Validation of Early Warning Systems for Severe Maternal Morbidity and Individualised Prediction of Severe Maternal Morbidity within Ethnic Groups



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Glossary

Administrative health data	Health data routinely collected as part of the administration of healthcare systems rather than at the point of care.
Advanced early warning score	A risk prediction score based on a statistical model that may incorporate the vital signs or other clinical data to predict a defined outcome.
Calibration	Degree of alignment between predicted probabilities and observed event rates.
Diastolic blood pressure	The blood pressure in the diastolic phase of the cardiac cycle, when the left ventricle of the heart is relaxed.
Discrimination	Ability of a tool to assign a higher risk to those who experience an event compared to those who do not.
Early warning score	An integer summary score based on the measurement of the vital signs for which clinical actions (e.g. escalation) are recommended according to a protocol.
Ethnicity	A form of personal social identity based on shared culture, family background, and heritage.
Escalation	The communication of an abnormality to another healthcare worker to provide clinical input into further investigation or treatment.
HELLP ('haemolysis, elevated liver enzymes, low platelets') syndrome	A severe complication of pregnancy, considered to represent a variant or complication of pre-eclampsia, involving endothelial injury and subsequent clotting and hepatic dysfunction.
Maternal Early Warning Score (MEWS)	The national (English) early warning score based on a centile-based approach to the distribution of the vital signs, developed through the '4P' study.
Maternity	A woman's pregnancy, ending in either a live birth or stillbirth, including the 42 days following birth.
Meta-analysis	The statistical process of combining the results from individual studies into a summary result.
Modified MEWS	A model based on the national (English) early warning score to which additional prognostic factors have been added.
Multiple imputation	The statistical process of filling in missing data with multiple values, conducting analyses using these multiple values, and then combining the results of these multiple analyses into one result.
Multiple imputation using chained equations	A multiple imputation procedure by which the multiple values are generated by iterating through a series of regression models.
Net benefit	A measure of how clinically useful a tool is based on the balance of true positives and false positives that it produces at a specified risk threshold.
Primary medical record	Contemporaneous clinical documentation produced by healthcare workers at the point of care.
Prognostic factor	An independent variable used to predict a dependent variable without any assumptions regarding its potential causal effect.
Recognition	The act of identifying and affirming that an abnormality exists so that further action can be considered.

Response	The clinical actions that occur as a result of escalation.
Severe maternal morbidity	The population-level measure of a range of severe complications that may occur to women during or following pregnancy, which may be defined in various ways.
Signals	Information that a healthcare worker may recognise and act on, used to refer to both signs and symptoms.
Signs	The clinical manifestations of a disease that are apparent on examination but that a woman herself does not experience, including early warning scores themselves.
Symptoms	The clinical manifestation of a disease that a woman experiences herself.
Structural inequalities	Systematic differences, including social and economic, between ethnic groups that are the product of policies over time as opposed to the actions of individuals.
Systolic blood pressure	The blood pressure in the systolic phase of the cardiac cycle, when the left ventricle of the heart is contracted and blood is ejected into the arterial circulation.
Vital sign	Measurements of the body's basic physiological functions that include the heart rate, respiratory rate, blood pressure, temperature, and oxygen saturation.

Abbreviations

ARDS	Acute respiratory distress syndrome
ARF	Acute renal failure
AMMOI	Australian Maternal Morbidity Outcome Indicator
AUS	Australia
BPM	Beats per minute
CAN	Canada
CDC	Centers for Disease Control and Prevention
CoA	Complications of anaesthesia
CPR	Cardiopulmonary resuscitation
CPSS	Canadian Perinatal Surveillance System
DBP	Diastolic blood pressure
DIC	Disseminated intravascular coagulation
DKA	Diabetic ketoacidosis
DREaMED	Defining, Recognising and Escalating Maternal Early Deterioration: Decreasing inequality through improved outcomes
EMMOI	English Maternal Morbidity Outcome Indicator
EWS	Early warning score
HELLP	'Haemolysis, elevated liver enzymes, low platelets'
HES	Hospital Episode Statistics
HDU	High-Dependency Unit
HR	Heart rate
ITU	Intensive treatment unit
LD	Liver disease
LoC	Loss of Consciousness
MBRRACE-UK	Mothers and Babies: Reducing Risk through Audits and Confidential Enquiries across the UK
MEWS	Maternal Early Warning Score
MI	Myocardial infarction
MSW	Midwifery support worker
MW	Midwife
NIHR	National Institute for Health and Social Care Research
NIS	National Inpatient Sample
NPEC	National Perinatal Epidemiology Centre
NL	The Netherlands
NPEU	National Perinatal Epidemiology Unit
PE	Pulmonary embolism
PET	Precision effect test
PEESE	Precision-effect estimate with standard error
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RF	Respiratory failure
RR	Respiratory rate
Sats	Oxygen saturation
SBP	Systolic blood pressure
SCASMM	Scottish Confidential Audit of Severe Maternal Morbidity
SDE	Secure Data Environment
SE	Status epilepticus

SMM	Severe maternal morbidity
SMM-RT	Definitions of severe maternal morbidity that do not include ‘any blood transfusion’
SMM-T	Definitions of severe maternal morbidity that include ‘any blood transfusion’
VST	Venous sinus thrombosis
WHO	World Health Organization

Abstract

Research problem

There is insufficient evidence to understand whether early warning scores, based on the maternal vital signs, facilitate appropriate early intervention or how they affect ethnic health inequalities. An advanced early warning score that uses additional clinical information alongside the vital signs may improve performance and reduce health inequalities.

Aim

The aim of this work was to understand the performance of early warning scores in maternity, including their use in clinical practice, how their performance differs between ethnic groups, and how an advanced tool may improve performance and reduce ethnic health inequalities.

Methods

Systematic reviews of outcome definitions for severe maternal morbidity and of prognostic factors for severe maternal morbidity were conducted to inform the validation and modification of the existing national Maternal Early Warning Score. Qualitative interviews with healthcare workers were conducted and analysed alongside medical records of women with severe complications and a secondary analysis of qualitative interviews with women who experienced severe complications was conducted to understand how early warning processes function in clinical practice. The existing national Maternal Early Warning Score was validated and modified using data from the electronic health records of a prospective cohort of women to inform the development of an advanced early warning tool.

Key Findings

There were a range of adaptive and maladaptive early warning processes that may compromise the function of safety systems but which may be necessary adaptations given the constraints of staffing and the perceived clinical meaning of existing early warning scores. Maladaptation meant that early warning signs may not be recognised or escalated, which could disproportionately affect women according to their ethnic group. Women face barriers to recognising their early warning symptoms and barriers to accessing maternity services when they do recognise warning symptoms. The performance of the national Maternal Early Warning Score differed between ethnic groups. Although net benefit was highest among Black women, there was evidence of under-prediction among this group. There was modest but positive clinical net benefit across all ethnic groups when the national early warning score was modified with additional prognostic factors.

Implications

An advanced early warning tool to predict severe maternal morbidity that includes generalisable prognostic factors could be used to strengthen equitable early warning in clinical practice. An advanced tool could support the individualisation of prediction, reduce the burden of false positives, and is an opportunity to strengthen early warning processes thereby ensuring that healthcare workers can address early warning scores meaningfully for all women and ethnicities. However, an advanced tool should be feasible within resource-constrained maternity services and its output should be meaningful to healthcare workers who use it. Women should be supported to recognise their early warning symptoms and seek help prior to assessment using an early warning score. Further characterisation of the acute physiological status in addition to baseline prognostic factors may lead to more substantial improvement in performance and may further address under-prediction among Black women.

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1 Chapter I: Introduction

1.1 Background

1.1.1 Ethnic inequalities

Across high-income settings, the risk of a woman developing a severe complication or dying in pregnancy differs based on her ethnic group. In the UK, women who were Black had more than twice the risk of dying during or following pregnancy, compared with women who were White(1). Similarly, women who were Black African or who were Bangladeshi were at greatest risk of severe maternal morbidity, compared with women who were White(2). The reasons for this inequality are diverse and may relate to both the health status a woman has at conception and the care she receives in pregnancy. Evidence-based interventions to reduce health inequalities in pregnancy are limited(3). Societally, socioeconomic differences based on ethnic groups exist because of historical and contemporary injustices(4). These processes are recognised as structural inequalities, whereby health status is viewed as the product of larger systems rather than solely individual decisions(5). Viewed from the lens of structural inequalities, the conditions that shape health(6) may be considered social determinants of health(7). These intersecting determinants of health affect an individual's health status over the life course. Ethnic health inequalities are not due to genetic or biological differences between groups based on their phenotype but acquired health differences may arise over a woman's life course due to these social determinants of health(8). Health may therefore be considered a reflection of an individual's experiences(4). Both a woman's access to and the quality of healthcare may be impacted by structural inequalities, because of where she lives or the resources she has available to her, as well as interpersonal biases. This means that when acquired health differences do arise, the treatment that a woman receives may differ according to her ethnic group(9), potentially affecting the trajectory of her subsequent health status and defining

her baseline health in the periconception period. A similar process may then unfold as women access(10) and interact with maternity services and healthcare professionals(11, 12).

Throughout this research, the term “ethnicity” was used in accordance with guidance from the Office for National Statistics (UK)(13), which groups individual ethnic identities into high-level ethnic groups, e.g. “Black” ethnicity is comprised of Black, African, Caribbean, and Black British ethnic groups. In the UK, ethnicity should be self-reported at the first antenatal appointment in pregnancy, although data on ethnicity may be missing or may be conflated with other aspects of an individual’s identity in practice, such as nationality or religion(14). In this thesis, ethnicity is regarded as a socially-constructed characteristic that may reflect an individual’s subjective identity, culture, ancestry and migratory history, whilst recognising that it is ultimately defined by the individual. Observed inequalities are considered products of differential exposure to the social determinants of health, structural inequalities, interpersonal biases, and the experience of health care. Although ethnicity is therefore a simplification of a wide range of dimensions of individual identity, standardised measurement allows inequalities to be identified at a population level and to be acted on.

In the context of such health inequalities, and within the scope of what maternity services can reasonably achieve, there are several steps maternity services could potentially take to reduce the risk that either pre-existing differences in health status or the way women access and receive care lead to differences in maternal health outcomes. These steps include ensuring access to routine care and screening and delivering interventions to reduce the risk of obstetric morbidity (primary prevention) as well as ensuring access to acute care and delivering interventions to reduce the risk of established complications progressing (secondary prevention). Any system designed to reduce the risk of severe complications has the potential to reduce health inequalities if it performs equally well among individual ethnic groups and if the preventative actions it leads to are effective. Additionally,

the way tools are developed and the way they function in clinical practice can also be optimised to further reduce health inequalities. One range of tools intended to facilitate access to acute care when a woman has a potentially early complication is 'early warning scores' (EWSs).

1.1.2 Early warning scores

Early warning scores are systems that are used in everyday medical care to systematically measure the vital signs and identify when they are abnormal. The principle of EWSs is that abnormalities of the vital signs may be indicative of either undiagnosed complications or subclinical abnormalities that may progress to more severe complications. EWSs facilitate earlier intervention to reduce this risk of progression. These vital signs include the maternal heart rate, respiratory rate, blood pressure, temperature, and oxygen saturation. In routine clinical practice across the UK, these vital signs are measured at regular intervals or at scheduled contacts with women or when new problems arise. The value of an individual vital sign is assigned a number and the numbers for the various vital signs are then summed to produce an 'early warning score'. An associated matrix determines the thresholds of individual vital signs for different scores, reflecting degrees of abnormality(15). Normal vital signs produce a score of zero, which means that unless there are other clinical concerns, routine care can be continued. Although the scoring matrices vary, the principle is that the higher the score the greater the clinical concern. The purpose of EWSs is to trigger 'escalation' (communication of the score to a healthcare worker able to decide on and initiate investigation or treatment)(16). Existing EWSs are therefore integer-based scores(17). This means that they are based on the simple concept that when a vital sign reaches a threshold, the score increases. The principle is that adding together the scores for the individual vital signs represents a useful summary of a woman's physiological status and is sufficient to identify abnormality that may require intervention.

The first national EWS for the general adult population was introduced in the UK in 2012(18). However, pregnancy induces both physiological and pathophysiological changes that affect the vital

signs and what may be regarded as normal. For example, the heart rate increases in a healthy pregnancy(19) which means that EWSs for the general adult population may generate an alert even though a woman does not have a medical problem. Similarly, EWSs for the general adult population may generate an alert for hypertension at a threshold that is considered life-threatening in pregnancy(18). Accordingly, clinicians across maternity services developed 'modified' versions of national EWSs to reflect these physiological changes, leading to a high degree of variation(17). These modifications are usually based on expert opinion. A different approach was used to reflect the physiological changes of pregnancy for the development of a national maternity-specific EWS. This national maternal EWS was based on physiological reference ranges for the vital signs among a healthy pregnant population at baseline(15).

The frequency with which the vital signs are measured and EWS calculated varies between maternity services but it is typically used when women present with new symptoms or concerns, during higher-risk periods such as following birth, and routinely for all women who are admitted to hospital. Few EWSs have been developed or validated according to best practice(20) and we do not know whether they reduce or contribute to health inequalities. There are no adequately validated maternity EWSs that have been developed for use in a UK-based maternal population and we do not know whether the performance of EWSs varies between ethnic groups.

1.1.3 An advanced early warning score

Simple, integer-based scores were well suited to a vision of healthcare that depended on representing patterns of the vital signs using paper charts, which was a novel intervention(21). These charts provided a portable and visual summary that made trends in the vital signs appreciable. However, in the modern NHS this represents a simplistic approach to risk assessment; the capacity to capture and use a much wider range of data far exceeds the current application to early warning. The complexity of existing scores is based on the limitations of an individual human's capacity to

measure, chart, sum, and interpret a limited array of data. Individual healthcare workers may perform more complex risk assessments but this mental process cannot easily be expressed as a set of rules nor deployed as a reproducible tool for use across healthcare teams. We do have the ability to develop statistical models of risk that can reproducibly express the relationship between a wide range of data and a specific clinical outcome(22). These are commonly developed using a regression modelling framework. Some statistical models, or 'prediction models', have the potential to better differentiate risk than individual healthcare workers or integer-based systems(23). Instead of integer scores based on the vital signs determined by experts' opinion or consensus, the scores from prediction models can be based on the relationships between the vital signs and a woman's clinical outcome. Practically, this would mean an 'advanced' tool based on a statistical model may be more likely to alert healthcare workers to women who proceed to experience a complication and less likely to falsely alert healthcare workers to women who do not proceed to experience a complication. Clearly, this has the potential to directly improve clinical outcomes and reduce the clinical time and resources spent investigating and treating women who are well. The development and use of prediction models for early warning using electronic health data is one way to bridge the well-characterised gap between digital capability and actual use in clinical practice(24, 25). Bridging this gap and implementing such advanced tools is a key part of the 10-year Health Plan, in which the Department of Health warned that the NHS is "behind the technological curve" and needs to 'predict and prevent' ill health "rather than simply diagnosing and treating it"(26).

1.1.4 Advanced early warning scores and health inequalities

The implementation of advanced EWSs into clinical practice requires a cautious approach to health inequalities. A tool that provides better prediction of adverse outcomes does not necessarily reduce health inequalities(27). Whilst these tools are more sophisticated, a disadvantage is that they have to be developed, or 'trained', on real data. Statistical models necessarily reproduce the patterns within that training data. These patterns, and the level of risk the prediction model subsequently

assigns to an individual, may be influenced by the quality of the data used; the definition and prevalence of the outcome; the availability, definition, and prevalence of predictors; and the relationship between the predictors themselves. It is very well recognised that the patterns a prediction model learns from its training data, based on the group among whom it is developed, do not necessarily apply to new groups(28). This same principle applies across ethnic groups. The relationship between a set of predictors and an outcome developed among a group with a specific ethnic composition may not necessarily perform equally well in different ethnic groups(29). EWSs are an opportunity to recognise risk and intervene to reduce the risk of progression to severe maternal outcomes; therefore, their development should take into account these potential differences between ethnic groups(30). Otherwise, an advanced EWS may not perform as well within some groups or could cause harm to some groups. Further, a prediction model itself is only as clinically useful as its ability to trigger appropriate clinical interaction. As well as bias introduced during the development of prediction models, bias could conceivably arise in the way EWSs are used in clinical practice. Therefore, the development of an advanced EWS should also be informed by potential differences in use between different ethnic groups so that it can be made robust to potential biases.

To improve prediction of an adverse outcome, an advanced EWS therefore needs to be developed with respect to a particular severe outcome and may benefit from additional predictors alongside the vital signs. These additional predictors may provide more individualised prediction that accounts for a woman's individual background and circumstances that may modify the meaning of her individual vital signs. Therefore, the first consideration for the development of an advanced EWS should be to define this outcome and identify the predictors, or 'prognostic factors' that may be used to improve prediction. The potential impact of these aspects across ethnic groups should be considered at each stage.

The ways that existing EWSs are used in clinical practice may also have implications for how the perceived performance of an advanced EWS as developed translates into its actual clinical performance. It is important to understand the broader process of early warning in clinical practice, from the recognition of potential problems by women or healthcare workers through to clinical intervention, including healthcare workers' use of EWSs and whether this varies across ethnic groups. Therefore, the second consideration for the development of an advanced EWS should be to describe and understand how EWSs are actually used and how and why they either do or do not lead to appropriate intervention. An advanced EWS may then be developed and its performance tested among individual ethnic groups to understand whether the patterns between the identified predictors and the outcome could lead to benefit within all ethnic groups.

1.2 Rationale

The rationale for this work is that in order to maximise the potential for an advanced EWS both to predict and to facilitate the prevention of severe maternal morbidity (SMM) or mortality, both overall and within ethnic groups, it ought to be:

- developed with respect to a definition of severe maternal morbidity that reliably captures life-threatening complications that occur across all ethnic groups;
- developed using prognostic factors whose association with severe maternal morbidity is likely to be generalisable, ensuring that prognostic factors that may have a higher prevalence in minority ethnic groups or a different magnitude of association across ethnic groups are incorporated;
- informed by how early warning occurs in clinical practice and how healthcare workers actually use early warning tools, including an understanding of whether and how early

warning practice could vary between ethnic groups and how tools can be made robust to this variation;

- validated within individual ethnic groups with an understanding of why an underlying statistical model may predict severe maternal morbidity better or worse across ethnic groups and whether the addition of prognostic factors alongside the vital signs may improve prediction fairly across groups.

1.3 Aim and objectives

The aim of this research is to understand the performance of maternity early warning scores and how they are used in clinical practice, including within individual ethnic groups, to inform the development of an advanced early warning tool, by:

1. Understanding how severe maternal morbidity should be defined so that the national maternity early warning score can be validated with respect to the clinical outcome of women within individual ethnic groups;
2. Understanding the strength of evidence for prognostic factors contained within electronic maternity records that could be used to develop an advanced maternal early warning score;
3. Describing how early warning signs and early warning scores are currently recognised and acted on in clinical practice;
4. Understanding the reasons for variation in how early warning signs are recognised and acted on by healthcare workers, and whether this may vary in women from different ethnic groups;
5. Describing how women themselves recognise and act on early warning symptoms;
6. Estimating the performance of the national maternity early warning score among women from individual ethnic groups;

7. Understanding reasons for potential heterogeneity in the performance of the national maternity early warning score between ethnic groups.

1.4 Thesis overview and structure

The approach to conducting and presenting this work reflects the sequential process of developing a new EWS. First, the selection of an outcome definition (objective 1, chapter 2); second, the identification of valid prognostic factors that may be incorporated into a new tool (objective 2, chapter 3); third, understanding challenges to recognising and acting on early warning signs/scores in clinical practice and how they could be improved (objectives 3-4, chapter 4); fourth, understanding women's experiences of early warning and how potential unmet needs may be addressed in a new tool (objective 5, chapter 5); and finally validating the national maternity early warning score and understanding the reasons for any difference in performance between ethnic groups (objectives 6-7, chapter 6).

This thesis incorporates multiple forms of research including quantitative and qualitative designs. These individual studies each related to one individual dimension of the overarching research aim. The findings from all of these individual studies were applied to the quantitative validation study of the national MEWS in chapter 6 and a comprehensive overview of the findings across all chapters and their application to the development of a new, advanced, early warning tool are detailed in chapter 7.

1.5 Research approach and the use of multiple methods

The work presented in this thesis was conducted from a subtle realist position that recognises ontologically that reality is independent of our understanding, while epistemologically any

understanding of reality is indirect and subject to the limitations of the tools and conceptual frameworks used to measure it(31). This applied equally to the quantitative and qualitative studies, both of which entailed the development of different types of 'model' of reality in order to improve healthcare processes practically. Quantitative elements of this thesis involved the estimation of associations between prognostic factors and outcomes and the validation of the national early warning score. Both involved selecting appropriate approaches with which to model these relationships and identifying potential weaknesses in these approaches in a way that was sufficiently credible to inform new safety systems(32). Similarly, when validating an EWS, there were a range of perspectives to consider and integrate when thinking about its 'performance'(30) and therefore what its effect may be in reality. The consequent estimates reflected uncertainty and informed the ability to make inferences about the target population. Conversely, qualitative elements involved the description of healthcare processes and the development of concepts and relationships between concepts, in order to explain and identify solutions to challenges across these processes(33). In qualitative work, reflexivity(34) required the subjective consideration of different perspectives, motivations, biases, and ways of accessing and understanding knowledge. Although reflexivity is not a part of the discourse of quantitative research, there is a need for reflexivity in quantitative research, i.e. critical examination of the researcher's assumptions and biases, and assumptions and biases introduced by either the epidemiological design or statistical aspects of the research, to avoid "naïve realism"(35) based on unexamined assumptions about the data or how they are used. Whilst differences rather than similarities between quantitative and qualitative methodologies have sometimes been over-emphasised(36), this research was led by its research questions and the most suitable methods to answer them. Subtle realism provides an epistemological framework to combine approaches: asserting that description was not a mirror of reality, i.e. that findings reflected how they were measured and interpreted; that the knowledge developed through this research was fallible, i.e. imperfect and subject to further development; and that validity was based on the plausibility of findings and the credibility of evidence, rather than dependent on a specific

method(31). Whilst this approach did not demand the use of multiple methods, it was consistent with the integration of different perspectives. Multiple methods provided diverse and complementary forms of knowledge on the phenomenon of clinical early warning. Both quantitative and qualitative elements presented in this thesis produced model-based representations of a more complex healthcare system and were combined to strengthen the understanding of this system and how it could be improved. Statistical estimates and thematic analyses both represented warranted claims that referred to the same reality. The credibility of these diverse forms of evidence was evaluated to develop revisable conclusions to inform healthcare improvement.

1.6 Relationship between thesis and NIHR DREaMED programme

The work presented in this thesis was aligned with the NIHR 'DREaMED' (Defining, Recognising and Escalating Maternal Early Deterioration: Decreasing inequality through improved outcomes) programme of work(37). The ongoing DREaMED programme incorporates a range of work streams, including:

- Developing definitions for near-miss and 'pre-near miss' morbidity for use with routine healthcare data (Workstream 1);
- Assessing the ability of existing EWSs to identify new near-miss and 'pre-near miss' events (Workstream 2);
- Developing a candidate variable list for a new advanced EWS and develop the advanced EWS (Workstream 3);
- Developing escalation and response pathways and the interface of a new advanced EWS (Workstream 4);
- Evaluating the new advanced EWS in a controlled before-and-after study (Workstream 5);
- Dissemination of the findings (Workstream 6).

The end product is the development and implementation of an advanced national maternal EWS based on the maternal vital signs and other routinely-collected electronic health data. The DREaMED programme commenced in May 2023. The work presented in this thesis was planned and designed in relation to and running alongside the DREaMED programme. Several members of the supervisory team who oversaw the design and conduct of the work presented in this thesis are investigators on the DREaMED programme. Whilst this work was informed by the aim of the DREaMED programme, at the design stage the objectives were defined so as to represent a separate but complementary body of work focussed on health inequalities. This work was conducted independently of the programme by the DPhil candidate, under supervision.

Nevertheless, there was some overlap to report. There was involvement of the candidate in the DREaMED programme, including attendance at management meetings and involvement in programme-related work that represented natural extensions or applications of the work presented in this thesis. For example, contribution to the development of and activities related to the development of a definition of severe maternal morbidity and a definition of pre-severe maternal morbidity as well as other aspects where the work in this thesis had implications for the development of the DREaMED advanced EWS. When contributing to such activities, it is possible that the decisions made within the remit of the thesis were influenced by discussions as part of the DREaMED programme. This represents a natural process of ensuring that work is relevant and has the potential for impact. However, any use of specific outputs developed as part of the DREaMED programme have been transparently identified below.

1.6.1 The DREaMED Data Set

NHS trusts were recruited by members of the DREaMED project team who approached NHS trusts according to the approvals obtained as part of DREaMED. The candidate did not provide input into the ethics application for DREaMED to obtain approval to collect or to use these data and has used

these data strictly in line with the permissions obtained through DREaMED. The ethical approval for other components of this work that were obtained by the candidate are detailed in the relevant chapters. The data were collected by members of the DREaMED project team. The data were extracted and deposited into a secure data environment by the relevant NHS trust. A member of the DREaMED project team verified that the data met the specifications of the protocol and did not contain any identifiable information. The data were then assembled (i.e. the individual list of submitted files combined into a research data set), cleansed (e.g. data converted into the appropriate type, dates and times extracted in the appropriate format, the data labelled, the plausibility of the values of each variable evaluated, and the logic of relationships between variables evaluated), and analysed by the candidate. For the qualitative work conducted as part of this thesis, ethical approval was sought and obtained by the candidate.

1.6.2 Public and Patient Involvement

Access to the DREaMED management meetings facilitated public and patient feedback from the two co-investigators of DREaMED with lived experience of maternity care. These representatives have provided feedback on work completed as part of this thesis, which was presented at monthly management meetings, that has informed the interpretation of the work and how work completed could inform the subsequent stages of this research. The involvement of these representatives has ensured that the understanding of what represents a severe complication has been informed by not only a medical perspective but by women's experiences. When measuring severe maternal morbidity, women's experiences of severe complications has been identified as a dimension that has been neglected(38). Therefore, the definition of SMM developed during this thesis was informed by the experience of public and patient representatives, particularly regarding conditions for which a low consensus was identified in the existing literature. Additional work to involve the perspectives of women with experience of maternity care has been conducted by the candidate but using the

DREaMED public and patient involvement group to inform refinement of the analyses and interpretation of the findings.

2 Chapter II: Defining Severe Maternal Morbidity

2.1 Introduction

Few EWSs in use in maternity care in the UK have been validated with respect to a particular clinical outcome(20). This means that there is an assumption that an abnormal score indicates that a woman is at risk of an (unspecified) adverse outcome. It also means that there is an assumption that directing clinical resources towards a woman with an abnormal score can potentially prevent this unspecified adverse outcome. These assumptions may be reasonable but they are crude and open to different interpretations between healthcare workers. When an outcome is specified, this outcome can be modelled on the predictors, including the vital signs, in order to estimate the relative importance of different predictors and to account for more complex relationships between predictors. This also means that the performance of different tools can be evaluated and compared. Selecting an individual outcome is challenging because most EWSs are developed with respect to a single outcome that must capture all relevant conditions. The aim of an EWS is to identify and treat complications at an early stage, reduce the risk of clinical deterioration, and reduce the risk of a severe outcome. However, early warning tools are also used for conditions for which early warning may not be possible and the same tool will likely also need to alert healthcare workers to acute deterioration when morbidity is already established.

Maternal mortality is a very rare event in high income countries (HICs), contributed to by both direct (obstetric) and indirect (non-obstetric conditions exacerbated by pregnancy) disease processes, with 54% of deaths attributable to indirect causes(1). This outcome is rare for the purpose of clinical prediction, particularly when prediction occurs at the level of the individual set of vital signs meaning that there may be even more sets of vital signs without an event per woman than there are with an event. SMM is more common and captures disease processes that are precursors of maternal

mortality. The World Health Organisation (WHO) Maternal Morbidity Working Group defined maternal morbidity as “any health condition attributed to and/or complicating pregnancy and childbirth that has a negative impact on the woman’s wellbeing and/or functioning”(2). A continuum from maternal morbidity, through potentially life-threatening conditions, life-threatening complications, to maternal near-miss morbidity (or maternal death) has been conceptualised (3, 4). In its definition of “severe acute maternal morbidity”, the WHO provided a standardised definition for “women who nearly died but survived a complication during pregnancy, childbirth or postpartum”(39). The purpose of the WHO’s definition was predominantly for the evaluation of the quality of obstetric care through case-based reviews, whilst remaining sufficiently rare so as not to “overload clinicians and data collection personnel within a facility”(39). For the purpose of predicting SMM with a view to early intervention, the definition may be less restrictive because it is not only complications that nearly led to death that can potentially be prevented using an EWS. It would be beneficial to aim to predict and intervene prior to any severe complication and therefore it is important to identify how SMM has been defined in epidemiological practice, including definitions used with administrative health data, at scale. SMM has been defined and informed by the degree of intervention, acuity, or end-organ injury(5). The WHO definition nevertheless represents a core set of the most severe indicators that ought to be reflected in any definition of SMM. Several composite definitions of SMM have been developed based on or informed by the WHO definition but the range of disease processes and the way those disease processes have been identified differs.

Conceptual definitions of SMM which have been translated into clinical epidemiological definitions could inform the development of an advanced EWS(12). Unfortunately, the WHO definition is not directly applicable to administrative health data that can be scaled to a national level. In particular, the WHO near-miss definition is based on detailed clinical signs that are not routinely documented in a structured manner using electronic health records and would need to be individually extracted from the medical record of each patient. This approach would be impractical if a tool were to be

applied across hospital systems. Different research teams have taken different approaches to defining SMM, potentially influenced by the setting, purpose of their definition, the source of data, or clinical or research systems in which the process occurs.

The aim of this systematic review was to identify definitions of SMM to inform the selection of an outcome with which to validate and then modify the national Maternal Early Warning Score (MEWS), by

- Describing existing definitions of SMM
- Describing how these definitions were developed
- Identifying agreement or variation between definitions of SMM across high-income settings
- Identifying which components should be included in an ideal definition of SMM for the validation or subsequent development of an advanced EWS

The rationale for this systematic review was that identifying definitions of SMM and understanding the approaches to their development facilitated the curation of a composite definition of SMM suitable for the purpose of clinical prediction using an EWS (thesis objective 1). This was conducted to inform the subsequent validation of EWSs (thesis objective 6) and to understand reasons for potential differences in performance between ethnic groups (objective 7).

2.2 Method

A prospectively-registered (PROSPERO CRD42023421377) systematic review of definitions of SMM was conducted. The conduct and report of this research was based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement(40). Preliminary searches identified relevant terms to inform the search strategy, reported in Appendix Table A2.1. The search strategy

was approved by a research librarian with expertise in women's health. Records were identified through PubMed, Embase, and Google Scholar that were published between 01/01/1993 and 31/08/2024. The first 1,000 records identified in Google Scholar were screened. Grey-literature searches were conducted using Bielefeld Academic Search Engine, Jisc, and OpenGrey. Observational or interventional studies in HICs that developed a unique definition of SMM and that incorporated both direct and indirect measures of SMM were included. SMM was defined as a composite outcome of at least two diagnoses, measures, or processes reflective of SMM that occurred during pregnancy and up to 6 weeks following birth. The time period is in accordance with the WHO definition of maternal near-miss(41). Morbidity and mortality that occurs after the postnatal period is less likely to be pregnancy-related and is driven by different processes(42). Definitions that included a non-severe component (i.e., a non-life-threatening condition in pregnancy, such as gestational diabetes, compared with a potentially life-threatening condition(39)) or a component conditional on a specific exposure (e.g., the inclusion of 'postoperative ventilation' but not 'ventilation') were excluded. No studies were excluded based on language. Definitions of only/predominantly direct measures of SMM were excluded given that the majority of maternal deaths in the UK are caused by indirect causes. The limitation of an outcome definition to indirect measures would likely restrict the ability of an advanced EWS to prevent SMM and maternal mortality for all causes. For example, a definition comprised of eclampsia, severe haemorrhage, and sepsis only would have been excluded because these would miss indirect ('non-obstetric') severe complications, such as cardiac disease. Screening, full-text reviews and systematic citation searches were conducted in duplicate by two reviewers (IH and RL). Data were extracted using a piloted data collection form using Covidence. Disagreement between reviewers was resolved by discussion and the input of a third reviewer (SG) if necessary.

The data were summarised using counts and percentages and a narrative synthesis was conducted, providing description and comparison of the identified measures. Study characteristics, narrative

summaries of the approach to SMM development, and components of SMM definitions were reported. Definitions were grouped and reported according to their intended use with administrative health data or with the primary medical record. Administrative health data included International Classification of Disease codes (ICD)(43), here ICD-9 or ICD-10, or procedural codes that reflect what critical care or surgical interventions were provided. ICD codes and procedural codes were used across all definitions developed for administrative data. Although the version and exact specification of the ICD system differed between studies and countries, the underlying approach to identifying SMM using administrative data was consistent and the clinical conditions included were identifiable across coding systems. Definitions for use with the primary medical record were those that depended on detailed clinical data that would require extraction from clinical documentation produced at the point of clinical care; for example, a near-miss clinical criteria of "gasping". When evaluating the degree of consensus on the inclusion of complications between definitions, a threshold of 70% was used to signify a high degree of consensus. The constituent diagnostic and procedural codes within clinical concepts across definitions for use with administrative data from different settings (Australia, Canada, England, Finland, Sweden, and USA) were compared. A formal risk of bias assessment was not conducted for this systematic review of outcome definitions because there are no established standards for the development of a composite outcome; instead, the development of outcome definitions was described. Missing data on definitions were acquired from associated publications from the same authors.

2.3 Results

The search identified 7,852 unique records. The PRISMA flow diagram is shown in Figure 2.1. Of the 467 studies retrieved for full-text review, 278 studies used a composite outcome already identified; 79 did not include a relevant composite outcome; 25 related to abstracts only; 21 occurred outside the time period of interest; 10 developed composite outcomes for specific disease pathways; and 14

were duplicate records. There were 40 studies included in total, with 28 studies that identified 32 composite definitions of SMM developed for use with routine administrative data, reported in Table 2.1**,** and 13 studies that identified 13 composite definitions for use with/abstraction from the primary medical record, reported in Table 2.2.

Figure 2-1 PRISMA Flow Diagram

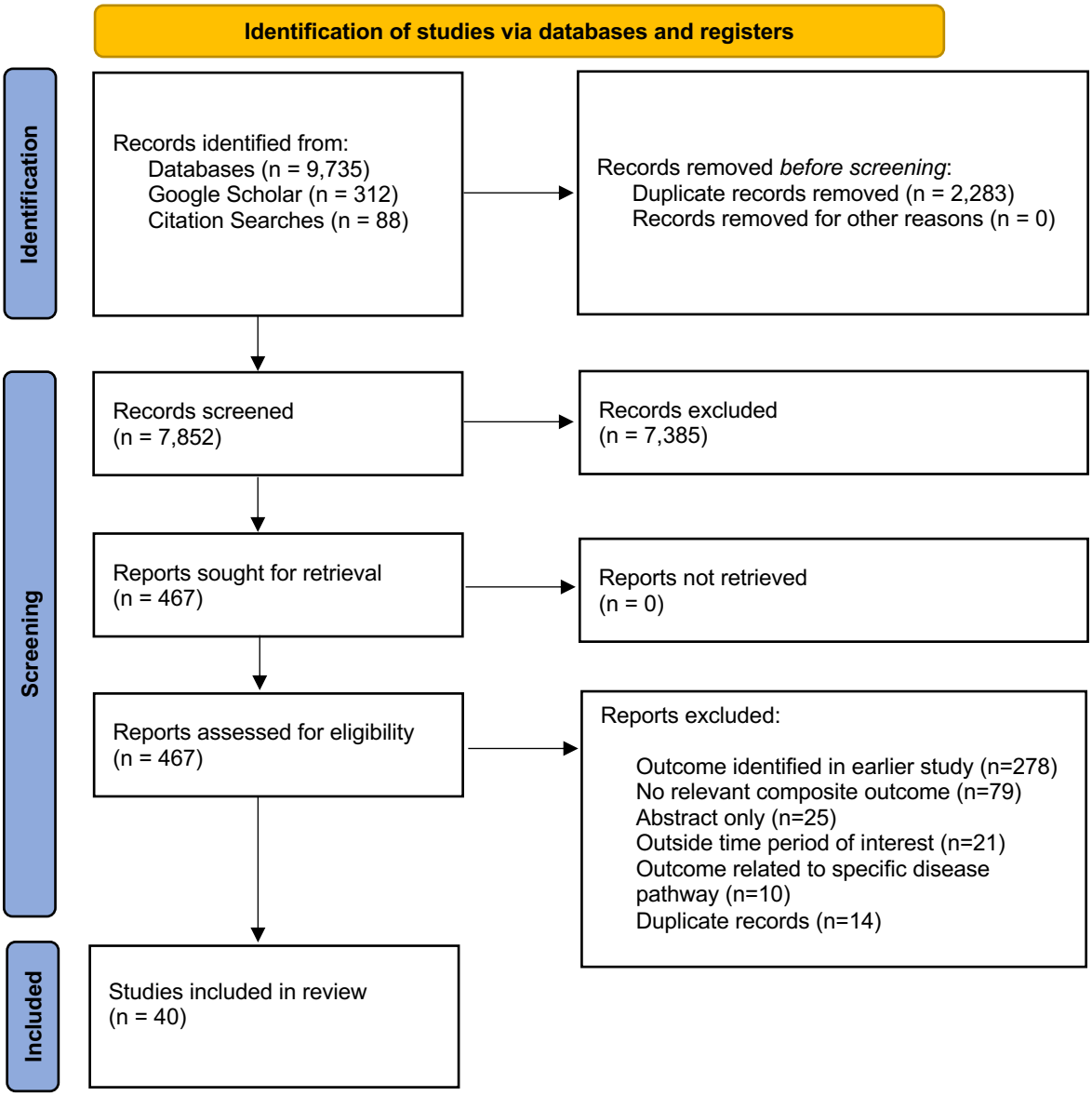


Table 2-1 Definitions of SMM Developed for Use with Administrative Data

Definition	Data	Development	Description	Prevalence (/1000)[a]
Wen 2005(44)	DD (Canada), ICD-9	"[N]ear miss conditions with potential to cause maternal death" reliably identifiable from discharge data; case fatality rates compared with reference rates.	**Cardiac arrest, HF, or cerebral anoxia after obstetric surgery (combined 24%)**, pulmonary oedema, MI, RF, ARDS, ARF, stroke, VST, **CoA (11%)**; eclampsia, PE, **uterine rupture (17%)**; **haemorrhage with transfusion (21%)** or with hysterectomy, ventilation.	Del 4.4 (1991-2001)
Olive 2005(45)	Universal perinatal database, DD (NSW, Australia)	Unspecified development of 'major maternal morbidity' outcome with respect to an exposure of placenta praevia.	ARF, ventilation, shock, death; **PPH with transfusion (63%), DIC, transfusion of platelets/coag. factors/FFP (combined 12%)**, hysterectomy, surgical management of haemorrhage, **ITU (21%)**.	11.2 (1998-2002)
CDC, Callaghan 2008(46)	NHDS (USA), ICD-9-CM	Informed by near-miss/SMM case review in Geller 2002(47) and SMM in Wen 2005(44); internal validation with respect to length of stay.	Original CDC list comprised of cardiac arrest, MI, HF (including cardiogenic pulmonary oedema), cardiomyopathy, RF, ARF, LD, stroke, VST, CoA; **eclampsia (14%)**, AFE, PE, shock, septicaemia; CPR/cardioversion, ventilation, **hysterectomy (12%)**, invasive monitoring, and **transfusion (whole blood or red cells, 48%)**. Diagnostic codes qualified by length of stay ≥3 days.	Del 5.1 (1991-2003)
AMMOI, Roberts 2008(48)	DD (NSW, Australia)	Literature review and consultation. Codes refined by comparison with case review of clinically-validated SMM, informed by availability/reliability of data.	Cardiac arrest, HF, pulmonary oedema, MI, SA, ARF, stroke, SE, coma, acute psychosis, shock, peritonitis, appendicitis, sickle crisis, CoA; AFE, PE, DIC, uterine rupture; CPR/cardioversion, ventilation, hysterectomy, surgical management of haemorrhage, evacuation of haematoma, repair of organs, repair of inverted uterus, reclosure of CS wound, dialysis, **transfusion (any product, 75%; from Roberts 2009)(49)**.	Del 14.6 (2002), Roberts 2008; del 12.5 (1999-2004), Roberts 2009(49)
Kuklina 2009(50)	NIS (USA), ICD-9-CM	Informed by WHO SMM (Say 2004) and non-composite indicators of SMM identified in Kuklina 2008(51).	Cardiac arrest, HF, pulmonary oedema, RF, ARDS, ARF, stroke, VST, shock, CoA; eclampsia, DVT, PE, septicaemia and sepsis, DIC; ventilation, hysterectomy, **transfusion (56%)**.	Del 8.1 (2004-05)
CPSS, Joseph	DD (Canada),	From Wen 2005(44),	As per Wen 2005 with addition of pre-existing hypertensive cardiac	Del 13.8 (2003-07)

Definition	Data	Development	Description	Prevalence (/1000)[a]
2010(52)	ICD-10CA	supplemented with additional codes/compared with Roberts 2008(48).	disease, cardiomyopathy, SA, LD, SE, coma, acute psychosis, shock, peritonitis, appendicitis, sickle crisis, HIV disease, death; AFE, sepsis/septicaemia; APH/IPH with coag. defect, DIC; CPR/cardioversion, surgical management of haemorrhage, evacuation of haematoma, repair of organ injury, dialysis, **transfusion (whole blood/red cells, 47%)**.	
Mhyre 2011(53)	NIS (USA), ICD-9 CM	Review of literature (44, 46, 50) and ICD-9 CM manual for severe, life-threatening complications reflecting end-organ injury-based definition; association of components with inpatient death or discharge to medical facility considered.	**Cardiac arrest or HF (19% combined)**, pulmonary oedema, MI, RF, **ARDS (20%)**, SA, **ARF (13%)**, **LD (21%)**, stroke, VST, SE, coma, delirium, shock, DKA, major transfusion reaction, panhypopituitary syndrome, CoA; AFE, PE, **sepsis (13%), DIC (22%)**. Qualified by either LoS >99th percentile or medical transfer, or death.	1.3 (2003-6)
CDC, Callaghan 2012(54)	NIS (USA), ICD-9-CM	Review of ICD-9 codes associated with inpatient mortality; Callaghan 2008(46); Kuklina 2009(50).	Expansion of CDC definition (Callaghan 2008) with aortic disease, ARDS, sickle crisis, intracranial injuries, internal injuries (non-iatrogenic), procedures on heart and pericardium. Major components were **DIC (10%)** and **transfusion (75%)**. Diagnostic codes qualified by LoS >90th percentile for mode of birth (vaginal, primary CS, repeat CS).	Del 12.9 (2008-9)
CDC+, Lyndon 2012(55)	DD, vital statistics (CA, USA)	Based on Callaghan 2008(46) and Kuklina 2009(50).	Cardiac arrest, HF, RF, ARDS, ARF, stroke, VST, shock, CoA, death; haemorrhage with coag. defect, DVT, PE, sepsis, DIC, uterine rupture, wound complication; ventilation, **hysterectomy (13%)**, haemorrhage with transfusion or surgical management, curettage, unplanned postnatal operation, ITU. Diagnostic codes qualified by LoS >90th percentile for type of birth.	Del 5.8 (2005-7)
Wahlberg 2013(56)	National registry (Sweden)	Informed by WHO definition in Say 2009(39).	Cardiac arrest, hypertensive HF, pulmonary oedema, MI, acute ischaemic heart disease, arrhythmia, aortic disease, ARDS, RF, ARF, LD, stroke, VST; **HELLP, eclampsia, DIC (23% combined)**, AFE, PE **(15%, obstetric embolism), uterine rupture or obstetric laparotomy (40%**	2.9 (1998-2007)

Definition	Data	Development	Description	Prevalence (/1000)[a]
			combined), sepsis, **shock or hysterectomy (11%).**	
Bateman 2013(57)	Medicaid healthcare utilisation dataset (USA)	Developed from Callaghan 2008(46), Callaghan 2012(54), Mhyre 2011(53); end-organ injury based definition.	**HF (20%)**, **pulmonary oedema (10%)**, MI, **ARDS/RF (14% combined)**, SA, ARF, **LD (11%)**, stroke, VST, shock, coma, SE, delirium, death; PE, **sepsis (22%)**, **DIC (14%)**.	11.6 (2000-7)
Non-transfusion CDC, Creanga 2014(58)	SID (USA), ICD-9-CM	As per Callaghan 2012(54).	CDC components with the omission of transfusion-only cases.	Del 6.4 (2008-10)
Lisonkova 2014(59)	State registry (WA, USA), ICD-9	SMM defined as any potentially life-threatening condition.	Cardiac arrest, HF, pulmonary oedema, MI, cardiomyopathy, malignant hypertension, arrhythmia, haemopericardium, aortic disease, pulmonary arterial aneurysm, RF, ARDS, ARF, LD, stroke, VST, shock; AFE, DVT, PE, DIC, **chorioamnionitis/infection/ sepsis (71% combined)**; hysterectomy, **transfusion (17%, any product)**. Defined with and without **"obstetric trauma"** (uterine rupture or inversion, pelvis or pelvic organ injury, cervical/high vaginal laceration, third and fourth degree perineal tear; **76%, combined, SMM with trauma cases**).	26.3 (2000-08), without trauma (late-onset pre-eclampsia model)
Pallasmaa 2015(60)	National registry (Finland), ICD-10	Based on review of all diagnostic and procedural codes assigned to deliveries over a five year period.	Pulmonary oedema, ARDS, shock, peritonitis; haemorrhage with coag. defect, AFE, DVT, PE, VST, uterine rupture, uterine inversion, ileus/bowel obstruction, **sepsis (52%)**, CoA; hysterectomy, surgical management of haemorrhage, repair of wound dehiscence, **laparotomy (haemorrhage) (13%)**, laparotomy (other causes), laparoscopy.	D42 12.8 (2007-12)
Schummers 2015(61)	Perinatal registry (British Columbia, Canada)	Apparent subset of CPSS codes.	Cardiac arrest, HF, pulmonary oedema, MI, ARDS, ARF, cardiomyopathy, stroke, VST, shock, death; APH with coag. defect, PE, AFE; repair of organ injury. Components not reported individually.	6.0 (2004-12)

Definition	Data	Development	Description	Prevalence (/1000)[a]
EMMOI, Nair 2016(62)	HES (England, UK)	Based on Roberts 2008(48); modified according to the quality of administrative data in the UK.	Supplementation of AMMOI with diagnostic codes for eclampsia and puerperal sepsis. Excluded isolated transfusion. Major components included **uterine rupture (13%)**, **eclampsia (19%)**, **sepsis (11%)**; **evacuation of haematoma (13%)**.	4.7 (2012-13)
Main 2016	DD-vital records (CA, USA), ICD-9 CM	Validation study.	Various modifications of the CDC index with the addition of either ≥4 units transfusion (any) or ≥4 units transfusion (red cells) or ITU admission or pLOS or ITU/pLoS	8.6; 8.0; 13.5; 16.4 17.0, respectively
CDC-NYS, Lazariu 2017(63)	DD-vital records (NY, USA), ICD-9 CM	Expansion of CDC criteria based on literature review.	CDC with additional 'New York supplemental codes' (NYS) qualified by pLOS or ITU admission. Supplementary codes for pulmonary oedema, cardiac complications, LD, ARDS, shock, anaemias, coma, DKA, delirium, SA, SE, thyroid crisis, oliguria; haemorrhage, DIC, eclampsia, sepsis, PE, DVT, VST, thrombocytopenia. Substantial components included **transfusion (22%**) and **anaemias/sickle cell (47%, combined)** based on 2013 numerator rate and 2008-13 denominator rate.	Del 25.5 (95% 25.2, 25.7), 2008-13
Abe 2018(64)	Diagnosis Procedure Combination database (Japan), ICD-10	Unspecified; disease-specific and management based selection of life-threatening conditions.	HF, MI, acute pericarditis, cardiomyopathy, aortic disease, cardiac CoA **(all cardiovascular combined 14%)**, pulmonary oedema, ARDS, RF, respiratory CoA, pneumonia, **(all respiratory combined 10%)**, ARF, stroke; PE, sepsis; **transfusion on day of delivery (red cells, 53%)**, **transfusion on day of delivery (FFP, 37%)**, shock treated with vasopressors.	Selected population
Non-transfusion CPSS, Aoyama 2019(65)	DD (Canada), ICD-10CA	As per Joseph 2010.	CPSS components with the omission of transfusion-only cases. Major components included **septicaemia during labour/puerperal sepsis (22%)**.	17.7 (2004-15)
CPSS, Dzakpasu 2020(66)	DD (Canada), ICD-10CA	From Joseph 2010. Candidate components reviewed according to incidence, length of stay, and mortality rates.	As per Joseph 2010 with addition of **severe pre-eclampsia, HELLP (35% combined, with eclampsia)**, acute fatty liver disease with transfusion, uterine inversion at vaginal birth, and **ITU (12%)** and removal of HIV, pre-existing hypertensive cardiac disease, and evacuation of	Del 16.1 (2012-16)

Definition	Data	Development	Description	Prevalence (/1000)[a]
			haematoma without transfusion. Transfusion (red cells) included only with defined diagnostic codes. Other major components were **haemorrhage + transfusion/coag. defect, curettage + transfusion (31% combined)**, and **surgical complications/evacuation of incisional haematoma + transfusion, repair of organ injury, reclosure of CS wound + transfusion (12% combined)**.	
Duke 2020(67)	Victorian Admitted Episode Dataset (Victoria, Australia)	Developed from WHO MNM tool(39) and Main 2016(68).	Cardiac arrest, HF, cardiomyopathy, RF, ARF, LD, **CoA/anaphylaxis (12%)**, Addisonian crisis, complication of transplanted organ; DIC, **severe pre-eclampsia/HELLP (25%),** eclampsia, AFE, PE, **sepsis (17%),** uterine rupture, **early pregnancy loss-related (11%)**; CPR/cardioversion, ventilation, hysterectomy, **PPH + surgical management/transfusion and coagulopathy/transfusion of coag. factors (17%)**, repair of organ injury, laparotomy, dialysis.	35.4 (95% CI 35.0, 35.8) (2001-2017)
CDC 2019-Bateman, Snowden 2021(69)	State-wide birth cohort/vital record-DD (CA, USA)	Compared agreement between multiple CDC-based and birth certificate-based measures. The use of this definition was to consider the effect of different sets of codes.	CDC index without transfusion with additional diagnostic codes from Bateman 2013(57). Components not reported individually.	9.7 (2007-12)
EMMOI-ITU, Masterson 2022(70)	Scottish Morbidity Record (Scotland)	Based on EMMOI(62)	EMMOI supplemented with **ITU (18%).** The other major component was **sepsis (35%)**.	10.4 (2005-18)
CDC, AIM 2022(71)	NA	Based on Callaghan 2012(54)	As per Callaghan 2012 with rolling update. Removal of invasive monitoring and transfusion.	-
Fridman 2023(72, 73)	DD (CA, USA), ICD-10-CM	Modification of CDC(71) to exclude indicators that are not predictable, pre-existing	CDC index with the exclusion of aneurysm, sickle crisis, AFE, transfusion and conditions present on admission. Components not reported individually.	4.4 (2016-18)

Definition	Data	Development	Description	Prevalence (/1000)[a]
		conditions or their precipitating factors, including diagnoses present on arrival.		
Tsamantioti 2024(74)	Birth register-DD (Sweden), ICD-10-SE	Review of CDC(54, 71) and CPSS definitions(66) by a multidisciplinary group of experts to evaluate validity. Concurrent comparison of LOS for components. Addition of severe mental health components.	Cardiac arrest, HF, pulmonary oedema, MI, cardiomyopathy, ARDS, ARF, LD, stroke, shock, CoA, SE, coma, sickle crisis, acute psychosis, inpatient psychiatric care; haemorrhage with transfusion/coag. defect (**PPH with transfusion, 39%**), DIC, **severe pre-eclampsia/HELLP (37%, combined)**, eclampsia, AFE, PE, VST, sepsis, obstetric haematoma, suicide attempt; CPR/cardioversion, ventilation, hysterectomy, uterine rupture with transfusion or repair of rupture with transfusion, **curettage/manual exploration of uterine cavity with transfusion (20%)**, dialysis.	27.2 (95% CI 26.8, 27.2) (1999-2019)
CDC-Scotland, Kearns 2024(75)	DD-vital record (Scotland), ICD-9 and ICD-10	Adaptation of CDC criteria(71) for use with Scottish administrative data.	CDC criteria with additional qualifier of critical care admission applied to postpartum haemorrhage and to sepsis due to over-estimation.	Selected population

[a] The denominator varies across rows. These are per maternity unless specified. Where specified, Del denotes the incidence of SMM at the delivery episode only, D42 denotes delivery episode and up to 42 days postnatal.

CDC Centres for Disease Control and Prevention, CPSS Canadian Perinatal Surveillance System, AMMOI Australian Maternal Morbidity Obstetric Indicator, EMMOI English Maternal Morbidity Obstetric Indicator, WHO World Health Organization, DD Discharge data, NSW New South Wales, NHDS National Hospital Discharge Survey, NIS National Inpatient Sample, HES Hospital Episode Statistics, HF heart failure, MI myocardial infarction, RF respiratory failure, ARDS acute respiratory distress syndrome, SA status asthmaticus, ARF acute renal failure, LD liver disease (acute), SE status epilepticus, CoA complications of anaesthesia, DKA diabetic ketoacidosis, PPH postpartum haemorrhage, APH antepartum haemorrhage, AFE amniotic fluid embolism, DVT deep venous thrombosis, PE pulmonary embolism, VTE venous thromboembolism, DIC disseminated intravascular coagulation, ITU intensive treatment unit, LoS length of stay, pLoS prolonged length of stay.

Components of definitions which represented more than 10% of cases of SMM are noted (%) and shown in bold. Components are not mutually exclusive.

Table 2-2 Definitions of SMM Developed for use with the Primary Medical Record

Definition	**Data**	**Development**	**Description**	**Prevalence (/1000)[a]**
Mantel criteria, Mantel 1998(76)	Prospective case review (Pretoria region, South Africa)	Unspecified.	Cardiac arrest, **pulmonary oedema (16%)**, RF, ARF, oliguria, coma, haemorrhagic stroke, DKA, thyroid crisis, CoA; pre-eclampsia with jaundice; ventilation, **hysterectomy (29%)**, **hypovolaemia with ≥5 units whole blood/red cells (27%)**, acute thrombocytopenia with platelet transfusion, ITU	10.9 (1996)
SCASMM precursor, Brace 2004(77)	Prospective systematic case surveillance (Scotland)	Based on Mantel 1998(76). Components based on pathophysiological measures rather than interventions were preferenced.	Cardiac arrest, pulmonary oedema, **ARF (10%)**, anaphylaxis, cerebrovascular disease ("including haemorrhage or thrombosis"), coma, SE, CoA; **haemorrhage transfused ≥5 units (50%)**, **eclampsia (13%),** septicaemic shock; **ITU (33%)**.	3.8 (2001-02)
Geller criteria, Geller 2004(78)	Retrospective review of selected cases.	Case review of SMM to characterise and differentiate near-miss from non-near-miss/"less severe morbidity".	'Five-factor scoring system' included organ system failure ("failure of either cardiac, pulmonary, hematologic, renal, liver/gastrointestinal, or central nervous system"); extended intubation, ITU, surgical intervention, transfusion ≥4 units.	NA
SAMM, Zwart 2008(79)	Prospective systematic surveillance ('LEMMoN study', NL)	Literature review; agreement of National Maternal Mortality Committee.	Severe complications as per treating obstetrician (including potential indirect processes), eclampsia, HELLP with liver haematoma/rupture, uterine rupture, **haemorrhage with transfusion ≥4 units red cells or embolization/hysterectomy (45%)**; **ITU (33%)**	7.1 (2004-6)
WHO SMM/near-miss, Say 2009(39), WHO 2011 (41)	NA	WHO systematic review of maternal morbidity and mortality(80). Organ dysfunction criteria based on the Sequential Organ Failure Assessment score. Development by an expert	<u>Severe maternal complications:</u> severe PPH, severe pre-eclampsia, eclampsia, sepsis or severe systematic infection, ruptured uterus, severe complications of abortion <u>Critical interventions of intensive care unit use:</u> ITU, interventional radiology, laparotomy, use of blood products	NA

Definition	Data	Development	Description	Prevalence (/1000)[a]
		working group and field tests of identification criteria.	Maternal vital status: maternal death In addition to categories that indicate "near-miss": Clinical criteria: acute cyanosis, gasping, respiratory rate >40 or <6/min, shock, oliguria not responding to fluids/diuretics, clotting failure, LOC ≥12 hours, LOC with absence of pulse, stroke, uncontrollable fit/total paralysis, pre-eclampsia with jaundice. Laboratory criteria: oxygen saturation <90% for ≥60 min, PaO_2/FiO_2 <200 mmHg, creatinine ≥300 µmol/l or ≥3.5 mg/dl, bilirubin>100 µmol/l or > 6.0 mg/dl, pH <7.1, lactate >5 mmol/L, acute thrombocytopenia <50 000 platelets, LOC with glycosuria and ketonuria. Management criteria: continuous vasoactive drugs, hysterectomy following infection or haemorrhage, transfusion ≥5 units of red cells, intubation and ventilation ≥60 minutes not related to anaesthesia, dialysis for ARF, CPR.	
Murphy 2009(81)	Prospective systematic case surveillance (Dublin, Ireland)	Based on Mantel 1998(76).	As per Mantel 1998 with the addition of eclampsia, radiologically-proven PE, and anaphylactic shock. Major components included **hypovolaemia requiring ≥5 units of red cells (47%)**, **acute thrombocytopenia + platelet transfusion (19%)**, **eclampsia (15%)**, and **ITU (13%)**.	3.2 (2004-05)
SMMG, NPEC 2013(82)	Primary record (Ireland)	From the Severe Maternal Morbidity Report 2011 (NPEC 2013, earliest instance identified). Review of literature; modelled on SCASMM.	Cardiac arrest, pulmonary oedema, acute respiratory dysfunction, ARF, LD, stroke, CoA, coma, SE; eclampsia, VST, septicaemic shock; **haemorrhage ≥2500 ml or with ≥5 units of blood (53% combined)**, hysterectomy, interventional radiology, **ICU (40%)**.	6.3 (2021)

Definition	Data	Development	Description	Prevalence (/1000)[a]
SCASMM, Marr 2014(83)	Prospective systematic case surveillance	Based on Mantel 1998(76) and Brace 2004(77).	Cardiac arrest, pulmonary oedema, ARF, LD, stroke, coma, SE, CoA, anaphylaxis; eclampsia, massive PE, VST, septicaemic shock; ventilation, **haemorrhage ≥ 2500ml or ≥5 units red cells or treated coagulopathy (67%)**, **ITU (21%)**.	6.1 (2003-12)
ACOG, Main 2016(68)	Routine screen then case review (CA, USA)	Screening criteria of a CDC code, pLoS, ITU, or transfusion. Case review by expert panel which developed criteria from Geller 2002(47) and Geller 2004(78) using a modified Delphi process.	Example-based guidance, including rule-out criteria (omitted here). Summary of main criteria: <u>Cardiac</u> Pre-existing cardiac disease + ITU for treatment, peripartum cardiomyopathy, arrhythmia + >1 dose antiarrhythmic or ITU, ITU admission for treatment <u>Respiratory</u> ARDS, pulmonary oedema, postoperative pneumonia, DVT or PE; ventilation <u>Renal</u> Acute tubular necrosis or dialysis, oliguria + >1 dose diuretic, acute creatinine elevation <u>Haemorrhagic</u> Haemorrhage with either: • transfusion ≥4 units • <4 units + pulmonary oedema + >1 dose of diuretic • return to theatre (major procedure) • uterine artery embolization • 2-3 units + uterine balloon/compression suture • ITU + invasive monitoring/treatment • Unplanned hysterectomy	7.3 (2012-13)

Definition	Data	Development	Description	Prevalence (/1000)[a]
			Hypertensive Pre-eclampsia with severe/refractory hypertension, hepatic haematoma or severe injury + ITU, HELLP; eclampsia or status epilepticus, antihypertensive infusion, non-responsiveness or loss of vision Infective Septic shock requiring fluid resuscitation/vasopressors, infection + pulmonary complication Other Organ injury, prolonged ileus, small bowel obstruction, CoA, invasive monitoring	
'EPIMOMS study', Siddiqui 2018(84)	Prospective systematic case surveillance	National Delphi-Rand process	Cardiac arrest, pulmonary oedema, decompensation of pre-existing cardiomyopathy, troponinaemia >1 µg/L, RF, ARF, LD, stroke, TIA, coma, death; **'severe hypertensive disorder' including placental abruption with haematological dysfunction, severe pre-eclampsia (birth <32/40), HELLP, eclampsia (19% combined)**, acute anaemia, DIC, PE, severe acute psychiatric disorder or acute decompensation of chronic psychiatric disorder or suicide attempt; **'severe obstetrical haemorrhage' including PPH ≥1500 ml, transfusion ≥4 units red cells or surgical management, hysterectomy (65% combined)**, laparotomy, ITU	NA
'PreCARE' study, Linard 2018(85)	Abstraction from primary record (Paris, France)	Unspecified.	Convulsions, DKA, death; haemorrhagic shock, placental abruption, **severe pre-eclampsia (28%)**, eclampsia, DVT, PE, uterine rupture, severe sepsis, **3rd/4th degree perineal tear (22%)**; **haemorrhage with second-line medical management and transfusion ≥2 units red cells or surgical management/hysterectomy (18% combined)**, **ITU (16%)**, **surgical reintervention (14%)**.	28.4 (2010-12)
Brakewood	Abstraction	Unspecified	Pulmonary oedema, ARF; sepsis, DIC, DVT, PE; hysterectomy, blood	Selected population

Definition	Data	Development	Description	Prevalence (/1000)[a]
2024(86)	from primary record (Rhode Island, USA)		transfusion, ITU. Components not reported individually.	
Boulet 2024(87)	Retrospective review of primary record (Atlanta, USA)	Modification of ACOG guidance (Main 2016)(68) with further specification of the examples from Main 2016.	As per Main 2016 with additional quantification of haemorrhage (1,000 mls, accompanied by treatment as per original definition); degree of fluid resuscitation in septic shock (≥3,000 mls); and addition of sickle crisis and DIC. Major components included **hypertensive disease (69%)**, **haemorrhage (20%)**, **pulmonary complications (18%)**, and **renal disease (10%)**.	Selected population; single centre, high risk population, Del 74 (2016-18)

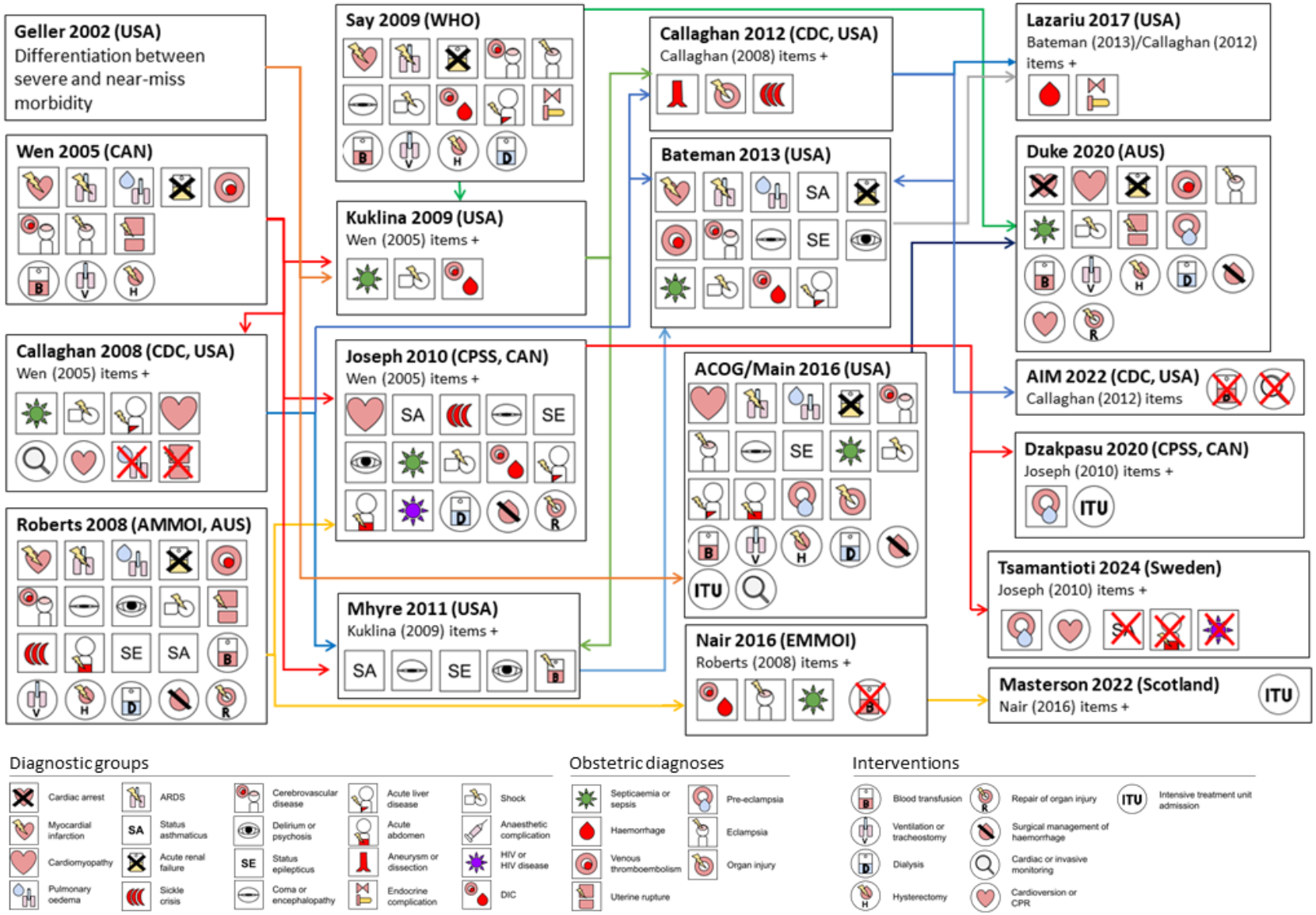
[a] The denominator varies across rows. These are per maternity unless specified. Where specified, Del denotes the incidence of SMM at the delivery episode only, D42 denotes delivery episode and up to 42 days postnatal.

RF respiratory failure, ARF acute renal failure, DKA diabetic ketoacidosis, ITU intensive treatment unit, SCASMM Scottish Confidential Audit of Severe Maternal Morbidity, SE status epilepticus, CoA complications of anaesthesia, SMM severe maternal morbidity, SAMM severe acute maternal morbidity, LEMMoN 'Landelijke Studie naar Etnische determinanten van Maternale Morbiditeit in Nederland' (National Study into Ethnic Determinants of Maternal Morbidity in the Netherlands), NL the Netherlands, HELLP 'haemolysis, elevated liver enzymes, low platelets' (syndrome), WHO World Health Organization, PPH postpartum haemorrhage, CPR cardiopulmonary resuscitation, LOC loss of consciousness, SMMG Severe Maternal Morbidity Group, NPEC National Perinatal Epidemiology Centre, LD liver disease, VST venous sinus thrombosis, ACOG American College of Obstetricians and Gynecologists, CDC Centers for Disease Control and Prevention, DVT deep vein thrombosis, TIA transient ischaemic attack

Components of definitions which represented more than 10% of cases of SMM are noted (%) and shown in bold. Components are not mutually exclusive.

Of the 28 studies of definitions for use with administrative data, 13 were from the USA(46, 50, 53-55, 57-59, 63, 68, 69, 71, 72); 5 from Canada(44, 52, 58, 61, 65, 66); 3 from Australia(45, 48, 67); 2 from Scotland(70, 75), 2 from Sweden(56, 74) and one each from England(62), Finland(60), and Japan(64). Of these, 2 studies (2/28, 7%) developed or reported definitions with reference to the primary medical record(48, 68) and 1 study cited previous case review evidence(46); 4 studies informed the development of a definition by comparing the case fatality rates of candidate components(44, 46, 53, 54); 3 informed the development of definitions by comparing the length of stay for candidate components(46, 66, 74); 3 studies developed definitions informed by the WHO definition of SMM (4/28, 14%)(50, 56, 67); 3 studies developed definitions from a literature review (3/28, 11%)(48, 53, 63); 12 modified or were based on previous definitions other than the WHO definition (16/28, 57%)(46, 52-55, 57, 58, 62, 65, 66, 68, 70-72, 74, 75) and 2 validation studies reported definitions as part of a theoretical comparative process without application of the definitions(68, 69). Additionally, 4 studies compared components or SMM overall according to length of stay, prolonged length of stay, mortality, or ITU admission following development of the definition(52, 65, 67, 70). The incidence of SMM according to these original studies ranged from 1.3 per 1,000(53) to 35.4 per 1,000(67) with a median incidence of 11.4 per 1,000. Of the 13 studies of definitions for use with the primary medical record, we identified the WHO(39); 4 studies from the USA(68, 78, 86, 87); 2 from Scotland(77, 83); 2 from France(84, 85); 2 from Ireland(81, 82), and one each from the Netherlands(79), and South Africa(76). Of these, 3 studies (3/13, 23%) developed definitions with direct reference to the primary medical record(39, 68, 78); 3 involved a consensus process (3/13, 23%)(68, 79, 84); and 5 modified or were based on previous definitions (5/13, 38%)(77, 81-83, 87). The incidence of SMM according to these original studies ranged from 3.8 per 1,000(77) to 28.4 per 1,000(87) with a median incidence of 6.7 per 1,000. The relationships between select definitions for administrative data and comparison of the components is shown in Figure 2.2.

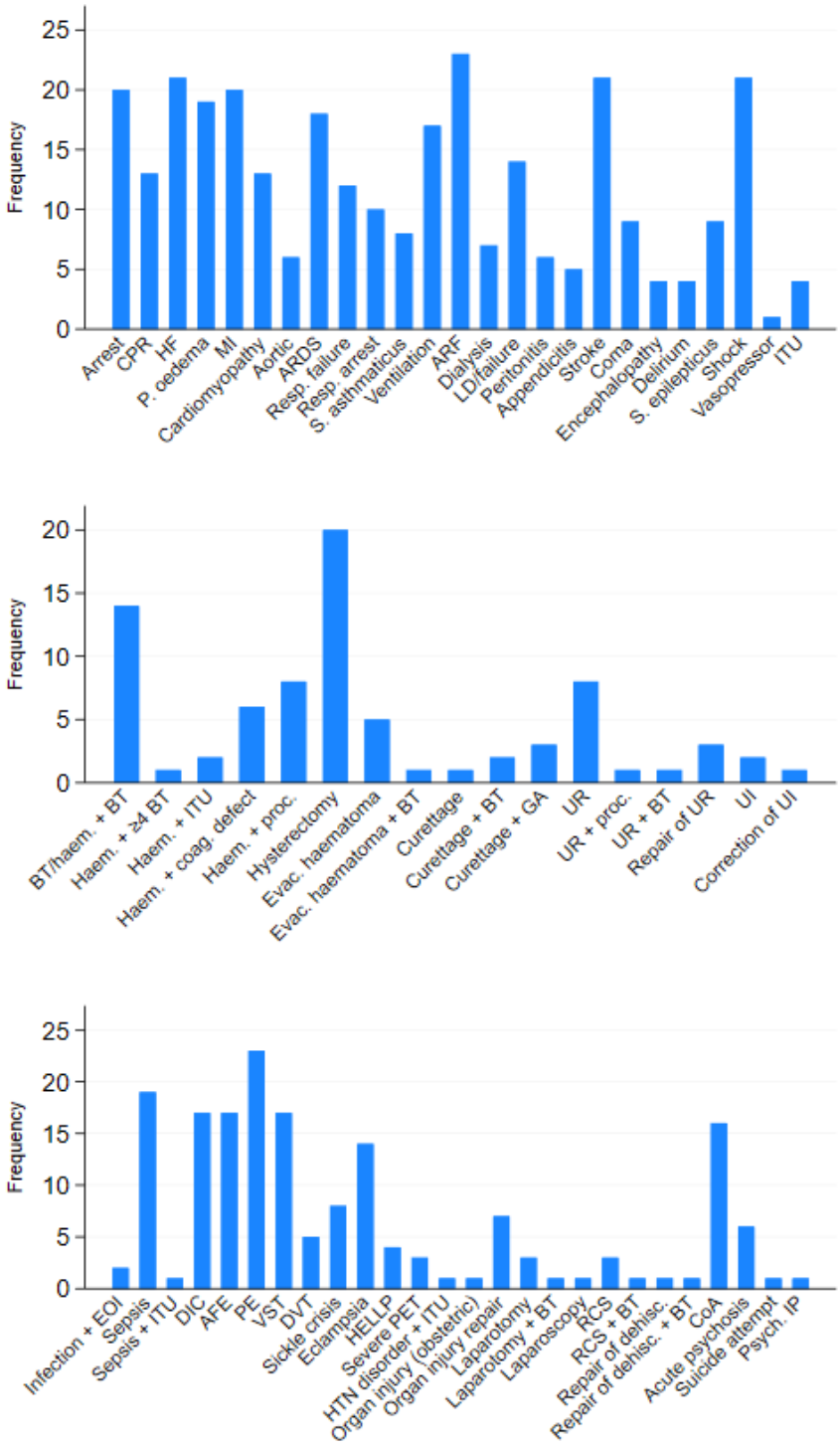
Figure 2-2 Relationship between Definitions of SMM



2.3.1 Components of definitions

Among 24/32 definitions for use with administrative data, the most common components were acute renal failure (ARF; 23/24 definitions), pulmonary embolism (PE; 23/24); shock (22/24), sepsis/severe infection (22/24); heart failure (HF), stroke (21/24); cardiac arrest (20/24), myocardial infarction (MI; 20/24), pulmonary oedema (19/24), and acute respiratory distress syndrome (ARDS; 18/24). The commonest interventions were hysterectomy (20/24), ventilation (17/24), and transfusion (15/24). Conversely, examples of components included in only one SMM definition included acute fatty liver(66), transplant complication(67), panhypopituitarism(53), acute ischaemic cardiac disease(56), and Addisonian crisis(67). The frequency with which components were included is shown in Figure 2.3. The coverage of the WHO definition by the identified diagnostic and procedural codes is shown in Table 2.3. Among 11/13 studies that included definitions for use with the primary medical record, the most common components were ARF (10/11) eclampsia, pulmonary oedema, cardiac arrest, stroke, coma (8/11); severe sepsis/septicaemic shock, uncontrollable fit/status epilepticus (7/11) and acute liver disease, or severe pre-eclampsia/pre-eclampsia with complications (6/11). The commonest interventions were ITU admission (11/11); a transfusion of ≥4/≥5 units of blood products (9/11), hysterectomy (8/11), and ventilation (7/11). Components found in a single definition included symptom-based (e.g., gasping), vital-signs based (e.g., respiratory rate >40 or <6/minute) and laboratory-based (e.g., PaO_2/FiO_2 <200 mmHg, pH <7.1, lactate >5 mmol/L) components of the WHO definition(39) although these may map to similar diagnostic components elsewhere.

Figure 2-3 Frequency of Components within SMM Indicators for Use with Administrative Data



CPR, cardiopulmonary resuscitation; HF, heart failure; P., pulmonary; MI, myocardial infarction; ARDS, Acute respiratory distress syndrome; Resp., respiratory; S., status; ARF, acute renal failure; LD, liver disease; ITU, intensive treatment unit; BT, blood transfusion; Haem., Haemorrhage; proc., Procedure; evac., Evacuation; GA, general anaesthetic; UR, uterine rupture; UI, uterine inversion; EOI, end organ injury; DIC, dissemination intravascular coagulation; AFE, amniotic fluid embolism; PE, pulmonary embolism; VST, venous sinus thrombosis; DVT, deep venous thrombosis; PET, pre-eclampsia; HTN, hypertensive; RCS, reclosure of caesarean section; dehisc., Dehiscence; CoA complications of anaesthesia; psych., psychiatric; IP, inpatient.

Table 2-3 Mapping of Identified International Classification of Disease Codes onto the World Health Organization Definition of Life-Threatening Complications

Clinical criteria	**Approximation**
Acute cyanosis	Respiratory failure, ARDS
Gasping ("terminal respiratory pattern")	ARDS
Respiratory rate >40 or <6/min	None
Shock	Shock during/following labour and delivery, shock (cardiogenic, hypovolaemic, septic, other, unspecified), shock due to anaesthesia, anaphylactic shock
Oliguria that did not respond to fluids or diuretics	Acute renal failure, postpartum acute renal failure, unspecified kidney failure
Clotting failure	Disseminated intravascular coagulation, other/unspecified coagulation defect, postpartum coagulation defects
Loss of consciousness ≥12 hours	Coma
Loss of consciousness and absence of pulse	Cardiac arrest
Stroke	Anoxic brain damage, cerebral infarction, cerebral venous thrombosis, transient ischaemic attack/retinal artery occlusion, subarachnoid haemorrhage, intracerebral haemorrhage, other atraumatic haemorrhage, other strokes
Uncontrollable fit/total paralysis	Eclampsia, status epilepticus
Pre-eclampsia with jaundice	Severe pre-eclampsia; pre-eclampsia + toxic liver disease or hepatic failure
Laboratory-based criteria	
Oxygen saturation <90% for ≥60 minutes	Respiratory failure, ARDS
PaO_2/FiO_2 <200 mmHg	Respiratory failure, ARDS
Creatinine ≥300 µmol/l or ≥3.5 mg/dl	Acute renal failure, postpartum acute renal failure, unspecified kidney failure
Bilirubin>100 µmol/l or > 6.0 mg/dl	Hepatic failure
pH <7.1	None
Lactate >5	None
Acute thrombocytopenia (<50,000 platelets)	None
Loss of consciousness and glycosuria and ketonuria	Type I diabetes mellitus with hyperosmolar coma
Management-based criteria	
Continuous vasoactive drugs	None

Clinical criteria	Approximation
Hysterectomy following infection or haemorrhage	Abdominal hysterectomy, vaginal hysterectomy, caesarean hysterectomy
Transfusion ≥5 units of red cells	Whole blood, packed cells
Intubation and ventilation for ≥60 minutes unrelated to anaesthesia	Continuous ventilation, invasive ventilation, tracheostomy, exteriorisation of trachea
Dialysis for acute renal failure	Dialysis, haemodialysis, insertion of peritoneal dialysis catheter, replacement/removal of peritoneal dialysis catheter
Cardio-pulmonary resuscitation	Restoration of cardiac rhythm, performance of cardiac output

ARDS Acute respiratory distress syndrome

There were five approaches to incorporating transfusion/haemorrhage into definitions using administrative data, including 'any transfusion', 'diagnosis of haemorrhage with transfusion', 'procedure with transfusion', 'transfusion with specified blood products', and 'transfusion ≥4 units', including combinations of approaches. Alternatively, definitions incorporated neither a diagnosis of haemorrhage nor transfusion and recognised only surgical management of haemorrhage, end-organ complications, or critical interventions. Definitions for use with the primary medical record were more nuanced with combinations of transfusion at different thresholds (≥2 units, ≥4 units, ≥5 units), in conjunction with thresholds of estimated blood loss (≥1,500 mls, ≥2,500 mls), or management criteria (second-line medical, surgical or radiological management, including hysterectomy). In most definitions for administrative data that included 'any transfusion'/haemorrhage with 'any transfusion', this was the most common condition among cases (9/12, 75%). For the remaining definitions that did not include 'any transfusion' and reported on individual components, common conditions (assigned to >10% of cases) included sepsis (7/8, 75%), dissemination intravascular coagulation (DIC)/coagulopathy (3/8, 38%), and LD (2/8, 25%). Sepsis was the most common condition in the majority of these definitions (4/8, 50%).

2.3.2 Diagnostic and procedural codes for example definitions from different countries using routine data

Diagnostic codes for the majority of components were defined similarly. The CDC (Centers for Disease Control and Prevention) definition excluded first trimester diagnoses, where this level of definition was available. The codes for pulmonary oedema, HF, cardiomyopathy, ARDS, coma, status epilepticus (SE), appendicitis, psychosis, amniotic fluid embolism (AFE), uterine rupture, and DIC were near-identical across the definitions from Canada, Finland, Sweden, the USA, and the UK, shown in Table 2.4. Codes for respiratory conditions demonstrated variation. The CDC definition included codes for respiratory distress, failure, and arrest as well as procedure-related insufficiency whereas other definitions focussed on ARDS or else captured respiratory failure through ventilation only. Separate codes for procedure-related diagnoses also led to variation for cardiac arrest, ARF, cerebrovascular disease, and sepsis. Complications of anaesthesia (CoA) were represented across several ICD categories for pregnancy, labour and delivery, or the puerperium and whilst most codes were consistent, there was variation in the time periods included. The CDC definition included additional codes for transient ischaemic attack (TIA), vascular syndromes, and encephalopathies, and the CDC and CPSS (Canadian Perinatal Surveillance System) included additional codes for MI. Haemorrhage was defined using diagnostic codes for antepartum haemorrhage (APH)/intrapartum haemorrhage (IPH) with clotting abnormality (CDC, CPSS, Finnish), codes for haemorrhage without clotting abnormality qualified by additional procedural/transfusion codes (CPSS), any transfusion (CDC, AMMOI), hysterectomy (all), surgical or radiological management (AMMOI, EMMOI, CPSS, Finnish), or balloon tamponade (CPSS, Finnish), specific complications that may relate to haemorrhage such as DIC (CDC, AMMOI, EMMOI, CPSS, Swedish), or through end-organ complications or shock (all). For hypertensive disease, most included eclampsia (CDC, EMMOI, CPSS, Swedish), fewer included HELLP syndrome (CPSS, Swedish), or severe pre-eclampsia (CPSS), or no diagnostic codes, instead relying on end-organ complications and critical interventions (AMMOI).

Puerperal sepsis codes were included in most definitions and additional severe sepsis and septic shock codes were included in the CDC definition whereas the CPSS definition included “septicaemia during labour”. Further additions included sepsis due to specified organisms, included in the CDC (streptococcus, listeria, other), and Wahlberg (streptococcus, listeria, actinomycosis, candida) definitions.

Table 2-4 Comparison of Example Diagnostic and Procedural Codes

	'CDC', USA ICD-10	**'AMMOI', Australia** ICD-10-AM	**'EMMOI', England** ICD-10	**'CPSS', Canada** ICD10-CA	**Pallasmaa, Finland** ICD-10	**Wahlberg, Sweden** ICD-10
DIAGNOSTIC, OBSTETRIC						
Haemorrhage						
APH, clotting abnormality	O46.002-.003, O46.009, O46.012-.013, O46.019, O46.022-.023, O46.029, O46.092-.093, O46.099			O46.0		
IPH, clotting abnormality	O67.0			O67.0	O67.0	
IPH, transfusion				O67 +transfusion		
Placental abruption, clotting abnormality	O45.002-.003, O45.009, O45.012-.013, O45.019, O45.022-.023, O45.029, O45.092-.093 O45.099			O45.0 +transfusion		
Placenta praevia				O44.1 +transfusion		
PPH + surgical management				O72 +procedural code		
Hypertensive disease						
Eclampsia	O15		O15	O15		O15
HELLP syndrome				O14.2		O14.2

	'CDC', USA ICD-10	**'AMMOI', Australia** ICD-10-AM	**'EMMOI', England** ICD-10	**'CPSS', Canada** ICD10-CA	**Pallasmaa, Finland** ICD-10	**Wahlberg, Sweden** ICD-10
Severe pre-eclampsia				O14.1		
Other						
Acute fatty liver				O26.6 +transfusion		
Complication of obstetric procedure, other					669.4	
Uterine inversion					O71.2	
Amniotic fluid embolism						
AFE, 1st trimester						
AFE, 2nd/3rd/unspecified trimester, childbirth, puerperium	O88.112-113, O88.119,	O88.1	O88.1	O88.1	O88.1	O88.1
Uterine rupture						
Uterine rupture		O71.0, O71.1	O71.0, O71.1		O71.0, O71.1	O71.0, O71.1
Uterine rupture + transfusion or surgical management				O71.0, O71.1 +procedure code		
DIAGNOSTIC, NON-SPECIFIC						
Abdominal						
Acute abdomen						
Acute or unspecified appendicitis		K35, K37	K35, K37	K35, K37		

	'CDC', USA ICD-10	**'AMMOI', Australia** ICD-10-AM	**'EMMOI', England** ICD-10	**'CPSS', Canada** ICD10-CA	**Pallasmaa, Finland** ICD-10	**Wahlberg, Sweden** ICD-10
Peritonitis (generalised, unspecified, pelvic)		K65.0, K65.9, N73.3, N73.5	K65.0, K65.9, N73.3, N73.5	K65, N73.3, N73.5	K65.0, K65.9	
Peritonitis (peritoneal abscess, spontaneous bacterial, choleperitonitis, sclerosing mesenteritis, other)						
Paralytic ileus and intestinal obstruction without hernia					K56	
Anaesthetic						
Pulmonary complications, pregnancy		O29.0		O29.0		
Other cardiac complications, 1st trimester		O29.1	O29.1	O29.1		
Other cardiac complications, 2nd/3rd/unspecified trimester	O29.192, O29.193, O29.199					
Cerebral anoxia due to anaesthesia, 1st trimester		O29.2	O29.2	O29.2		
Cerebral anoxia due to anaesthesia, 2nd/3rd/unspecified trimester	O29.212, O29.213, O29.219					
Other CNS complications, 1st trimester						
Other CNS complications, 2nd/3rd/unspecified trimester	O29.292, O29.293, O29.299					
Aspiration pneumonitis due to anaesthesia, labour and delivery	O74.0	O74.0	O74.0	O74.0	O74.0	
Cardiac complication (arrest or failure) due to anaesthesia, labour/delivery	O74.2	O74.2	O74.2	O74.2		
CNS complication (anoxia) due to anaesthesia, labour/delivery	O74.3	O74.3	O74.3	O74.3		

	'CDC', USA ICD-10	**'AMMOI', Australia** ICD-10-AM	**'EMMOI', England** ICD-10	**'CPSS', Canada** ICD10-CA	**Pallasmaa, Finland** ICD-10	**Wahlberg, Sweden** ICD-10
Other pulmonary complication due to anaesthesia, labour/delivery	O74.1		O74.1	O74.1		
Pulmonary/cardiac/CNS complications of anaesthesia, puerperium	O89.0, O89.1, O89.2	O89.0, O89.1, O89.2	O89.0, O89.1, O89.2	O89.0, O89.1, O89.2		
Malignant hyperthermia	T88.3XXA					
Cardiovascular						
Acute HF/pulmonary oedema						
Acute pulmonary oedema	J81.0	J81	J81	J81	J81	J81
Left ventricular failure	I50.1	I50	I50	I50		
Systolic HF	I50.21, I50.23, [I50.20]					
Diastolic HF	I50.31, I50.33, [I50.30]					
Combined HF	I50.41, I50,43, [I50.40]					
Right heart failure/cor pulmonale	I50.810, I50.811, I50.813, I50.814					
Heart failure (biventricular, high output, end stage)	I50.82, I50.83, I50.84					
Heart failure (other/unspecified)	I50.89, I50.9					
Post-procedure heart failure	I97.13					
Heart failure due to anaesthesia, 1st trimester		O29.1	O29.1	O29.1		
Heart failure due to anaesthesia, 2nd-3rd/unspecified trimester	O29.122, O29.123, O29.129					
Hypertensive disease (+/- CKD +/- ESRF) with heart failure						I11.0

	'CDC', USA ICD-10	**'AMMOI', Australia** ICD-10-AM	**'EMMOI', England** ICD-10	**'CPSS', Canada** ICD10-CA	**Pallasmaa, Finland** ICD-10	**Wahlberg, Sweden** ICD-10
Aortic aneurysm/dissection (intact/ruptured)	I71					I71.0, 171.1, 171.5, 171.8
Aneurysm of aorta in other diseases	I79.0					
Cardiac arrest						
Cardiac arrest/ventricular fibrillation	I46	I46	I46	I46		I46
Cardiac arrest due to anaesthesia, 1st trimester		O29.1	O29.1	O29.1		
Cardiac arrest due to anaesthesia, 2nd-3rd/unspecified trimester	O29.112, O29.113, O29.119					
Cardiac arrest, intra-/post-operative	I97.12, I97.711			O75.4 (inclusive of arrest)		
Ventricular fibrillation/flutter	I48.0					
Other cardiac arrhythmias				I49		I49.0 (ventricular)
Cardiomyopathy						
Peripartum cardiomyopathy		O90.3	O90.3	O90.3		
Cardiomyopathy		I42, I43	I42, I43	I42, I43		
Myocardial infarction						
Myocardial infarction, acute	I21	I21	I21	I21		I21
Myocardial infarction with subsequent STEMI/NSTEMI	I22			I22		
Ischaemic heart disease, other acute/unspecified						I24.8, I24.9

	'CDC', USA ICD-10	**'AMMOI', Australia** ICD-10-AM	**'EMMOI', England** ICD-10	**'CPSS', Canada** ICD10-CA	**Pallasmaa, Finland** ICD-10	**Wahlberg, Sweden** ICD-10
Respiratory						
ARDS	J80			J80	J80	J80
Acute respiratory distress/respiratory arrest	R06.03, R09.2					R09.2
Acute pulmonary insufficiency/failure, postoperative	J951, J95.2, J95.82					
Chronic pulmonary insufficiency, post-operative	J95.3					
Respiratory failure (acute, acute and chronic)	J96.0, J96.2					J96.0
Respiratory failure (acuity unspecified)	J96.9					
Status asthmaticus						
		J46	J46	J45.01, J45.11, J45.81, J45.91		
CNS						
Coma						
Coma, persistent vegetative state		R40.2	R40.2	R40.2		
Cerebral oedema		G93.6	G93.6	G93.6		
Cerebrovascular disorders (puerperal)						
Ischaemic						
Anoxic brain damage						G93
Cerebral infarction	I63	I63	I63	I63		I63
Cerebral infarction, DVT in cerebral vein					I63.6	
Cerebral venous thrombosis, 1st trimester				O22.51		O22.5

	'CDC', USA ICD-10	**'AMMOI', Australia** ICD-10-AM	**'EMMOI', England** ICD-10	**'CPSS', Canada** ICD10-CA	**Pallasmaa, Finland** ICD-10	**Wahlberg, Sweden** ICD-10
Cerebral venous thrombosis, 2nd trimester-puerperium or unspecified	O22.50, O22.52, O22.53			O22.5		
Cerebral venous thrombosis, puerperium	O87.3		O87.3	O87.3	O87.1	O87.3
Cerebrovascular infarction (perioperative)	I97.81, I97.82					
TIA/related syndromes, transient retinal artery occlusion	G45, H34.0					
Vascular syndromes of brain	G46					
Haemorrhagic						
Haemorrhage, atraumatic (subarachnoid, intracerebral, other/unspecified)	I60, I61, I62	I60, I61, I62	I60, I61, I62	I60, I61, I62		I60, I61, I62
Other						
Cerebrovascular disorders in other diseases	I68					
Hypertensive encephalopathy	I67					I67.4
Occlusion/stenosis of arteries without infarct	I65, I66					
Other encephalopathy, cerebral compression, oedema	G93.49					G93
Other cerebrovascular diseases	I67					
Progressive multifocal leukoencephalopathy	A81.2					
Stroke not specified as haemorrhage or infarction		I64	I64	I64		
Psychosis						
Puerperal psychosis		F53.1	F53.1	F53.1		
Brief psychotic episode		F23	F23	F23		

	'CDC', USA ICD-10	**'AMMOI', Australia** ICD-10-AM	**'EMMOI', England** ICD-10	**'CPSS', Canada** ICD10-CA	**Pallasmaa, Finland** ICD-10	**Wahlberg, Sweden** ICD-10
Status epilepticus						
Status epilepticus (grand mal only)						
Status epilepticus (grand mal, petit mal, complex partial, other, unspecified)		G41	G41	G41		
Haematological						
DIC	D65	D65	D65	D65		D65
Other/unspecified coagulation defect	D68.8, D68.9					
Postpartum coagulation defects	O72.3					
Sickle cell disease with crisis						
SCD with crisis (Hb-SS)	D57.0	D57.0	D57.0	D57.0		
SCD with crisis (Sickle/Hb-C, Sickle thalassaemia, other)	D57.21, D57.41, D57.81					
Thromboembolism (and air embolism)						
PE with acute cor pulmonale	I26.0				I26.0	I26
PE without acute cor pulmonale	I26.90, I26.92, I26.93, I26.94, I26.99				I26.9	
Air embolism, 1st trimester						
Air embolism, 2nd trimester-puerperium or unspecified	O88.012, O88.013, O88.019, O88.02, O88.03	O88.0	O88.0	O88.0	O88.0	O88.0
Thromboembolism, 1st trimester		O88.2	O88.2	O88.2	O88.2	O88.2

	'CDC', USA ICD-10	**'AMMOI', Australia** ICD-10-AM	**'EMMOI', England** ICD-10	**'CPSS', Canada** ICD10-CA	**Pallasmaa, Finland** ICD-10	**Wahlberg, Sweden** ICD-10
Thromboembolism, 2nd trimester-puerperium or unspecified	O88.212, O88.213, O88.219, O88.22, O88.23					
Pyemic/septic embolism, 1st trimester		O88.3	O88.3	O88.3	O88.3	O88.3
Pyemic/septic embolism, 2nd trimester-puerperium or unspecified	O88.312, O88.313, O88.319, O88.32, O88.33					
Other embolism, 1st trimester		O88.8	O88.8	O88.8	O88.4	O88.8
Other embolism, 2nd trimester-puerperium or unspecified	O88.812, O88.813, O88.819, O88.82, O88.83					
Iatrogenic air embolism	T80.0XXA					
Phlebitis and thrombophlebitis, lower limb					I80.1, I80.20, I80.29	
Portal vein, subclavian, vena cava, other venous thrombosis					I81, I82.80, I82.88, I82.29	
Deep phlebothrombosis, puerperium					O87.1	
Hepatic						
Toxic liver disease (drug-induced cholestasis/hepatitis/fibrosis/other/unspecified)				K71		
Hepatic failure				K72		K72.0
Renal						
ARF/postpartum ARF	N17, O90.4	N17, O90.4	N17, O90.4,	N17, O90.4		N17, O90.4

	'CDC', USA ICD-10	**'AMMOI', Australia** ICD-10-AM	**'EMMOI', England** ICD-10	**'CPSS', Canada** ICD10-CA	**Pallasmaa, Finland** ICD-10	**Wahlberg, Sweden** ICD-10
Intra-/post-operative complications/disorders of the genitourinary system		N99.0	N99.0	N99.0		
Unspecified kidney failure		N19	N19	N19		
HIV disease						
Symptomatic HIV/AIDS				B20, O98.7		
HIV leading to malignant neoplasms, other diseases resulting from HIV, acute HIV				B21-24		
Severe infection/sepsis						
Puerperal sepsis	O85		O85	O85, O75.3	O85	
Severe sepsis (without/with septic shock)	R65.20, R65.21					
Sepsis or septic shock following a procedure/obstetric procedure	T81.44XA, T81.12XA, O86.04					
Septic arterial embolism	I76					
Sepsis (streptococcal, listerial, other)	A40, A41, A32.7					A40, A41
Sepsis (actinomycosis)						A42.7
Disseminated candidiasis/candidal sepsis						B37.7
Shock						
Shock during/following labour and delivery	O75.1	O75.1	O75.1	O75.1	O75.1	
Shock (cardiogenic, hypovolaemic, septic, other, unspecified)	R57	R57	R57.0-.02, R57.8, R57.9	R57		R57
Shock due to anaesthesia	T88.2XXA					

	'CDC', USA ICD-10	**'AMMOI', Australia** ICD-10-AM	**'EMMOI', England** ICD-10	**'CPSS', Canada** ICD10-CA	**Pallasmaa, Finland** ICD-10	**Wahlberg, Sweden** ICD-10
Anaphylactic shock, unspecified, initial encounter	T78.2XXA					
Shock following a procedure	T81.10XA-.12XAT81.19XA					
Anaphylactic reaction due to […] administered medicament	T88.6XXA	T88.6	T88.6	T88.6		
Anaphylactic reaction due to serum		T80.5	T80.5	T80.5		
PROCEDURAL, OBSTETRIC						
Curettage						
Curettage of uterus + GA		✓	✓			
Dilatation and curettage/aspiration/ evacuation + transfusion				✓		
Evacuation of haematoma						
Evacuation of vulval/vaginal haematoma			✓			
Evacuation of incisional haematoma + transfusion				✓ + transfusion		
Evacuation of incisional perineal haematoma		✓				
Evacuation of non-incisional perineal/vaginal haematoma		✓				
Evacuation of caesarean wound haematoma		✓				
Aspiration of haematoma of organ			✓			
Open drainage of abdominopelvic abscess			✓			
Image-guided drainage of abdominopelvic abscess		✓	✓			

	'CDC', USA ICD-10	**'AMMOI', Australia** ICD-10-AM	**'EMMOI', England** ICD-10	**'CPSS', Canada** ICD10-CA	**Pallasmaa, Finland** ICD-10	**Wahlberg, Sweden** ICD-10
Hysterectomy						
Abdominal hysterectomy	✓	✓	✓	✓	✓	✓
Vaginal hysterectomy						
Abdominal hysterectomy (without fixation/pelvic floor repair)				✓		
Caesarean/peripartum hysterectomy				✓	✓	✓
Abdominal re-intervention						
Reclosure of abdominal wound		✓	✓			
Re-exploration of abdomen +/- arrest of bleeding			✓			
Re-opening of abdomen		✓	✓		✓	
Opening of abdomen and exploration of groin			✓			
Secondary suture of skin, resuture of skin			✓		✓	
Refashioning of scar			✓			
Control of postoperative bleeding/thrombosis after intra-abdominal vascular procedure		✓				
Control of postoperative haemorrhage after gynaecological surgery		✓			✓	
Reoperation/laparotomy for deep infection/drainage in obstetric surgery					✓	
Reoperation for insufficiency of anastomosis/suture in					✓	

	'CDC', USA ICD-10	**'AMMOI', Australia** ICD-10-AM	**'EMMOI', England** ICD-10	**'CPSS', Canada** ICD10-CA	**Pallasmaa, Finland** ICD-10	**Wahlberg, Sweden** ICD-10
gynaecological surgery						
Repair of abdominal organs						
Repair of obstetric laceration to bladder/urethra		✓		✓		
Repair of ruptured bladder		✓	✓			
Repair of rupture of urethra			✓			
Repair of ruptured uterus		✓				✓
Surgical correction of inverted uterus		✓				
Repair of uterine laceration				✓ + transfusion		
Surgical management of haemorrhage						
Embolisation of artery		✓	✓	✓	✓	
Open embolisation			✓			
Ligation of artery		✓	✓	✓	✓	
Ligation of vein			✓			
Transluminal procedures of vein			✓	✓		
Compression suture of uterus				✓		
Balloon compression of uterus/tamponade				✓	✓	
PROCEDURAL (AND TREATMENT-BASED ICD CODES), NON-SPECIFIC						
Exploratory laparotomy					✓	✓
Exploratory laparoscopy					✓	
Cystotomy		✓	✓			

	'CDC', USA ICD-10	**'AMMOI', Australia** ICD-10-AM	**'EMMOI', England** ICD-10	**'CPSS', Canada** ICD10-CA	**Pallasmaa, Finland** ICD-10	**Wahlberg, Sweden** ICD-10
Repair of fistula			✓			
Bowel resection and anastomosis (jejunectomy, ileectomy)		✓	✓			
Resection of small intestine with formation of stoma		✓				
Other procedures to ileum			✓			
Colectomy and anastomosis/exteriorisation/ileostomy		✓	✓			
Endoscopic procedures on lesion of distal bowel/sigmoid			✓			
Excision of rectum			✓			
Repair of mesentery of small intestine/colon			✓			
Endoscopic resection of lesion of peritoneum			✓			
Formation of ileostomy reservoir		✓				
Suture of intestine		✓		✓		
Other repair of intestine		✓		✓		
Cardiovascular						
Restoration of cardiac rhythm	✓					
Performance of cardiac output	✓					
Transfusion (in isolation)						
Whole blood or packed cells	✓	✓		With diagnostic codes		
Platelets						
Coagulation factors or other serum						
Exchange transfusion		✓				

	'CDC', USA ICD-10	**'AMMOI', Australia** ICD-10-AM	**'EMMOI', England** ICD-10	**'CPSS', Canada** ICD10-CA	**Pallasmaa, Finland** ICD-10	**Wahlberg, Sweden** ICD-10
Intensive treatment unit						
Ventilation						
Tracheostomy	✓	✓	✓	✓		
Cricothyroidostomy			✓			
Exteriorisation of trachea			✓			
Tracheostomy-related		✓				
Continuous ventilation	✓	✓				
Non-invasive ventilation		✓	✓			
Invasive ventilation			✓	✓		
Renal (dialysis)						
Haemodialysis		✓	✓	✓		
Dialysis (all)						
Insertion of peritoneal dialysis catheter		✓	✓			
Replacement/removal of peritoneal dialysis catheter		✓				

CDC Centers for Disease Control and Prevention, AMMOI Australian Maternal Morbidity Outcome Indicator, EMMOI English Maternal Morbidity Outcome Indicator, CPSS Canadian Surveillance System, ICD International Classification of Diseases, APH antepartum haemorrhage, IPH intrapartum haemorrhage, PPH postpartum haemorrhage, AFE amniotic fluid embolism, HF heart failure, CKD chronic kidney disease, ESRF end-stage renal failure, STEMI ST (segment) elevation myocardial infarction, NSTEMI non-ST (segment) elevation myocardial infarction, ARDS acute respiratory distress syndrome, CNS central nervous system, DVT deep vein thrombosis, DIC disseminated intravascular coagulation, SCD sickle cell disease, PE pulmonary embolism, ARF acute renal failure, GA general anaesthetic.

2.4 Discussion

There were 32 composite definitions developed for use with administrative health data and 13 for use with the primary medical record that incorporated both direct (obstetric) and indirect (medical) measures of SMM. Among definitions for use with administrative data, there was strong consensus (>70%) on a core set of components that included diagnostic codes reflective of end-organ injury or failure across cardiovascular (heart failure, cardiac arrest, myocardial infarction, pulmonary oedema); respiratory (acute respiratory distress syndrome); renal (acute renal failure); cerebrovascular (stroke); haematological (disseminated intravascular coagulation) systems. There was also consensus for severe direct obstetric complications, including haemorrhage, sepsis, eclampsia, pulmonary embolism, venous sinus thrombosis, and amniotic fluid embolism, and interventions including hysterectomy and ventilation. Together, these core components represented the working definition of SMM for use with structured data from the electronic health record (Chapter 6). Among definitions for use with the primary medical record, there was strong consensus on acute renal failure, cardiac arrest, pulmonary oedema, and stroke, as well as coma, and interventions including ITU admission, transfusion of at least 4 units of blood products, and hysterectomy. The components not already identified were considered for potential inclusion following further development (Chapter 6). A principal source of variation to be addressed was the definition of haemorrhage, which had high consensus at the conceptual level but which was defined using a wide range of measures. The inclusion of transfusion was the most influential component on the prevalence of severe maternal morbidity, and was typically the most common component within these composite definitions.

To use these definitions with structured data from the electronic health record, a definition needs to be developed that reflects severe complications and that can be used reliably across different maternity services. Therefore a useable phenotype(88) for SMM needs to be developed from these

definitions. The division of definitions into those based on the primary medical record or secondary sources of administrative health data enables comparison of how SMM may be 'ideally' defined if it were possible to review all cases individually and how SMM may need to be defined practically, at scale, when integrated with the electronic systems that could facilitate individualised EWSs. Definitions for individual case review are able to differentiate between severe and non-severe manifestations of specific disease pathways in detail(89) whereas definitions for administrative data had to take other approaches. Some definitions used combinations of codes(66) or more complicated algorithms(67) for the identification of SMM using administrative data. As diagnostic and procedural codes are routinely derived from clinical documentation across the UK, the use of administrative data ensures availability across services and therefore supports consistency, also termed fitness for reuse(90). However, the reliability of administrative data is dependent on the construction of an accurate clinical narrative, its correct interpretation by a clinical coder, and the appropriate assignment of diagnostic or procedural codes(62). For these potential reasons, several components that were common among definitions for use with administrative data have been found to have poor positive predictive values when validated against the primary medical record(91). The benefits of administrative data nevertheless outweigh these limitations because the ability to identify larger numbers of cases enables prediction models for SMM to be developed and validated. These phenotypes must be carefully curated. The development of a phenotype of SMM using data from the electronic health record is an opportunity to use additional structured data entered at the point of care to improve the specificity of diagnostic codes and to introduce reliable thresholds for disease severity where these are not available within administrative data.

There was consensus for a core set of clinical concepts among the definitions for administrative data that reflected end-organ injury and failure, life-threatening physiological states, and critical interventions based on diagnostic and procedural codes. There were several areas where the definition may be further developed. First, acute liver disease had only moderate consensus and was

not included in the preliminary set of conditions. It was represented in the WHO definition by the laboratory criterion for bilirubin(39), which represents acute liver dysfunction, but is captured by a diverse array of ICD-10 diagnostic codes(43). Second, eclampsia had moderate consensus among the definitions for administrative data and strong consensus among those based on the primary medical record. The reason for omitting eclampsia from definitions for administrative data included that it did not appear to have been regarded as a life-threatening complication(64) despite its alignment with the WHO definition(39) but also concern with the quality of administrative codes(48). Components with moderate consensus may be considered for inclusion in the composite outcome based on the specific phenotype within electronic health records. Third, some components for which there was a high degree of consensus, including sepsis and acute renal failure, may represent a wide spectrum of disease in practice. The validity of diagnostic codes for sepsis has been found to vary substantially(92). Similarly, an AKI is not necessarily a life-threatening event, encompassing a spectrum of severity from a mild and transitory impairment of renal function through to renal failure that requires renal replacement therapy(93). Evidence from the general adult population also showed that diagnostic codes for AKI were not necessarily reflective of biochemical measures of renal function(94). The clinical concept of 'severe pre-eclampsia', or rather 'pre-eclampsia with severe features' also represents a potentially wide spectrum, and diagnostic codes may not reflect severe disease(95). These diagnoses would benefit from further phenotypic development in the electronic health record to ensure validity.

There was variation in the proportion of cases identified by individual components within definitions; for example, the proportion of women who had haemorrhage with transfusion varied between 21% and 75% of women with SMM in the definitions for administrative data. This raised two related issues. First, the inclusion of 'any transfusion' may substantially increase the number of women labelled as having experienced SMM despite its potentially low positive predictive value(96). Second, there may be a substantial imbalance between the components of composite measures of

SMM. Whereas in clinical trials such imbalance may lead to misleading claims(97), in clinical prediction such imbalance may modify a model's function if early warning processes are reoriented towards one dominant component. Combined, this could lead to the particularly problematic situation whereby prediction is driven by a less important component of the outcome(98). In the worst case, this could mean that an EWS may direct care and resources towards women at risk of transfusion but who are not at risk of a severe complication and away from women potentially at risk of a severe complication. Further, the inclusion of interventions like transfusion may make the outcome contextual and clinician-dependent(99). Clinical prediction models could cause harm due to the influence of a prediction on clinical behaviour(100), which could pose a problem if the clinical threshold for transfusion were lowered or increased inappropriately, for example. The application for the validation and modification of EWSs is that the included components should be appropriately matched to the intended use of the tool. The composite definition of SMM should capture a balanced mix of all severe complications for which it is expected to provide early warning whilst excluding non-severe disease.

2.4.1 Strengths and limitations

The strength of this systematic review was its detailed approach to comparing definitions of SMM at the concept and coding levels. This component of work was limited to mapping the existing definitions of SMM only. These definitions were limited to those that included both direct and indirect severe complications only that would be most useful to develop a general EWS for use in maternity. Therefore, the definitions do not represent an exhaustive list encompassing every conception of SMM possible. A further limitation is that these definitions were restricted to those identified in high-income settings because the prevalence of SMM, its determinants, and underlying disease processes differ across the classifications of country-level income. The focus of this work was to inform the development of an advanced EWS in a high-income setting in the first instance. The actual use of these definitions beyond their initial development was not considered; some

definitions have been widely adopted whereas others have not. However, the aim of this work was to understand what definitions exist, how these were developed, and how they can be applied to the validation of EWSs.

2.5 Conclusion

This systematic review has identified areas of consensus on the definition of SMM, including end organ injury and failure, life-threatening physiological states, and critical interventions. Areas of less consensus included obstetric and medical diagnoses. This has informed a working definition of SMM (thesis objective 1) that will be applied to electronic health data with which a reliable and generalisable phenotype will be developed for the validation (thesis objective 5) and exploration of differences in performance between ethnic groups (thesis objective 6). The working definition following this chapter included heart failure, cardiac arrest, myocardial infarction, pulmonary oedema, acute respiratory distress syndrome, acute renal failure, stroke, disseminated intravascular coagulation, haemorrhage, sepsis, eclampsia, venous sinus thrombosis, pulmonary embolism, amniotic fluid embolism as well as hysterectomy or ventilation.

In the next chapter, the prognostic factors that were associated with SMM were considered (thesis objective 2), which represents the next stage of the development of an advanced EWS. Based on the differences between definitions identified in the present chapter, prognostic factors were analysed for definitions of SMM that include or do not include 'any blood transfusion' separately so that differences were apparent. In the later stage of this work, the definition of SMM developed here was adapted for use with electronic health data (chapter 6). The definition was adapted according to the limitations of the electronic data collected but adhered as closely as possible to the WHO definition with input from a multidisciplinary group of experts. The definition was developed further to include

a time point at which SMM occurred so that the prospective prediction of SMM over different periods of time could be evaluated (chapter 6).

3 Chapter III: Prognostic Factors for Severe Maternal Morbidity and Related Severe Outcomes

3.1 Introduction

In chapter 2, definitions of severe maternal morbidity (SMM) were identified and the potential implications for the prediction of SMM were considered to develop a preliminary definition of SMM (thesis objective 1). The next stage is to identify the prognostic factors that relate to those outcomes of SMM (thesis objective 2). In this chapter, the prognostic factors for SMM, including within individual ethnic groups, will be identified and their implications for the individualised prediction of SMM will be discussed. Ultimately, the aim is to use this research to inform the development of an advanced EWS. These prognostic factors are therefore relevant because a key difference between existing EWSs and an advanced EWS is the ability to base predictions on a wider range of clinical information contained within electronic health records. However, the vast array of data available requires curation so that an advanced EWS is not needlessly complex, which may impair its performance. This chapter addresses the need to evaluate the evidence in support of the association between prognostic factors and SMM (thesis objective 2). The term 'prognostic factors', drawn from the discourse of prediction modelling, is used to emphasise that risk factors are not necessarily causal risk factors.

Maternal morbidity may arise from the complex interaction of processes through the life course(101), from the social environment a woman may be born into, to the acquisition of comorbidities(102, 103) and to care and interventions near to the time she gives birth(42). Currently, EWSs are simple, integer score-based prediction models that predominantly use the vital signs and sometimes other bedside clinical signs and symptoms to understand the acute physiological status.

The normal vital sign ranges for these simple scores may be determined by expert opinion on what the appropriate ranges are for pregnancy(17) or may be based on pregnancy-specific physiological reference ranges(15). The application of EWSs to reduce SMM may be limited by this universal approach to pregnancy physiology in which all women are compared to a single standard set of 'normal' vital signs. In reality, a woman's risk of experiencing SMM may be understood from the vital signs, from her known clinical risk factors, and from the relationship between the two. Individualised prediction refers to the more nuanced understanding of an individual woman's condition and her individual risk of developing a severe complication based on a wider range of information(104). If informed by a wider range of prognostic factors, the prediction of SMM may be improved. For example, the vital signs could be interpreted through the lens of that individual woman's age, body mass index, and pre-existing morbidities.

It is also important to recognise that the prevalence of SMM during a maternity is unequal across different ethnic groups. Women who are Black are at greater risk of SMM(105, 106) and at twice the risk of SMM progressing to death(107), compared with women who are White. Black women are at greater risk of death in pregnancy in the UK, compared with White women(1). Further, prognostic factors can differ between ethnic groups(108). The prevalence and magnitude of prognostic factors within groups should be understood so that this important safety system can recognise risk and potentially prevent morbidity in all women equally. A modified EWS based on an individual's risk factors has the potential to reduce health inequality if it predicts SMM as well within all ethnic groups and if alerts that lead to preventative action occur reliably and at the same level of physiological abnormality in all groups. Improved prediction could disproportionately increase the recognition of risk in groups at higher risk. Second, this review is an opportunity to identify prognostic factors that have been studied within individual ethnic groups to ensure that a modified EWS includes relevant predictors even if these may not be predictive of SMM in the population as a whole. Where possible, differences should not be assigned to ethnicity itself, a form of biological

essentialism(109); this does not mean that socioeconomic inequality and racism do not contribute to health inequality, rather that the actual, acquired, biological causes of SMM are the product of structural inequalities. The inclusion of prognostic factors, including measures of structural inequalities that are collected as part of maternity care, may improve prediction.

As a tool for use in the acute setting, EWSs are necessarily directed towards the recognition of acute disease processes or obstetric complications. Although the EWS cannot intervene on the social determinants of health(103) or pre-existing morbidity, it is an opportunity to break the progression of structural inequalities to SMM. In practice, this means that whatever the distribution of prognostic factors across groups, an EWS should prevent SMM by directing staff time, investigations, high-dependency or critical care resources appropriately. This can only happen if those prognostic factors are identified, extracted and incorporated into these clinical prediction models. The rationale for this systematic review is that the identification of prognostic factors for SMM from the existing literature will inform both the subsequent modification of the national MEWS and the development of an advanced EWS. This represents a systematic approach to curating the list of candidate variables. Without this process, an EWS may not only be less effective but could also cause harm if it assigns a higher level of risk to one woman because an important prognostic factor in another women with similar vital signs has not been included in the model. The systematic identification of prognostic factors reduces the chance that important risk factors will not be identified. Similarly, a further step to identify prognostic factors within individual ethnic groups will ensure that key prognostic factors are not omitted because they do not appear to be informative of SMM risk in the population overall.

3.2 Methods

A systematic review and meta-analysis of studies of risk factors for SMM, ITU admission, cardiac arrest, or maternal death was conducted. This work was prospectively registered with the PROSPERO database (CRD42023416574; https://www.crd.york.ac.uk/prospero/display_record.php?RecordID=416574) and is reported in accordance with the 'Preferred Reporting Items for Systematic Reviews and Meta-analyses' (PRISMA) guidance(40).

3.2.1 Systematic search

Systematic searches were conducted in MEDLINE and Embase between 1 January 1993 and 30 June 2023. The first 1,000 records of Google Scholar were screened as a 'top up' search and citation searches were conducted in all included studies. Observational studies of prognostic factors for SMM, ICU, cardiac arrest, or maternal death among women who were either pregnant or who were up to 42 days postpartum were included. SMM was defined as a composite outcome that combined at least two diagnoses, measures, or processes reflective of severe complications and which contained no components that represented non-severe complications. Study populations were based in high income countries. The search strategy is shown in Appendix Table B3.1. Studies of populations selected according to ethnicity, including groups of different ethnicities often termed 'race', were included. Studies of populations selected for other demographic characteristics, comorbidities, or multiple pregnancy were excluded because an advanced EWS is for use among all women who are pregnant or postpartum. Studies with a study period prior to 1 January 1993 were excluded. A human translator was identified to translate any records that were not in English.

Two reviewers (IH and RL) screened titles and abstracts of records and reviewed eligible records in duplicate. Discrepancies were resolved by discussion and, if necessary, using a third reviewer (SG).

Where additional data were required to determine inclusion or exclusion or clarify inconsistencies, study authors were contacted using the corresponding author's email address in the first instance, other institutional email addresses in the second instance, followed by direct message through the 'ResearchGate' academic network.

3.2.2 Data extraction

The records were managed using the 'Covidence' systematic review tool in which an electronic data collection form was developed. Two reviewers (IH and RL) extracted data in duplicate on study and sample characteristics (author, year, design, region, sample size, ethnic composition, inclusion and exclusion criteria, time period, source of data); the measurement of outcomes and prognostic factors; methods including modelling strategy and handling of missing data; raw summary data and adjusted estimates. Discordance between reviewers was resolved as for the screening stage.

3.2.3 Quality assessment

Records were assessed in accordance with the 'Quality in Prognosis Studies' (QUIPS) tool(110) in duplicate by both reviewers. The tool is recommended for the assessment of studies of prognostic factors by the Cochrane Prognosis Methods Group(111). The QUIPS tool is divided into the domains of 'study participation', 'study attrition', 'risk factor measurement', 'outcome measurement', 'confounding', and 'statistical analysis and reporting'. Each domain details a list of prompting items to produce a domain-level risk of bias assessment. Domains are rated 'low' risk, with bias unlikely; 'moderate risk', where bias may have arisen; or 'high risk' where bias is very likely. The domain ratings inform an overall risk of bias assessment. Discordance between reviewers was handled as for the screening stage.

To identify candidate prognostic factors for future prediction models, evidence of the marginal associations between prognostic factors and outcomes was desirable. Accordingly, unadjusted estimates were meta-analysed to reflect the total prognostic information of each prognostic factor. The QUIPS tool includes the domains of analysis and confounding, introducing a causal approach. These domains were not relevant when understanding the risk of bias for the unadjusted associations. Consequently, a dual risk of bias assessment was applied. First, an overall QUIPS rating using all domains to understand the independence of predictors from its causal approach. Second, a sub-rating that excluded the domains of analysis and confounding to select studies for inclusion in the meta-analysis of unadjusted estimates. This approach ensured that studies contributed to the meta-analyses based on the risk of bias for the estimates that were being pooled. Additionally, to identify prognostic factors that are 'independent' of other variables, a meta-analysis of adjusted summary estimates was planned but due to a high degree of clinical diversity whereby no studies adjusted for the same covariables, this was not possible.

3.2.4 Synthesis

Prognostic factors were reported on modified harvest plots(112) according to the direction of association (positive, no association, negative) and risk of bias (low risk, moderate/potential risk, high/at risk). These were reported separately for prognostic factors without adjustment, with adjustment for demographic or socioeconomic covariables, with adjustment for comorbidities or lifestyle-related covariables; and any proximal variables (such as peripartum interventions). SMM was reported with 'any transfusion' (SMM-T, i.e. severe maternal morbidity-transfusion) and without 'any transfusion' ('restricted' to a higher volume of blood products or not including transfusion, SMM-RT, i.e. severe maternal morbidity-restricted transfusion) of blood products because this was a major difference between definitions identified in Chapter 2 and because prognostic factors may differ between haemorrhage and other severe complications. Where required, rates or proportions were extracted from figures using the 'WebPlotDigitizer' tool(113)

and, separately, calculated counts from rates and percentages. Data for maternal mortality or cardiac arrest were not extracted from composite outcomes of SMM if there were less than 5 events in each cell.

Restricted maximum likelihood random effects meta-analyses using inverse-variance weighting were conducted. For prevalence, proportions and their standard errors were calculated from count data. For prognostic factors, relative risks were calculated from count data and their standard errors, the log-transformed relative risks were pooled and then exponentiated to obtain summary relative risks with 95% confidence intervals, using the 'meta' command in Stata. Meta-analyses were performed where summary data were available from at least 3 studies with unadjusted estimates at low-moderate risk of bias. Meta-analyses were not conducted for peripartum interventions. Absolute heterogeneity was evaluated using the tau^2 statistic(114) and 95% prediction intervals, which express the degree of uncertainty for an additional study investigating the same association(115). Harvest plots included only one study for prognostic factors from identical populations. Meta-analyses included the largest study when populations were estimated to overlap by 20% or more based on geography/time period. Small study and publication bias were assessed by inspecting funnel plots for meta-analyses of ten or more studies. Asymmetry was also evaluated using the Harbord test for binary outcomes and the precision effect test (PET). Bias-corrected estimates were calculated using trim-and-fill and using the precision effect estimate with standard errors (PEESE). Statistical analyses were conducted in Stata 18 (StataCorp LLC).

Prognostic factors were reported based on the meta-analyses and divided into 'generalisable' prognostic factors, whose confidence and prediction intervals did not include a relative risk of 1, and 'potentially generalisable', whose confidence intervals did not but whose prediction intervals did include a relative risk of 1. This meant that although the association was present in the pooled sample, the strength or direction may be either context-specific or affected by the diversity of study

methods. For prognostic factors not suitable meta-analysis, 'strength of evidence' was evaluated using a scoring system(116) (strong evidence, ≥2 studies at low risk of bias; moderate evidence, ≥2 studies with 1 at low risk of bias; weak evidence, ≥2 studies, none at low risk of bias). Prognostic factors were reported within ethnic groups separately, which included interaction or mediation studies, and calculated ratios of relative risks with 95% confidence intervals to compare the strength of association between ethnic groups.

The approach to measuring identity differed across countries. The individual groups were reported as described in the primary studies. Either race or ethnicity were considered to be proxy measures for systemic socioeconomic or interpersonal bias that an individual may be subject to, which may reflect acquired differences in health status as the product of bias rather than baseline genetic differences. Therefore, these data were considered suitable for synthesis.

3.3 Results

Of 184 included studies, 153 investigated SMM; 28 maternal mortality; 18 ITU admission; and 8 cardiac arrest. The flow diagram is shown in Figure 3.1 and included studies in Table 3.1. There were 36 definitions of SMM but the most common were from the Center for Disease Control (CDC) with blood transfusion (CDC-T; 49%, 75/153) and without blood transfusion (CDC-NT; 37%, 56/153) and the Canadian Perinatal Surveillance System (CPSS) with blood transfusion (CPSS-T; 7%, 11/153). Almost all outcome definitions included the delivery episode (183/184). The most common pattern was only the delivery episode (64%, 117/184) followed by all periods (antenatal through to 42 days postpartum; 15%, 28/184). The exact timing was unclear for some (8%, 15/184). A total of 1,195 associations between prognostic factors and SMM-T were reported/calculated from summary data; 1,188 associations for SMM-RT; and 360 associations for other outcomes.

3.3.1 Risk of bias

There were 15 studies at low, 83 at moderate, and 86 at high risk of bias. Of these, 34 studies at moderate/high risk contributed unadjusted estimates at low risk and 59 studies at high risk contributed unadjusted estimates at moderate risk. The most common contributor to a high risk rating was over-adjustment for variables that may lie on the causal pathway between any reported exposure and an outcome without rationale; for example, adjustment for mode of birth or preterm birth was common. Separately, studies of peripartum interventions commonly introduced potential indication bias or severity bias. The most common contributor to a moderate risk rating was poor reporting of missing data or its inappropriate handling. The full risk of bias assessment is shown in Appendix Table B3.2 and a summary shown in Figure 3.2.

Figure 3-1 PRISMA Flow Diagram

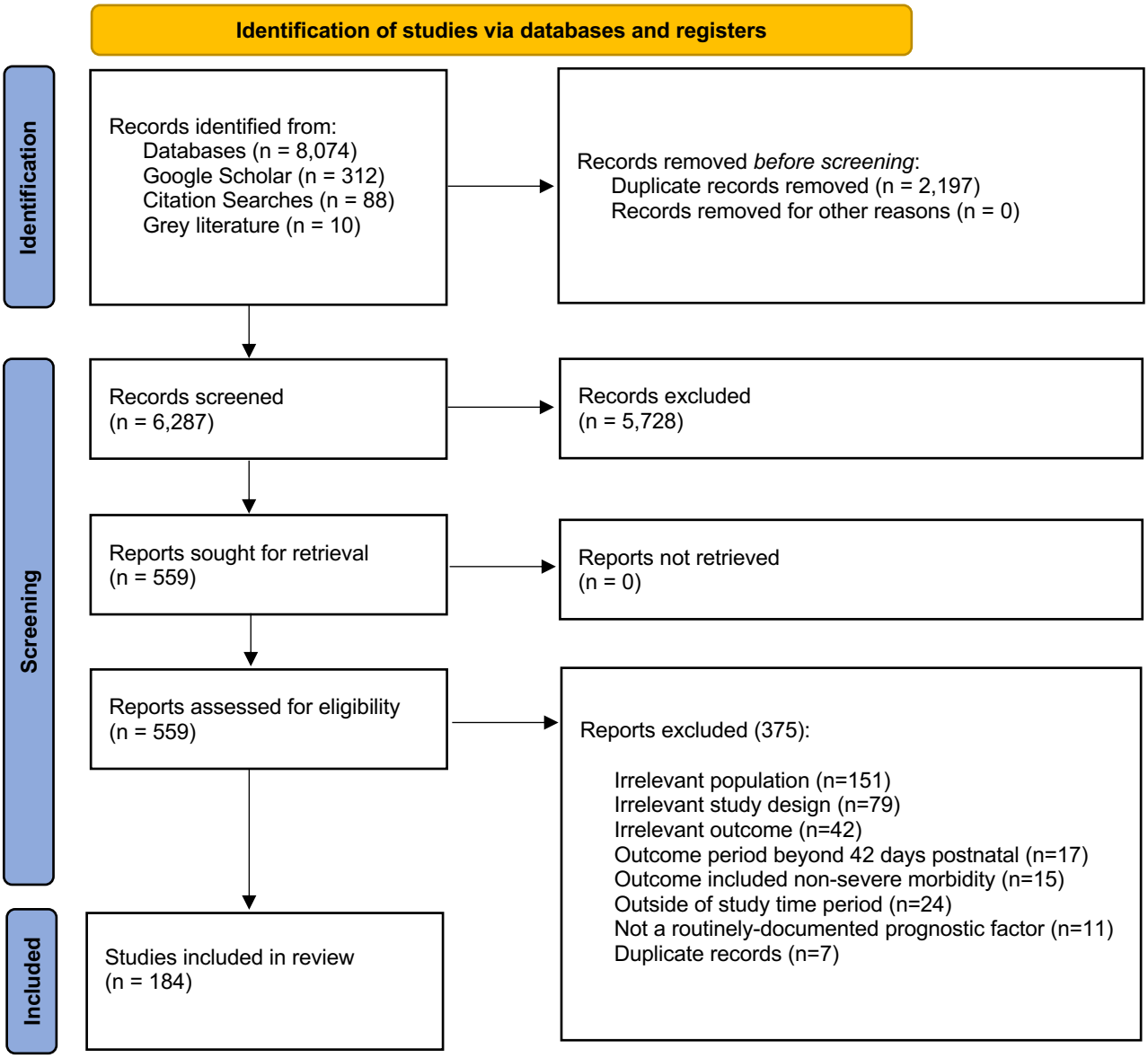


Figure 3-2 Summary of Risk of Bias Assessment for Included Studies

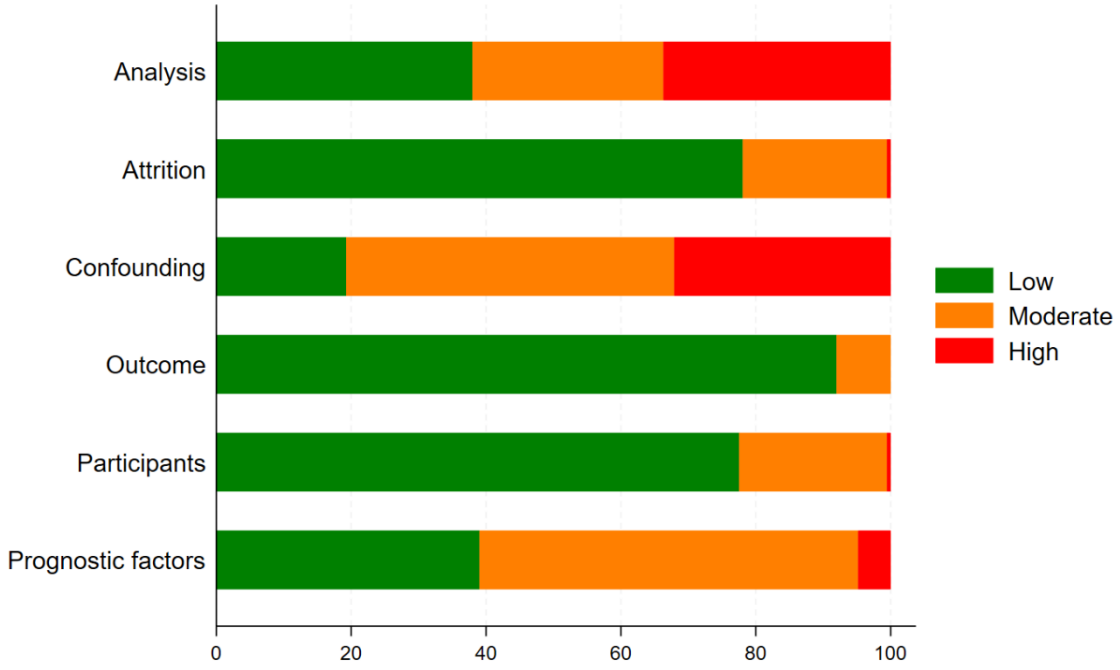


Table 3-1 Included Studies

Study	Setting	Period	Births	Outcome	Time	Main prognostic-factors
Adane 2020(117)	West AUS	2002-15	410,043	SMM	Del.	Ethnicity
Admon 2018(106)	USA	2012-15	2,523,528	SMM	Del.	Ethnicity
Admon 2019(118)	USA	2004-15	9,638,262	SMM	Del.	Substance use
Alexander 2003(119)	Europe	1999-2000	569,397	Death	All	Age, mode of birth
Aoyama 2019(120)	CAN	2004-15	3,162,303	SMM	All	Age
Bae 2021(121)	USA	2007-14	6,911,916	Death	Unclear	Sickle cell
Balayla 2022(122)	USA	2005-14	1,234	Death	All	Mode of birth
Balki 2017(123)	CAN	2002-15	3,568,597	Arrest	Del.	Obstetric morbidity
Bateman 2012(124)	USA	1995-2008	Weighted	Death	Del.	Hypertension
Belanoff 2016(125)	MA, USA	2004-10	458,918	SMM	Del.	Subfertility and ART
Ben-Ayoun 2023(126)	South Israel	2013-18	288	ITU	Del.	Non-specific
Black 2021(127)	USA	2016	390,430	SMM	Del.	Ethnicity, comorbidity, obstetric morbidity
Boulet 2020(128)	GA, USA	2016-18	3,723	SMM	Del-42d	Hypertension, mode of birth
Brown 2011(129)	NC, USA	1994-2005	12,774	SMM	Del-42d	Ethnicity
Brown 2017(130)	Ont, CAN	2002-12	386,706	SMM	Del.	IDD
Brown, C 2020(131)	USA	2016-17	1,480,925	SMM	Del.	Comorbidity
Brown, H 2021(132)	Ont, CAN	2003-18	1,802,704	SMM	Del.	Disability
Campbell 2013(133)	NYC, USA	1995-2003	1,084,862	Death	Del.	Comorbidity, obstetric morbidity
Carr 2022(134)	USA	2012-16	19,473,910	SMM	Del.	Age
Chen 2019(135)	USA	2011-13	8,656,791	SMM	Del.	Gestational weight gain
Chen 2021(136)	USA	2010-14	2,667,325	SMM	Del-42d	Non-specific
Clapp 2022(137)	USA	2016-20	18,420	SMM	Del.	Intrapartum risk-factors
Combier 2020(138)	France	2012-14	2,256,797	Death	Del-42d	Unplanned out of hospital birth
Conrey 2019(139)	OH & MA, USA	2008-13	1,229,564	SMM	Del.	Non-specific
Courchesne 2021(140)	USA	2016-19	1,346	SMM	Del-28d	Substance use
Creanga 2014(141)	USA	2008-10	3,476,392	SMM	Del.	Ethnicity
Cromi 2018(142)	Italy	2005-16	23,453	SMM	Del.	ART
Cudjoe 2023(143)	MD, USA	2015-20	204,140	SMM	Del.	Ethnicity
Dakin 2023(144)	Republic of Ireland	2000-19	162,462	SMM	Unclear	Demographic, lifestyle
Dayan 2018(145)	Ont, CAN	2013-14	114,409	SMM	AN-del.	IVF, BMI
Dayan 2019(146)	Ont, CAN	2006-12	59,099 (matched)	SMM	All	Fertility treatment
Dayan 2021(147)	Ont, CAN	2006-14	634,290	SMM	All	Non-specific
Decker 2021(148)	USA	2015-17	8,174,853	SMM	Del.	Epilepsy
Denoble 2022(149)	USA	2015-19	8,004,184	SMM	Del.	Cardiac disease
van Dillen	NL	2004-06	355,841	SMM	Unclear	Mode of birth

Study	Setting	Period	Births	Outcome	Time	Main prognostic-factors
2010(150)						
Dinsmoor 2022(151)	USA	2008-11	52,162	SMM, death	Del.	BMI
Diop 2022(152)	MA, USA	1998-2018	1,136,415	SMM	Del.	Ethnicity
Donoso 2003	Chile	1999	Unspecified	Death	All	Age
Donoso 2014	Chile	2005-10	1,452,052	Death	All	Age
Du 2023(153)	AR, USA	2013-16	72,183	SMM	Del-42d	Comorbidity index
Dzakpasu 2020(154)	CAN	2012-16	2,843,395	SMM	Del.	Non-specific
Early 2023(155)	USA	2021-22	5,401,899	SMM	Del.	Sickle cell disease, race
Eslier 2022(156)	France	2010-12	9,599	SMM	All	Immigration status
Fernandez 2011(157)	Spain	1999-2006	665	Death	All	Immigration status
Fitzpatrick 2017(158)	UK	2013-14	687	ITU	All	Age
Frederiksen 2017(159)	IA, USA	2009-14	196,788	SMM	Del.	Age
Freese 2020a(160)	PA, USA	2003-12	86,260	SMM	Del.	Non-specific
Freese 2020b(161)	PA, USA	2003-12	84,241	SMM	Del.	Gestational weight gain
Frey 2022(162)	OH, USA	2012-17	347,497	SMM	Del-42d	BMI
Friedman 2022(163)	USA	2000-18	15,213,024	SMM	Del.	Asthma
Garg 2022(164)	WA, USA	2007-14	407,808	SMM	Del.	Ethnic group
Gibson 2017(165)	WI, USA	2000-14	995,179	SMM	Del.	Non-specific
Gleason 2021(166)	USA	2002-08	223,385	SMM	Del.	Disability
Grobman 2014(167)	USA	2008-11	115,495	SMM	Del.	Non-specific
Guglielminotti 2019(168)	NY, USA	2013-14	403,116	SMM	Del.	Non-specific
Guignard 2021(169)	France	2012-13	6,191	SMM	All	Gestational anaemia
Gyamfi-Bannerman 2022(170)	USA	2008-14	2,748,784	SMM, death	Del.	Epilepsy
Ha 2023(171)	Unclear, USA	2011-20	17,493	SMM – del.	Del.	Sickle cell disease
Hage Diab 2022(172)	USA	2002-8	199,611	SMM	Unclear	Small for gestational age
Hailu 2022(173)	CA, USA	1997-2017	9,806,406	SMM	Del.	Race/ethnicity
van Hanegem 2011(174)	NL	2004-06	373,533	SMM	Del.	Asylum seeker status
Hansen 2022(175)	KY, USA	2017	48,608	SMM	Del.	Rural residence
Harden 2022(176)	SC, USA	1999-2017	860,535	SMM	Del.	Spatial cluster
Harrison 2021(177)	USA	2002-08	166,566	SMM	Unclear	Anaemia
Hayashi 2012(178)	Japan	2001-05	242,715	ITU, death	Unclear	Fertility treatment
Hitti 2018(179)	WA, USA	2013-17	7,025	SMM	Del.	Hypertensive disease
Horner-Johnson 2022(180)	CA, USA	2000-12	5,787,090	SMM	Del.	Disability
Howell 2016 A(181)	NYC, USA	2011-13	183,049	SMM	Del.	Race/ethnicity

Study	Setting	Period	Births	Outcome	Time	Main prognostic-factors
Howell 2016 B(182)	USA	2010-11	942,622	SMM	Del.	Race
Howell 2017(183)	NYC, USA	2011-13	216,126	SMM	Del.	Ethnicity
Howell 2020(184)	NY, USA	2010-14	591,455	SMM	Del.	Race/ethnicity; insurance
Howland 2019(185)	NYC, USA	2008-12	588,232	SMM	Del.	Race/ethnicity
Huang 2023(186)	USA	2016-18	539,950	SMM	Del.	Ethnicity, housing insecurity
Huennekens 2020(187)	IL, USA	2016-19	42,681	SMM	Del.	Non-specific
Huisman 2013(188)	NL	2004-06	371,021	SMM	All	Non-specific
Jarlenski 2020(189)	USA	2003-16	Weighted	SMM	Del.	Substance use disorder
Jeffers 2023(190)	USA	2008-11	234,917	SMM	Del.	Small-area inequality
Joseph 2010(191)	CAN	2003-07	1,336,356	SMM	Del.	Non-specific
Karamlou 2011(192)	USA	1998-2007	Weighted	Death	Del.	Congenital cardiac disease
Kilpatrick 2016(193)	CA, USA	2012-13	67,468	SMM	Del.	Gestational age
Knight 2009(194)	UK	2005-06	1,913	SMM	All	Ethnicity
Knight 2020(195)	UK	2009-17	7,001,210	Death	All	Ethnicity
Korb 2019(196)	France	2012-13	4,908	SMM	Del-42d	Age, mode of birth
Kozhimannil 2019(197)	USA	2007-15	6,793,342	SMM	Del.	Rurality
Kozhimannil 2020(198)	USA	2012-15	1,417,500	SMM	Del.	Ethnicity, rurality
Kramer 2023(199)	GA, USA	2009-20	1,172,752	SMM	Del.	Non-specific
Kuklina 2011(200)	USA	1995-2006	Weighted	SMM	Del.	Chronic cardiac disease
Lazariu 2017(201)	NY, USA	2008-13	1,352,600	SMM	Del.	Non-specific
Le Ray 2019(202)	France	2012-13	6,191	SMM	All	IVF
Leonard 2019A(203)	CA, USA	1997-2014	8,252,025	SMM	Del.	Race/ethnicity
Leonard 2019B(204)	CA, USA	2007-14	3,556,205	SMM	Del.	Mode of birth
Leonard 2020A(205)	CA, USA	2007-12	2,650,182	SMM	Del-42d	BMI, gestational weight gain
Leonard 2020B(206)	CA, USA	2016-17	919,546	SMM	Del.	Prediction model
Leonard 2022(207)	CA, USA	2011-17	3,309,554	SMM	Del.	Race/ethnicity, comorbidity
Lewkowitz 2019(208)	FL, USA	2005-6	1,362,567	SMM	Del.	Stillbirth
Liese 2019(209)	USA	2002-14	Weighted	SMM	AN, Del., 42d	Race/ethnicity
Linard 2018(210)	France	2010-12	9,117	SMM	AN-del.	Antenatal care pattern
Lindquist 2013(211)	UK	2005-10	3,400	SMM	All	Socioeconomic
Lindquist 2015A(212)	Victoria, AUS	2006-08	211,060	SMM	Del.	Non-specific
Lindquist 2015B(213)	AUS	Unclear	1,443	SMM	Del-10d	Socioeconomic
Lipkind 2019(214)	AUS, ENG, USA	2008-13	516,781	SMM	Del.	Non-specific

Study	Setting	Period	Births	Outcome	Time	Main prognostic-factors
Lisonkova 2014(215)	WA, USA	2000-08	670,120	SMM	Del.	Pre-eclampsia
Lisonkova 2016(216)	BC, CAN	2005-10	256,220	SMM	Del.	Rurality
Lisonkova 2017A(217)	WA, USA	2003-13	828,269	SMM	Del.	Age
Lisonkova 2017B(218)	WA, USA	2004-13	743,639	SMM	Del.	BMI
Liu 2019(219)	NY, USA	2011-13	244,854	SMM	Del.	Race/ethnicity
Liu 2020(220)	Sweden	2000-14	1,539,510	SMM	Del.	Residency status
Luke 2019(221)	USA	2004-13	1,477,522	ITU	Del.	Subfertility
Luke 2021(222)	USA	2012-17	4,494,089	SMM	Del.	Race, rurality
Lutomski 2012(223)	Rep. of Ireland	2005-09	330,955	SMM	Del.	Non-specific
Lyndon 2012(224)	CA, USA	2005-07	1,572,909	SMM	Del.	Non-specific
Lyndon 2015(225)	CA, USA	2005-07	1,475,593	SMM	Del.	Time/day of birth
Macdonald 2015(226)	USA	2007-11	4,190,599	SMM, death	Del.	Epilepsy
Madar 2019(227)	France	2012-13	6,150	SMM	All	Twin pregnancy
Main 2020(228)	CA, USA	2007-14	3,647,427	SMM	Del.	Comorbidity
Malhamé 2021(229)	RI, USA	2007-17	80,996	SMM	Del.	Prediction model
Männistö 2013(230)	USA	2002-08	223,512	ITU	Unclear	Thyroid disease
Martin 2016(231)	USA	2008-12	1,016,618	SMM	Del-42d	ART
Masters 2018(232)	OH, USA	2006-12	999,437	ITU	Del.	BMI
Masterson 2022(233)	Scotland	2005-18	762,918	SMM	All	Non-specific
Matas 2021(234)	USA	2016-17	6,193,852	NA	Del.	SMM
Matsuo 2022(235)	USA	2016-19	Weighted	SMM, death	Del.	Cancer
McKinley 2021(236)	USA	2010-14	15,658,650	SMM	Del.	Hospital-level
Meeker 2021(237)	PA, USA	2010-17	63,334	SMM	Del.	Non-specific
Mhyre 2011(238)	USA	2003-06	3,463,327	SMM	Del.	Maternal comorbidity
Mhyre 2014(239)	USA	1998-2011	Weighted	Cardiac arrest	Del.	Non-specific
Minkauskiene 2006(240)	Lithuania	2003-04	13,399	SMM	Any	Non-specific
Mitra 2021(241)	USA	2004-17	26,592	SMM	Del.	IDD
Montori 2021(242)	Spain	2007-18	27,455	ITU	Unclear	Age
Mooney 2022(243)	USA	2016-18	98,922	SMM	Del.	Non-specific
Mujahid 2021(244)	CA, USA	2007-12	3,010,525	SMM	Del.	Race and ethnic group
Mujahid 2023(245)	CA, USA	1997-2018	10,384,976	SMM	Del.	Deprivation
Murugappan 2020(246)	USA	2003-15	545,353	SMM	Del-42d	Fertility status
Nagata 2019(247)	Japan	2011-14	96,860	ITU	Unclear	Fertility treatment
Nair 2014(105)	UK	2005-13	5,063	SMM	All	Ethnic group
Nair 2016(248)	UK	2009-13	1,899	Death	All	Non-specific
Nam 2022(249)	S. Korea	2003-18	6,421,091	SMM	Unclear	Non-specific

Study	Setting	Period	Births	Outcome	Time	Main prognostic-factors
Olive 2005(250)	NSW, AUS	1998-2002	375,970	SMM	Unclear	Placenta praevia
Oot 2021(251)	IL. USA	2016-18	421,426	SMM	Del.	Non-specific
Osei-Poku 2023(252)	MA, USA	2016-20	324,012	SMM	Del.	Opioid use
Ozimek 2016(253)	LA, USA	2012-14	16,323	SMM	Del-30d	Non-specific
Pallasmaa 2008(254)	Finland	1997-2002	110,717	SMM	Del.	Mode of birth
Pallasmaa 2015(255)	Finland	2007-11	292,253	SMM	Del.	Comorbidity
Panelli 2021(256)	CA, USA	2007-1	2,668,442	SMM	Del-42d	Epilepsy
Park 2023(257)	CA, USA	2007-12	3,098,578	SMM	Unclear	Endometriosis
Phillips 2021(258)	PA, USA	2018-19	21,843	SMM	Del.	Prediction model
Phillips 2023(259)	PA, USA	2002-18	152,724	SMM	Del.	Gestational age
Platner 2019(260)	NYC, USA	2008-12	515,148	SMM	Del.	Gestational weight gain
Platner 2021(261)	NYC, USA	2008-12	570,997	SMM	Del.	BMI
Raineau 2022(262)	France	2012-13	4,252	SMM	AN	Non-specific
Ray 2018(263)	Ont, CAN	2002-17	1,953,943	Death	Del-42d	SMM
Ray 2020(264)	Ont, CAN	2007-10	737,393	SMM	All	Haemoglobin
Rezaeiahari 2023(265)	AR, USA	2014-17	77,172	SMM	Del-42d	Race/ethnicity
Rosenbloom 2019(266)	MO, USA	2004-14	19,249	SMM	Del.	Prediction model
Rossi 2019(267)	USA	2012-16	18,716,171	ITU	Unclear	Prediction model
Salahuddin 2020(268)	TX, USA	2011-14	1,434,441	SMM	Del.	Comorbidity index
Sastow 2021(269)	USA	2007-14	6,879,332	SMM	Del.	Race
Schummers 2015(270)	BC, CAN	2004-12	226,958	SMM	Del.	BMI
Selo-Ojeme 2005(271)	London, UK	1993-2003	99	ITU	All	Non-specific
Sheen 2018(272)	USA	2006-15	Weighted	SMM	Del.	Age
Siddiqui 2017(273)	USA	2002-13	Weighted	Death	All	Ethnicity
Siddiqui 2019(274)	France	2012-13	6,191	SMM	All	BMI
Siddiqui 2021(275)	NYC, USA	2010-14	591,455	SMM	Del.	Race/ethnicity, BMI
Snowden 2021(276)	CA, USA	2007-12	3,049,774	SMM	Del.	Methodological
Somerville 2019(277)	MA, USA	1998-2013	1,185,182	SMM	Del.	Comorbidity
Stanhope 2022(278)	GA, USA	2015-21	14,255	SMM	Del-42d	Multimorbidity
Sutton 2020(279)	PA, USA	2015-18	18,162	SMM	Unclear	Blood pressure
Tangel 2019(280)	USA	2007-14	6,872,588	Death	Del.	Race/ethnicity
Tangel 2020(281)	USA	2007-14	6,879,332	SMM	Del.	Race/ethnicity, route of anaesthesia
Thompson 2015(282)	USA	2000-10	12,524,118	SMM, death	Del.	Congenital cardiac disease
Ukah 2019(283)	WA, USA	2004-13	722,839	SMM	Del.	Gestational weight gain
Urquia 2015(284)	AUS, CAN, Denmark	1999-2010	2,322,907	SMM	Del.	Maternal birthplace

Study	Setting	Period	Births	Outcome	Time	Main prognostic-factors
Urquia 2017(285)	Ont, CAN	2002-12	1,252,543	SMM	Del.	Maternal birthplace
Vousden 2021(286)	UK	2016-18	1,099	ITU, SMM	AN-2d	Seasonal influenza
Wagner 2020(287)	USA	2014-17	8,815,877	SMM	Del.	Ethnicity (Asian)
Wahlberg 2013(288)	Sweden	1998-2007	914,474	SMM	Del.	Maternal birthplace
Wall-Wieler 2019(289)	CA, USA	1999-2011	6,459,842	SMM	Del.	Stillbirth
Wanderer 2013(290)	MD, USA	1999-2008	765,598	ITU	All	Non-specific
Wang 2016(291)	CA, USA	2012	6,543	SMM	Unclear	Fertility treatment
Wanigaratne 2015(292)	Ont, CAN	2002-11	1,154,121	SMM	Del.	Migration, HIV
Waterstone 2001(293)	England	1997-98	2,938	SMM	Del-42d	Non-specific
Zanconato 2012(294)	Verona, Italy	2005-09	9,395	SMM	All	Non-specific
Zwart 2008(295)	NL	2004-06	373,573	SMM	All	Non-specific
Zwart 2011(296)	NL	2004-06	358,874	SMM	All	Ethnic group

AUS Australia, CAN Canada, ENG England, NL the Netherlands
MA Massachusetts, GA Georgia, NC North Carolina, Ont. Ontario, NYC New York City, OH Ohio, MD Maryland, AR Arkansas, IA Iowa, PA Pennsylvania, WA Washington state, WI Wisconsin, New York state, KY Kentucky, SC South Carolina, CA California, IL Illinois, FL Florida, BC British Columbia, RI Rhode Island, NSW New South Wales, MO Missouri, TX Texas

AN denotes outcome measurement during the antenatal period prior to the delivery episode.
Del. Denotes outcomes measurement during the delivery episode.
Del-42d denotes outcome measurement during the delivery episode and up to 42 days.
'All' denotes the outcome was measured over the antenatal, delivery, and postpartum periods up to 42 days.

3.3.2 Synthesis of results

The pooled prevalence of SMM-T was 15.2 (95% CI 12.8 to 17.8) and of SMM-RT was 6.8 (95% CI 5.4 to 8.5) per 1,000 births. The most commonly studied exposures were ethnicity, maternal age, individual healthcare coverage, parity, body mass index (BMI), hypertension (HTN), diabetes (DM), and mode of birth. The harvest plots for SMM-T and SMM-RT are shown in Appendix Tables B3.3 and B3.4, respectively. Pooled estimates for prognostic factors for SMM-T are shown in Figure 3.3 and for SMM-RT in Figure 3.4. Overall, there was low heterogeneity for meta-analyses for SMM-T, with median tau^2 0.02 (IQR 0.01-0.045) and low-moderate heterogeneity for meta-analyses for SMM-RT, with median tau^2 0.04 (IQR 0.01-0.09).

Figure 3-3 Prognostic Factors according to Strength and Generalisability for SMM-T

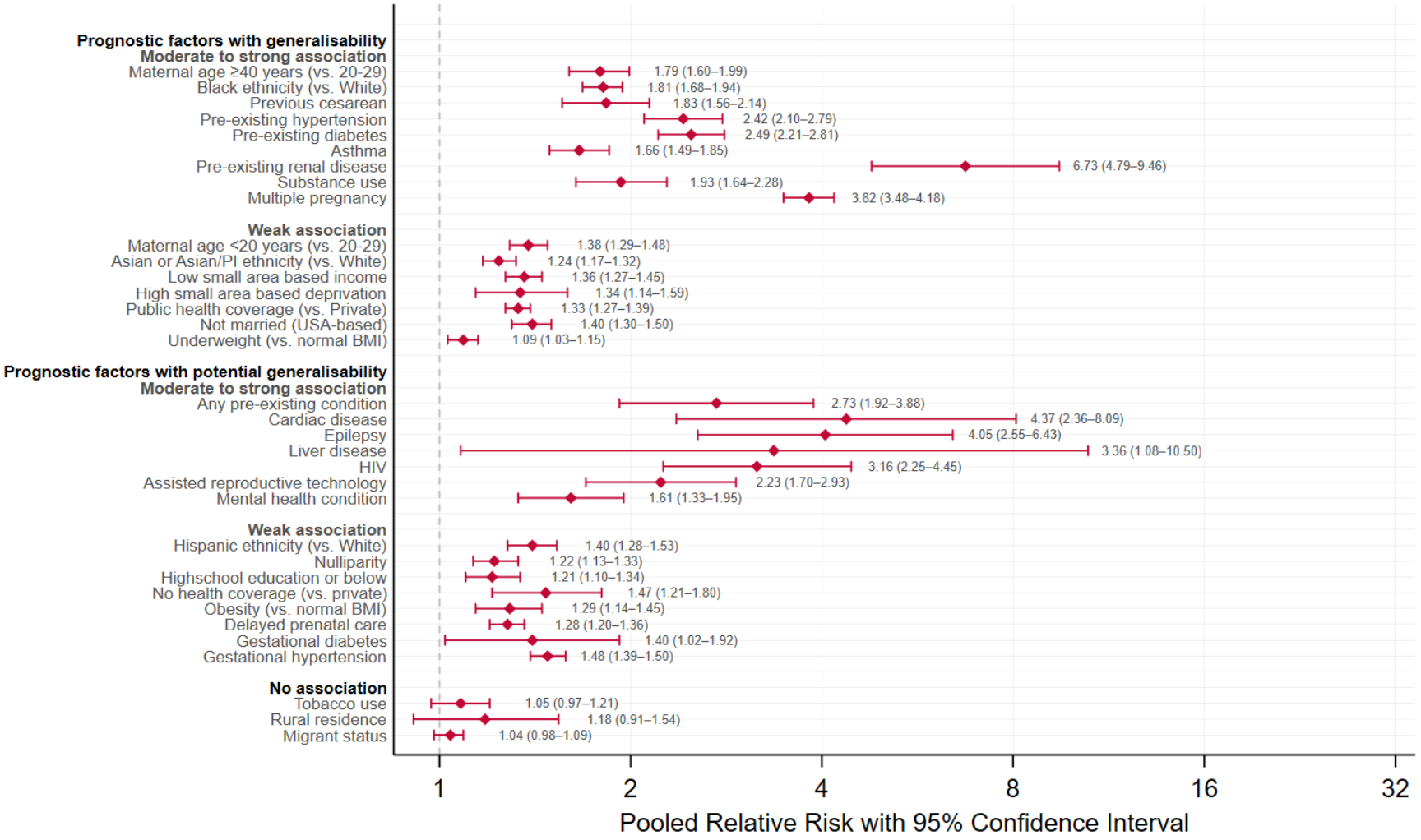
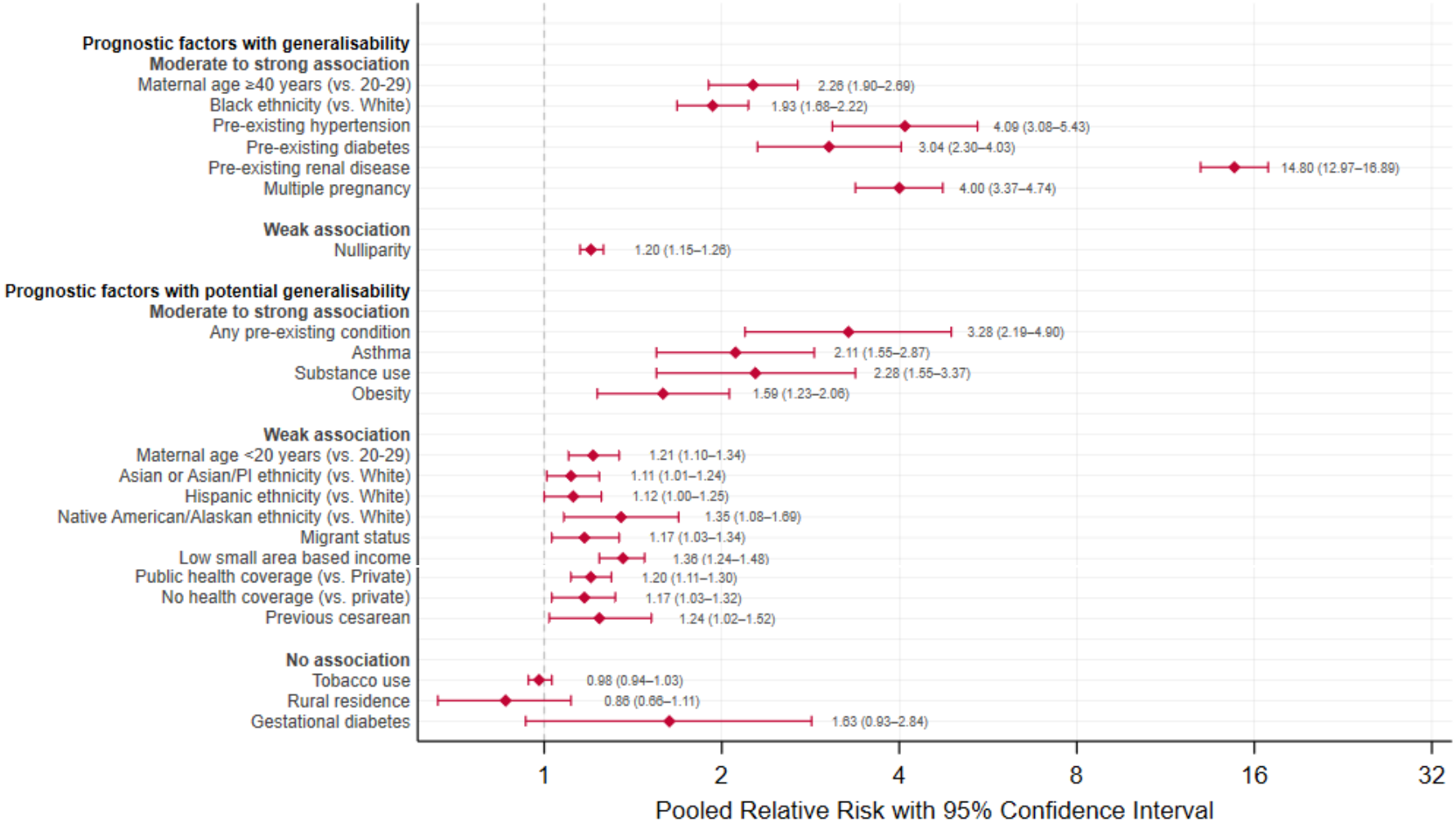


Figure 3-4 Prognostic Factors according to Strength and Generalisability for SMM-RT



Ethnicity

Black ethnicity (vs. White) was associated with both SMM-T (95% of studies, 35/37, unadjusted) and SMM-RT (100%, 28/28, unadjusted); summary estimates RR 1.81 (95% CI 1.68 to 1.94; 95% PI 1.31 to 2.49; 15 studies) and RR 1.85 (95% CI 1.61 to 2.12; 95% PI 1.04 to 3.28; 13 studies), respectively. All adjusted estimates showed this association. Most studies found a positive association between Hispanic/Latina ethnicity (vs. White) and SMM-T (87%, 26/30) and SMM-RT (56%, 14/25; unadjusted); RR 1.40 (95% CI 1.28 to 1.53; 95% PI 0.99 to 1.99; 12 studies) and RR 1.12 (95% CI 0.97 to 1.25; 95% PI 0.72 to 1.73; 11 studies), respectively. The direction of association varied following adjustment. Most studies of Asian ethnicity found a positive unadjusted association with SMM-T (82%, 14/17) and SMM-RT (72%, 13/18); RR 1.24 (95% CI 1.17 to 1.32; 95% PI 1.00 to 1.55; 10 studies) and RR 1.15 (95% CI 1.01 to 1.31; 95% PI 0.74 to 1.80; 7 studies), respectively, consistent after adjustment for demographic and socioeconomic as well as lifestyle and comorbidity variables but not peripartum exposures. There was moderate evidence for Native American or Alaskan ethnicity and SMM; all studies (8/8, unadjusted) found a positive association with SMM-T (vs. White), and a majority (75%, 6/8, unadjusted) for SMM-RT. The pooled estimate for SMM-RT was RR 1.35 (95% CI 1.08 to 1.69; 95% PI 0.61 to 3.03).

Immigration

There was no association between migrant status overall and SMM-T, RR 1.04 (95% CI 0.98 to 1.09; 95% PI 0.88, 1.23; 7 studies), but there was an association with SMM-RT, RR 1.17 (95% CI 1.03 to 1.34; 95% PI 0.62 to 2.20). For both outcomes, risk differed according to the type of immigrant and region of origin. Studies at low risk of bias identified increased risk among immigrants with refugee status(292), among those from the Caribbean and Sub-Saharan Africa, as well as 'East or Southeast Asia or the Pacific'(285), unadjusted. Conversely, immigration from 'European or Western' countries or 'South Asia' or the 'Middle East' appeared to be protective for SMM-T, in a multi-national study(284). Fewer studies considered the association between immigration and SMM-RT but

prognostic factors identified included being a 'non-Western' immigrant and having asylum-seeker status (same population)(174). One study with an unadjusted estimate at low risk of bias identified no association between immigrant status(207) and SMM-RT and another found an increased risk of SMM-RT(220). Estimates from different studies at moderate risk of bias supported increased risk among immigrants from Africa, the 'Middle East or Asia'(233), the Caribbean(147), and Sub-Saharan Africa(147, 274), across different settings.

Maternal age

Most studies investigated and identified a U-shaped association between maternal age and SMM-T (68%, 25/37, unadjusted) but a minority with SMM-RT (39%, 13/33, unadjusted). When compared individually, both age ≥40 years or below 20 years (both vs. 20-29 years) were associated with SMM. The summary estimate for age ≥40 years (vs. 20-29) was RR 1.79 (95% CI 1.60 to 1.99; 95% PI 1.12 to 1.99; 15 studies) for SMM-T and RR 2.26 (95% CI 1.90 to 2.67; 95% PI 1.12 to 4.57; 13 studies) for SMM-RT. The association remained across all patterns of adjustment. For age <20 years (vs. 20-29) and SMM-T, RR 1.38 (95% CI 1.29, 1.48; 95% PI 1.03 to 1.46), and for SMM-RT, RR 1.21 (95% CI 1.10 to 2.34; 95% PI 0.83 to 1.34).

Socioeconomic prognostic factors

Socioeconomic factors were weakly associated with SMM with evidence for the generalisability of small-area income, small-area deprivation and marital status. The summary estimates were RR 1.21 (95% CI 1.10 to 1.34; 95% PI 0.95 to 1.72; 7 studies) for high school education or below (vs. higher); RR 1.36 (95% CI 1.27 to 1.45; 95% PI 1.04 to 1.45; 5 studies) for lowest quantile of small-area household income (vs. all other); and RR 1.24 (95% CI 1.22 to 1.26; 95% PI 1.19, 1.28; 4 studies) for highest (vs. lowest) quantile of deprivation. The summary estimates for SMM-RT were RR 1.05 (95% CI 0.98 to 1.13; 95% PI 0.82 to 1.36; 5 studies) for high school education or below (vs. higher) and RR 1.36 (95% CI 1.24 to 1.48; 95% PI 0.47 to 1.48; 3 studies) for lowest quantile of small-area household

income (vs. all other). There was also strong evidence for the association between small-area deprivation (75%, 3/4, unadjusted) and SMM-RT. Across all of these exposures, a positive association was found following adjustment.

Additional socioeconomic prognostic factors included publicly-funded individual healthcare 'coverage', (vs. private insurance), SMM-T RR 1.33 (95% CI 1.27 to 1.39; 95% PI 1.10 to 1.61; 14 studies), SMM-RT RR 1.20 (95% CI 1.11 to 1.30; 95% PI 0.91 to 1.58; 9 studies) and not being married (vs. married), SMM-T RR 1.40 (95% CI 1.30 to 1.50; 95% PI 0.12 to 1.74; 6 studies; USA subgroup). No association was found with marital status outside the USA for either SMM-T(212, 223) or SMM-RT(274) (233).

Rurality

Rural (vs. urban) residence was not associated with either SMM-T, RR 1.18 (95% CI 0.91 to 1.54; 95% PI 0.43 to 3.22; 9 studies), or SMM-RT, RR 0.86 (95% CI 0.66 to 1.11; 95% PI 0.33 to 2.19) although absolute heterogeneity was high. When rural or urban residence were compared with intermediate groups, a U-shape(131, 222) (199); inverted U-shape(153); and negative associations(168) were found in the USA whereas all three Canadian studies showed a positive, mild association between rural (vs. intermediate) and SMM-T. There was moderate evidence that large metropolitan (vs. small-medium metropolitan or small city) was associated with SMM-RT but inconclusive (highly variable) evidence for SMM-T and for other comparisons, shown in Appendix Tables B3.3 and B3.4.

Lifestyle prognostic factors

All studies (9/9, unadjusted) that used standard WHO BMI categories found overweight and obesity were associated with SMM-T, 3 of which also found underweight and SMM-T to be associated: summary estimates for obesity (vs. not obese) and underweight (vs. normal BMI) and SMM-T were RR 1.29 (95% CI 1.14 to 1.45; 95% PI 0.83 to 1.99; 9 studies) and RR 1.09 (95% CI 1.03 to 1.15; 95% PI

0.90 to 1.32; 5 studies), respectively. Most found obesity (82%, 9/11, unadjusted), RR 1.57 (95% CI 1.42 to 1.73; 95% PI 0.50 to 4.88; 3 studies), and a minority overweight (45% 5/11, unadjusted) to be associated with SMM-RT. None (0/11, unadjusted) found an association between underweight (vs. normal) and SMM-RT. There was moderate evidence for both low and high gestational weight gain and SMM-T.

Half of studies found a positive association (50%, 5/10, unadjusted) between smoking and SMM-T. Most (73%, 8/11, unadjusted) found no association with SMM-RT but 4 found a negative association. The summary estimates for SMM-T and SMM-RT were RR 1.08 (95% CI 0.97 to 1.21; 95% PI 0.74 to 1.59; 5 studies) and RR 0.99 (95% CI 0.94 to 1.03; 95% PI 0.93 to 1.05; 6 studies), respectively. Substance use (any) was associated with both SMM-T, RR 1.93 (95% CI 1.64 to 2.28; 95% PI 1.07 to 3.50) and SMM-RT, RR 2.28 (95% CI 1.55 to 3.37; PI extremely wide). The full results for BMI, gestational weight change, and subtypes of substance use are shown in Appendix Tables B3.3 and B3.4.

Obstetric history

Nulliparity (vs. parity) was associated with SMM-T (75%, 9/12, unadjusted) and SMM-RT (53%, 9/17, unadjusted) in most studies, with similar pooled associations: RR 1.21 (95% CI 1.11 to 1.33; 95% PI 0.87 to 1.70; 9 studies) and RR 1.18 (95% CI 1.15 to 1.22; 95% PI 1.11 to 1.26; 7 studies), respectively. Nearly all studies found both nulliparity and a parity >1 (vs. parity of 1) to be associated with SMM, shown in Appendix Tables B3.3 and B3.4. Previous caesarean birth was associated with SMM-T (100%, 9/9, unadjusted) and SMM-RT (100%, 10/10, unadjusted): RR 1.83 (95% CI 1.56 to 2.14; 95% PI 1.01 to 3.32; 9 studies) and RR 1.24 (95% CI 1.02 to 1.52; 95% PI 0.49 to 3.16; 4 studies), respectively. Assisted reproductive technology was associated with SMM-T (100%, 7/7, unadjusted), RR 2.23 (95% CI 1.70 to 2.93; 95% PI 0.60 to 8.38; 4 studies) and in all studies for SMM-RT (100%, 5/5, unadjusted; weak evidence).

Pre-existing comorbidities

All individual conditions were associated with SMM-T and almost all with SMM-RT. All 'any pre-existing morbidity' exposures were associated with SMM-T (10/10, unadjusted) and SMM-RT (9/9, unadjusted). There was evidence of generalisability for hypertension, diabetes, asthma and renal disease, with summary estimates for SMM-T of RR 2.42 (95% CI 2.10 to 2.79; PI 95% 1.46 to 3.99); RR 2.49 (95% CI 2.21 to 2.81; 95% PI 1.62 to 3.83); RR 1.66 (95% CI 1.49 to 1.85; 95% PI 1.10 to 2.50) and RR 6.73 (95% CI 4.79 to 9.46; 95% PI 1.28 to 35.28), respectively. Cardiac disease, liver disease, epilepsy and HIV were also associated with SMM-T within the pooled sample: RR 4.37 (95% CI 2.36 to 8.09); RR 3.36 (95% CI 1.08, 10.50); RR 4.79 (95% CI 3.04 to 7.57); and RR 3.16 (95% CI 2.25 to 4.45) but the prediction intervals were extremely wide. For SMM-RT, only hypertension, diabetes, and renal disease had evidence of generalisability: RR 4.09 (95% CI 3.08, 5.43; 95% PI 1.47, 11.39); RR 3.04 (95% CI 2.30, 4.03; 95% PI 1.19, 7.81); and RR 14.80 (95% CI 12.97, 16.89; 95% PI 6.29, 34.84), respectively. There was also strong evidence that disability was associated with both SMM-T and SMM-RT although the strength of association was variable. The full range of comorbidities are shown in Appendix Tables B3.3 and B3.4.

Obstetric conditions and morbidity

Multiple pregnancy was associated with SMM-T in all studies (100%, 19/19, unadjusted), SMM-T RR 3.82 (95% CI 3.48 to 4.18; 95% PI 2.75 to 5.29; 10 studies), and SMM-RT in a majority (95%, 19/20, unadjusted). Gestational diabetes was associated with SMM-T in a minority (29%, 2/7, unadjusted) although these were the largest and only studies at low risk of bias, with RR 1.40 (95% CI 1.02 to 1.92; 95% PI 0.44 to 4.50; 6 studies); and a majority (75%, 6/8, unadjusted) showed a positive association with SMM-RT, with RR 4.00 (95% CI 3.37 to 4.74). A majority showed a positive association between gestational hypertension and either SMM-T (75%, 6/8, unadjusted) or SMM-RT (75%, 3/4, unadjusted). The pooled association between gestational hypertension (confirmed not to include pre-eclampsia) and SMM-T was RR 1.48 (95% CI 1.39 to 1.58; 95% PI 0.98 to 2.24).

Peripartum exposures and interventions

Caesarean birth prior to labour, intrapartum caesarean, and preterm birth (all strong evidence, all strong association) were associated with both SMM-T and SMM-RT, as was induction of labour (strong evidence, variable strength of association). Assisted vaginal birth was associated with SMM-T (strong evidence, moderate association) and with SMM-RT (weak evidence, moderate association). There was moderate evidence that non-cephalic presentation, chorioamnionitis, and stillbirth were associated with both SMM-T and SMM-RT and that abnormal placentation and birth weight <2500g or ≥4000g were associated with SMM-T (weak evidence for SMM-RT).

The forest plots from all meta-analyses are shown in Appendix Figures 3.1-54.

Prognostic factors within ethnic groups

There were 14 studies of either prognostic factors within ethnic groups or of differences between ethnic groups stratified by other prognostic factors. Most prognostic factors did not differ in direction or strength of association between ethnic groups but almost all prognostic factors differed in prevalence across ethnic groups. From single studies, parity ≥3 (vs. parity of 1), RRR 1.15 (95% CI 1.00 to 1.32); intermediate inadequate antenatal care (vs. normal care), RRR 1.34 (95% CI 1.01 to 1.77); and self-pay (vs. private insurance), RRR 2.50 (95% CI 1.41 to 4.43) were stronger prognostic factors in Black women (vs. White). The relative difference between rural and urban residency appeared lower for Black women (vs. White): small metropolitan RRR 0.70 (0.52 to 0.95); micropolitan RRR 0.69 (0.49 to 0.97); rural RRR 0.69 (0.53 to 0.91), (all vs. large metropolitan). The same was true for most deprived quartile of neighbourhood deprivation (vs. all others) with RRR 0.87 (0.77 to 0.98). One study identified educational attainment below high school level and two studies found level of antenatal care to be prognostic factors for SMM among Black women but not among other groups. These results are shown in Appendix Table B3.5.

Maternal mortality, ICU admission, and cardiac arrest

No additional prognostic factors were identified for these outcomes not already identified for SMM. Black ethnicity was associated with ITU admission, cardiac arrest, and maternal mortality. Black African or Black Caribbean ethnicity, Hispanic ethnicity, Asian/Pacific Islander ethnicity, and both immigration (any) and immigration from Africa or the Caribbean were identified as prognostic factors for maternal mortality, all in single studies at low or moderate risk of bias.

3.3.3 Small study and publication bias

There were 13 meta-analyses that included 10 or more studies in which small study and publication bias were investigated. Of these, the funnel plots for maternal age ≥40 years and SMM-T and for multiple pregnancy and SMM-T demonstrated asymmetry, slightly more than would be expected by chance. Neither demonstrated asymmetry in the lower left quadrant (i.e. studies with smaller associations which, if missing, are more indicative of publication bias). For age ≥40 years and SMM-T, the Harbord test provided evidence of asymmetry (p=0.020) but the PET did not (p=0.125). Trim-and-fill imputed one study with a bias-adjusted RR 1.85 compared with an original RR of 1.79 (95% CI 1.60 to 1.99). For multiple pregnancy and SMM-T, the Harbord test provided strong evidence of asymmetry (p=0.009) and the PET was significant (p=0.016). The PEESE bias-adjusted RR was 3.94 (95% CI 3.65, 4.26) compared with an original RR of 3.82 (95% CI 3.48, 4.18). Trim-and-fill did not impute any studies. Overall, there was no evidence that publication bias attenuated the association between maternal age and SMM-T or multiple pregnancy and SMM-T. We note possible small-study effects for multiple pregnancy and SMM-T but consider the estimates to be insensitive to bias. In both cases, the small upwards bias correction did not alter interpretation. The funnel plots are shown in Appendix Figures 3.56-67.

3.4 Discussion

This review of prognostic factors for SMM found strong evidence for a wide range of variables to inform an advanced EWS. Maternal demographic (age, ethnicity, marital status), socioeconomic (individual health insurance/coverage, educational attainment, small-area income and deprivation); obstetric history (parity, previous caesarean birth); comorbidity-related (BMI, pre-existing conditions, use of assisted reproductive technology); and obstetric (gestational hypertension, gestational diabetes) exposures were associated with SMM. The evidence on smoking was inconclusive, and on immigration and rural-urban classification nuanced. The strongest prognostic factors were pre-existing conditions and peripartum interventions; the latter group do not necessarily represent true (prospective) prognostic factors. There was strong and very consistent evidence of health inequality across all high-income settings but few studies considered how prognostic factors related to or interacted with ethnicity. Among studies that did, the prevalence of prognostic factors between ethnic groups differed whereas few differed in the magnitude of association.

Inequalities between ethnic groups for SMM was consistent across settings within high-income countries although the magnitude differed. The categories of 'race' investigated in the majority of studies combined women from a range of potentially very different cultural and migratory backgrounds. Although the exact historical and contemporary socioeconomic processes that contributed to and that perpetuate health inequalities differ between settings(297), women within either these combined groups of ethnicities other than White ethnicities or from individual ethnic groups or than White had a higher rate of SMM-T in the vast majority of studies. Across settings, the association between women who were Black and SMM was moderate to strong. Ethnic inequality was also present within some advantaged socioeconomic groups(280, 281). A smaller majority of studies for Asian and Hispanic ethnicity identified a positive association for SMM-RT compared with

SMM-T and a small number of studies identified a negative (protective) association. Whilst the numbers of events were lower, the summary estimates for both SMM-RT groups did not identify an association. This highlights how the definition of SMM affects the measurement of health inequality. Nevertheless, the aggregation of ethnic groups may mask inequality in individual groups. If transfusion practices were prejudiced (more restrictive) against women from Black, Hispanic, or minority racial/ethnic groups(298), a greater risk among women with SMM-RT may have been observed, compared with SMM-T, but this was not the case overall, although the management of haemorrhage may differ in other ways between ethnic groups that could make transfusion more or less likely. Studies that included 'any transfusion' had a higher period prevalence of SMM. By affecting the mix of cases of SMM, as discussed in Chapter 2, it may detrimentally affect the performance of a modified EWS to predict severe complications unrelated to haemorrhage. Consequently, the use of SMM-T may weaken the ability to address health inequality for these other measures or even mask inequalities for other measures (in the presence of under-transfusion).

Relatively few studies considered prognostic factors within individual ethnic groups or the interaction between other prognostic factors and ethnicity. There was no strong evidence with which to consider any difference in the strength of association between groups, although the degree of antenatal care was identified in two separate studies. In studies that reported the distribution of prognostic factors by ethnicity, women who were Black or Hispanic were socioeconomically disadvantaged, had a higher burden of pre-existing or pregnancy-related medical conditions, and women who were Black in particular had worse access to antenatal care, compared with White women. This may provide a basis for potential interaction between access to antenatal care and ethnic group. In the USA, women who are Black or Hispanic face higher economic barriers to access antenatal care(299) and both disadvantaged and minoritised women have described a range of intersecting structural and interpersonal barriers to care(300) yet groups with a higher prevalence of risk factors may benefit most from receiving that care. Ideally, women would not be selected for

escalation by an EWS based on their ethnic group but would have the same chance of treatment based on the alert produced by their vital signs and individual prognostic factors. Achieving this balance can be difficult(301, 302). Some researchers have advocated for the retention of ethnic group in prediction models, prioritising "fairness in outcome"(301). Critics of "race-based medicine" have identified the need to understand the purpose of including race or ethnicity in clinical prediction models, including how its inclusion might condition the attitudes of healthcare workers or adversely affect the treatment offered to women from individual ethnic groups(302, 303). For the purpose of an advanced EWS, the main requirement is to appropriately recognise prognostic factors within individual ethnic groups to trigger escalation.

Aside from ethnicity, maternal age, previous caesarean birth, pre-existing conditions, and the use of assisted reproductive technologies represented common prognostic factors that moderately-strongly increased the risk of SMM. Obesity was only a weak prognostic factor although healthcare workers may emphasise its importance(304). Parity demonstrated a U-shaped association with SMM with risk increasing before the traditional threshold of 'grand multiparity'(305). Some prognostic factors may not be useful for individual-level prediction. Rural/urban residence does not necessarily capture health status but may simply measure place of birth and peripartum transfusion can be commoner among rural residents(306), potentially due to a delay in definitive treatment. Smoking had an unclear relationship with SMM. Smoking could cause lower birthweight, reducing maternal complications but, equally, smokers at highest risk may experience pregnancy loss or preterm birth prior to later-pregnancy causes of SMM(307) and self-report of smoking could introduce bias. Contrastingly, the effect of smoking on perinatal outcomes is clear(308) and should be considered if smoking is used for prediction, meaning that a model may indicate that a woman is at lower risk of SMM whereas she may be at greater risk of fetal complications that do require intervention. The identified prognostic factors may support a theory-informed modelling approach(309) that reduces the risk of over-fitting(310). Applying these findings may increase the generalisability of clinical

prediction models for the prediction of SMM(311, 312) and strengthen patient benefit. The prognostic factors for which there was highest evidence and which were highly prevalent or strong prognostic factors can be prioritised for extraction and inclusion in a modified EWS. The latter is important where it is important to specify parsimonious models due to a limited sample size.

The handling of confounding was inconsistent across studies and therefore no meta-analyses of adjusted estimates were performed as no studies adjusted for the same set of potential confounders for a given prognostic factor. The associations were reported according to broad patterns of adjustment instead. Adjustment for peripartum interventions (induction of labour, mode of birth) and preterm birth was very common, despite obstetric interventions lying on the causal pathway between distal indications/prognostic factors, which may not be included, and SMM(313) or potentially indicating a more severe form of disease. The modelling strategy and subsequent interpretation of estimates was often unclear. Often relatedly, 'Table 2 fallacy'(314), where a single model is reported without considering the individual pathways between its variables and outcome, was common. Including these peripartum variables in clinical prediction models is problematic because the association between an induction of labour, an assisted vaginal or caesarean birth and SMM may differ based on the underlying indication that is potentially life-threatening(315). If the risk of SMM is assigned to the potentially life-saving intervention because the potentially life-threatening indication is not included in a model, i.e. due to unmeasured confounding by indication or severity, then a model could estimate a higher risk of SMM among all women who have a caesarean birth and may erroneously tend to direct clinical resources towards those women who do not have the same underlying clinical indication. For example, the ability of a caesarean section performed at maternal request in a well woman to predict SMM would not be the same as the ability of a caesarean section performed for severe pre-eclampsia to predict SMM where the indication is not included in the model. Although establishing the causality of risk factors (namely, peripartum interventions) is not necessary, it is necessary to establish that prognostic factors are

prospective and to understand that omitting indication or unmeasured severity could worsen the ability of models to direct clinical resources appropriately. This could exacerbate health inequality due to poorer model performance overall and additionally where the indication or severity differs between ethnic groups.

3.4.1 Strengths and limitations

The strengths of this research included the comprehensive approach to identification of the relevant literature; to risk of bias assessment; and to synthesis of the findings and consideration of how the findings can used. This included a conservative approach to the identification of prognostic factors based on the risk of bias assessment and the replication and consistency of findings across studies. Limitations included diversity and statistical heterogeneity, although mostly low or moderate. Some prognostic factors, such as rural residence, may be context-specific. The timing of outcome definitions also varied. Most studies measured SMM only over the delivery episode whereas some conditions are more likely after discharge. Prediction intervals were reported to guard against over-interpretation. Second, labels of ethnicity, and aggregations of ethnic groups, do not adequately measure the diverse geographical, historical, cultural, and socioeconomic processes that produce acquired differences in health. Nevertheless, categories facilitate the tracking of health inequality and differences were highlighted between more granular categories where these were reported in the literature reviewed. Third, there were methodological limitations within studies that limited synthesis of the findings; in particular, relating to modelling strategy, handling of confounding(313, 314), biases related to peripartum interventions, and transparent reporting. This meant that meta-analyses of adjusted estimates were not possible. It is important to stop thinking of ethnicity as an explanatory risk factor in itself and to think about its relationship with other prognostic factors. This problem is widely acknowledged but is not yet fully addressed in the SMM literature reviewed here. Although directed acyclic graphs can be used to clarify the assumed causal relationships between exposures, confounders and outcomes, this review encompassed a large number of risk factors.

Constructing a single DAG to represent all possible relationships would have been prohibitively complex and of limited interpretive value.

3.5 Conclusion

These prognostic factors may be used as the evidence base to develop prediction models for severe maternal morbidity (thesis objective 2) on which an advanced EWS may be based. Including prognostic factors that are more prevalent within individual ethnic groups at higher risk of severe outcomes could ensure recognition of early complications and therefore facilitate early intervention for women from all ethnic groups. These prognostic factors support the theoretically-informed prediction of SMM to improve the performance, generalisability and equity of clinical prediction models so that advanced EWSs can be developed to reduce health inequalities.

The evidence presented in this chapter related to the epidemiological associations between prognostic factors and outcomes. These can be incorporated into a statistical model predict SMM. However, these associations do not reflect how healthcare workers (HCWs) use information to make decisions in clinical practice or how they integrate clinical information with existing EWSs. Therefore, in the next chapter, how HCWs interpret and apply prognostic factors in practice will be explored as part of understanding how they assess a woman's individual risk and how early warning processes function (thesis objective 3). This may provide complementary insight into why ethnic health inequalities exist in particular and whether early warning processes appear to introduce differences based on a woman's ethnicity (thesis objective 4). In the later stage of this work, these prognostic factors will then be used to understand how differences in performance between ethnic groups could be addressed (thesis objective 7). Prognostic factors for which there was strong evidence and for which there was evidence of generalisability will be selected, including maternal age, pre-existing

hypertension, pre-existing diabetes, pre-existing renal disease, asthma, parity, previous caesarean birth, substance misuse, multiple pregnancy, small-area based deprivation, and body mass index.

4 Chapter IV: Pathways of Recognition, Escalation, and Response and the Reasons for Variation

4.1 Introduction

Defining SMM (thesis objective 1) and identifying prognostic factors (thesis objective 2) enables early warning score (EWSs) to be developed and tested. However, EWSs are complex health interventions(316). How they affect the care of women and how they affect health inequalities cannot be understood solely by modelling SMM and early warning processes (i.e., the broader system that includes subsequent clinical actions following measurement of an EWS). It is important to understand the clinical context in which they are used and how healthcare workers (HCWs) actually use them (thesis objective 3). An EWS is comprised of a system to measure and record the vital signs; a process to convert the vital signs and additional prognostic factors into a score; and a protocol to determine subsequent clinical actions. We do not know how these systems are used by HCWs in clinical practice. For example, confidential enquiries in the UK have identified a range of issues related to EWS processes, including the erroneous use of non-maternity EWSs in maternity(317-319); the inaccessibility of EWSs within electronic systems(317); not recording(320) or mis-documenting the vital signs(319, 320); and non-escalation(320, 321) or escalation in an untimely manner(322, 323). Crucially, the recognition of early warning signs does not necessarily lead to appropriate intervention(317, 320) meaning that these safety systems, whose aim is to prevent clinical deterioration, may not function for all women(324). These are multi-stage processes dependent on HCW's decisions, actions, and communications. Across this process, there may be both positive or negative adaptive behaviours that can be identified(325). These processes may also be susceptible to ethnic biases, which should be explored to inform the development of an advanced EWS (thesis objective 4).

The aim of the work in this chapter was to describe and understand the reasons for variation in how warning signs are recognised and how EWSs are used and responded to (thesis objective 3), including how potential variation may affect women from different ethnic groups (thesis objective 4). The research questions were:

1. What are HCWs beliefs regarding EWSs?
2. How do HCWs use EWSs and their associated protocols in practice?
3. What are the reasons for deviation from EWS protocols?
4. Does the use of EWSs, the recognition of warning signs, or their escalation differ between women from different ethnic groups?

The rationale for this approach was that describing pathways of recognition, escalation, and response to early warning signals (scores, symptoms, or other clinical signs) may identify positive behaviours or weaknesses that can strengthen the development of an advanced EWS. This work will identify how EWSs could better support HCWs to provide equitable early intervention and how EWSs could be made robust to unintended mechanisms of use in clinical practice.

4.2 Methodology

This was a qualitative study, based on interviews with HCWs and analysis of maternity records of women who experienced severe complications. The use of maternity records allowed a naturalistic approach to understanding early warning as documented by HCWs at the point of care, without introducing the risk of researcher effects from direct observation(326). Interviews provided an understanding of the individual perspectives and stories of HCWs on early warning in depth, and ensured that disclosures regarding adaptations to protocols or perspectives on ethnic groups or biases remained confidential. The research used an interpretive approach to understanding

participant's perspectives, within a subtle realist framework(31), as outlined in Chapter 1. This recognises the co-constructed nature of knowledge and the influence that social and cultural context has on its creation. This means that, when thinking about what represents credible knowledge in the context of early recognition, this research recognised that subjective interpretation of clinical events, tools and processes were integrated into a revisable model with implications for the development of new safety systems. This perspective extended both to the reported experiences of HCWs as situated in their clinical environment and culture, and also to the creation of the interview data. Multiple interpretations of healthcare interactions existed, informed by a HCW's role, experiences, social context, and environment. This work was guided by the belief that a thematic analysis(327) of HCW's reported experiences and views and maternity documentation, treated reflexively, produced actionable insights(33) into how early warning signs are recognised and responded to in maternity services. An applied approach was taken, such that thematic analysis was carried out reflexively without adopting the philosophical commitments of Braun and Clarke's more recent 'reflexive thematic analysis'(34, 328).

4.3 Methods

4.3.1 Data collection

Medical records of women who experienced severe complications

A purposive sample of 38 women was selected from those included in the MBRRACE-UK systematic case-based reviews of maternal deaths and of severe complications that occurred between 2013 and 2023(317-319, 322-324, 329). Women were selected from those who had haemorrhage, hypertension, infection and cardiovascular disease (at least 6 from each group) as well as those with thromboembolic disease, neurological complications, and anaesthetic complications (4 from each group). This was to ensure a range of conditions were included because warning signs and how they

are recognised may differ between conditions. Across all conditions, half of women were selected from those who survived SMM and half from those who died, in case the use of EWS differed according to survival. One third of the women were selected from Asian, Black, and other minority ethnic groups. Within condition, survival, and ethnicity subgroups, women were selected using a random number generator from either reviews of severe maternal morbidities for women who survived or from the most recent MBRRACE-UK enquiry for women who died. The medical records of women included all routine documentation from the first booking appointment (the first antenatal contact a woman has with her midwife) until the postnatal period, including documentation from antenatal appointments and clinics, charts of vital signs, entries from acute attendances and inpatient stays, and the results of investigations. Events that occurred in the community, primary care, and non-maternity departments were included so that the analysis reflected all contacts between women and HCWs from her journey through maternity services. Additional documents collected as part of investigations (such as Maternity & Newborn Safety Investigations) and pre-hospital documentation from ambulance services, where available, were included because these often provided additional information on acute care and the timeline of events.

Interviews of healthcare workers in maternity

Data were also collected using semi-structured interviews with midwives, doctors, and midwifery support workers. The interview guide, shown in Appendix Table C4.1, was developed based on the research questions and was informed by the initial descriptive findings from the analysis of medical records. Participants were sampled purposively according to role (midwives, obstetricians, anaesthetists, midwifery support workers), seniority within professional group, ethnic group, and were sought from different hospitals. Participants who worked in the NHS anywhere in the UK were recruited using professional networks (e.g., Royal College of Midwives research website), social media (e.g., 'X'), direct referrals ('snowballing'), and sharing of the study information by professional contacts within closed instant messaging groups and professional 'Facebook' groups. The invitation

email was provided when potential participants made contact, which summarised key study information and contained a link to the Participant Information Sheet (PIS), shown in Appendix Item C4.1 (the PIS for both midwives and doctors is shown). Questions were answered by email and, if contacts were interested in participation, the consent form was provided by email ahead of the scheduled interview. Interviews were offered in person, by telephone, or online (Microsoft Teams). The study details were then reiterated at the time of interview and the consent form was either signed by the participant or signed by the interviewer on their behalf and a copy sent to the participant. Due to a lack of recruitment of midwifery support workers, after reflection on potential barriers for midwifery support workers to participate, this group was provided with compensation for their time in the form of a £25 voucher. The first five interviews were transcribed by the researcher. Subsequent interviews were transcribed by a professional transcriber and checked and extensively corrected by the researcher.

The number of interviews was based on the diversity of the sample and range of clinical situations represented in the data. Data collection was considered potentially complete after a period of model testing, over which new interviews did not provide meaningfully different data and did not further develop, but rather confirmed, the analysis. Additional data collection continued beyond this point with HCWs from specific occupational groups to ensure as diverse a range of perspectives as possible were included. The interviewer had a historical professional relationship with 5 participants, having worked alongside them between 3 and 6 years prior to the interview. A participant identifier was assigned to each participant, comprised of their high-level occupation as midwife (MW), doctor (DR), midwifery support worker (MSW) and the participant number within that specific role, e.g. MW 1.

4.3.2 Data analysis

Descriptive analysis of medical records

Data from the medical records were charted into an Excel spreadsheet in order to manage the large volume of structured and free-text data. Each row represented one early warning 'event' (an abnormal EWS, symptom, or sign), organised by admission and the woman. Columns identified contextual factors, HCW interactions, and processes following the event. Direct quotes from the documents were included in this table. The table was used to identify patterns of events and to develop a map of the recognition, escalation, and response pathway, based on the principles of framework analysis(330). The pathway from events was described using these tabulated data, using counts and percentages. The pathway was further mapped using a process diagram to identify reasons why early warning did not result in appropriate clinical input, investigation, or treatment. Individual examples provided in the text were referenced according to a number for each woman, a number for her individual attendance, and a number of each individual event per attendance, e.g. (1.2.3) represents the third event during the second attendance documented in the first woman's medical record from the sample. Separately a structured table of objective measures of EWS practice (e.g. the presence of EWS charting errors; whether EWSs were documented on admissions and at ward rounds; whether escalation was always responded to), across columns, was used to summarise EWS-related care across individual women's care, per row, which informed an assessment of the quality of EWS-related practice and a subjective assessment of the degree to which EWSs were integrated into clinical practice (high, mixed, or low) based on the clinical experience of the researcher.

Thematic analysis of medical records and interviews

The tabulated data from the medical records was coded using preliminary codes that were developed deductively, based on the clinical processes surrounding EWSs and existing literature.

These codes were refined inductively during the analysis to respond to new information(331). All interviews were listened to at least twice and then the transcripts read during coding. Interviews were re-read at intervals as the analysis developed. Coding of interview transcripts was managed using NVivo software. An initial set of codes from the analysis of medical records were used to code the interview transcripts but was again then developed inductively. Although not a formal research question, differences between professional groups arose during interviews and were considered as themes were developed. Themes were developed through a reflexive interpretation of groups of codes that represented major determinants of EWS function(327), based on codes from both the documented evidence and interview data. These themes were developed sequentially to develop a model of care related to early warning practice. Themes that represented 'inputs' into the model were more descriptive whereas the intermediary and 'outputs'/effects of the model, related to behaviours, were more interpretive. Illustrative quotes were selected to exemplify and support the developed themes, labelled according to the high-level HCW role and the participant number within each group, as described. The description of doctors' roles adopted the terms used by HCWs themselves. These included historical terms that are no longer job titles in use in the NHS, including 'Senior House Officer' (SHO), who are doctors who have between 0-2 years of maternity-specific experience and 'Registrars', who are doctors who have at least 2 years of maternity-specific experience and who are either specialised in or on a specialist maternity-specific training pathway. Additionally, potential targets for the improvement of EWSs that were either directly suggested by HCWs or that were identified indirectly as gaps perceived to worsen early warning were collected separately to the model of early warning practice, based on either evidence form the medical records or from HCWs.

4.3.3 Reflexivity

I maintained a conscious awareness of potential sources of bias when developing the interview guide, communicating with potential participants, and collecting and analysing the data. This

included an awareness of my position as a male researcher from a White British background and a professional background in obstetrics(332). I made notes and diagrams when conducting interviews to support my engagement with the data and to record my immediate reactions to interview data, including informal personal reactions. Research notes were made to support the development of themes, including how personal and professional experiences had the potential to shape their development(328). I used the 'insider' status as a HCW when conducting interviews to try to remove professional barriers and mitigate the potential for social desirability bias. During the interviews, I maintained a reflexive approach, and was careful to confirm my interpretation of participants' views and experiences, asking probing follow-up questions to understand divergent views or experiences, and normalised potentially 'taboo' topics, such as observations or experiences of ethnic biases. I used self-disclosure and permission-giving statements, where appropriate. The impact of positionality is discussed in the strengths and limitations section below.

4.3.4 Ethical approval

Ethical approval for the interviews of HCWs was obtained from the Oxford Central University Research Ethics Committee (reference R80907/RE001), granted 01/05/2024. Permission for the secondary analysis of medical records originally obtained through MBRRACE-UK was sought from the Healthcare Quality Improvement Partnership through an extended output request, which was granted on 25/08/2023.

4.4 Results

4.4.1 Records and participants

The medical records of 38 women were analysed. Of these, 22 (58%) were White, 9 (24%) were Black, 4 (11%) were South Asian, and 3 (8%) were Arab. A total of 28 HCWs were interviewed; 14

(56%) doctors, 10 (40%) midwives, and 4 (14%) midwifery support workers. Of these, 16 (57%) were White, 5 (18%) were Black, 4 (14%) were South Asian, 2 (7%) were Arab, and 1 (4%) did not wish to disclose their ethnic group. The characteristics of the women and HCWs are summarised in Table 4.1.

Table 4-1 Characteristics of Included Women and Healthcare Workers

WOMEN (38)	n	%
Age, years		
<25	5	13
25-29	10	26
30-39	18	47
≥40	5	13
Ethnic group		
Arabic	3	8
Black	9	24
South Asian	4	11
White	22	58
Pre-existing medical condition	22	58
HEALTHCARE WORKERS (28)		
Role		
Consultant Anaesthetist	1	4
Consultant Midwife	1	4
Consultant Obstetrician	5	18
Midwife	9	32
Midwifery Support Worker	4	14
Registrar Anaesthetist	1	4
Registrar Obstetrician	4	14
Senior House Officer	3	11
Ethnic group		
Arabic	2	7
Black	5	18
South Asian	4	14
White	16	57
Prefer not to disclose	1	4

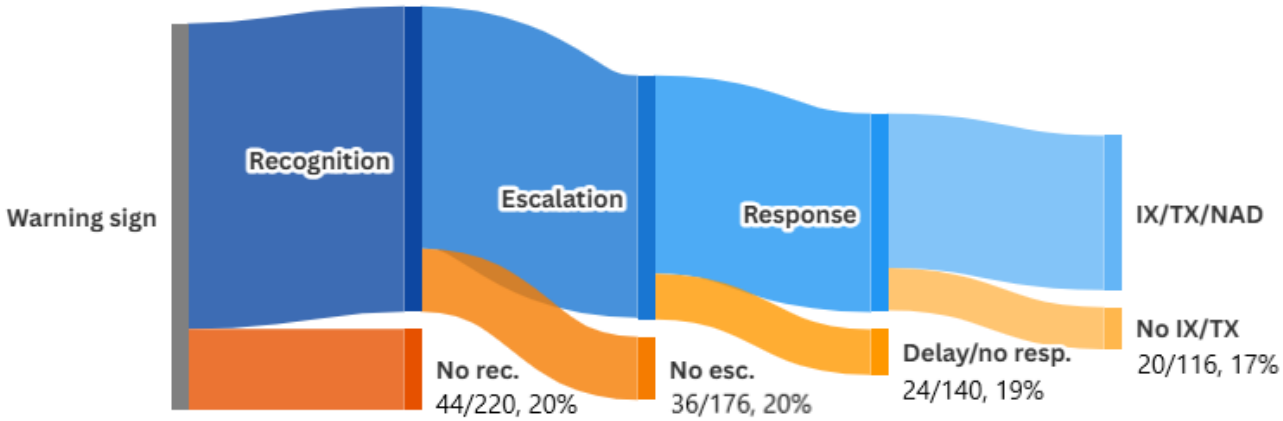
Registrar denotes a doctor with at least two years of maternity-specific experience.
Senior House Officer denotes a doctor with less than two years of maternity-specific experience.

4.4.2 Descriptive findings

There were 280 potential warning events across the medical records of the 38 women. These included both events that led to or that were associated with a severe complication but also potential early warning events that did not lead to complications. Of the 280 events in total, 60 events related to 2 women who were admitted with acute Coronavirus-19 pneumonia. These were excluded as they were unlikely to reflect typical clinical practice. Of the 220 events unrelated to Coronavirus-19 infection, 44 (20%, 44/220) involved the lack of recognition of at least one abnormal vital sign and/or other abnormality, most commonly including tachypnoea, tachycardia, and hypertension. Of these 44 events, 10 included unrecognised abnormalities other than the vital signs; for example, type 1 respiratory failure, ECG abnormalities, and diabetic ketoacidosis. Of the recognised abnormalities, in 36 (20%, 36/176) events escalation did not occur, most commonly for tachypnoea, tachycardia and hypotension. Some of these were severe abnormalities. In a further 7 events, escalation was delayed. Of all escalated events, there was either no response or a significantly delayed response in 26 (19%, 24/140) events, including severe tachypnoea, post-operative hypotension, and hypertension. Of events that were responded to appropriately, appropriate treatment was not provided for 20 (17%, 20/116) events; examples included lack of investigation for severe tachypnoea and severe tachycardia, lack of treatment for hypertension, a missed diagnosis of septic shock, no oxygen or IV fluids in septic shock, advice to drink water with symptomatic and severe post-operative hypotension. The broad pattern of care following an event, represented by the preceding percentages, is shown quantitatively in Figure 4.1. A process map of the handling of warning signs is shown in Figure 4.2. In addition to this overview, 25 events did not elicit a full set of observations, 12 events involved mis-plotted or uninterpretable vital signs (including crowding and invalid values for electronic charts), 5 events involved a HCW not recognising relevant recent information across shift changes, and 19 events involved

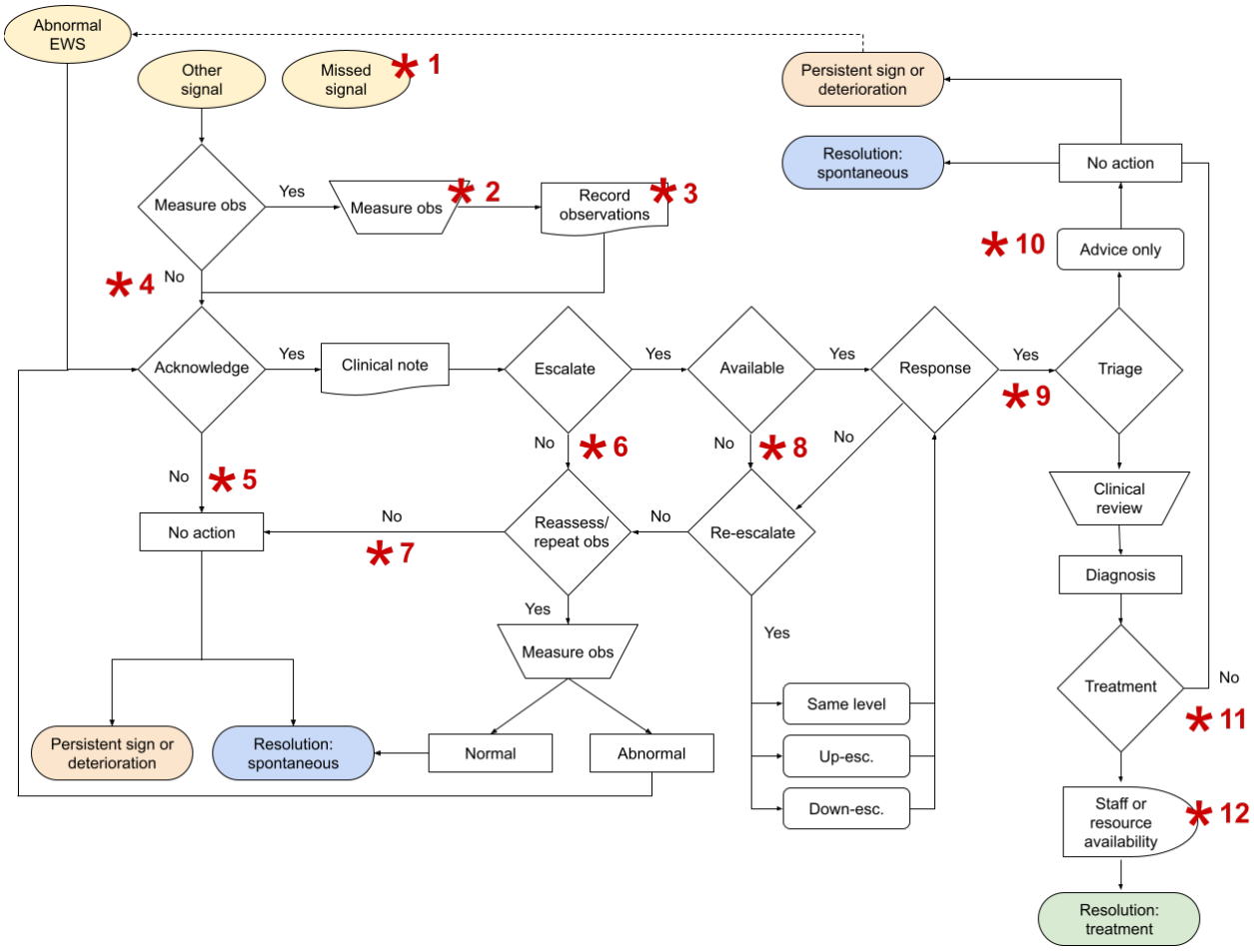
delayed/omitted escalation to a consultant or escalation that did not lead to consultant involvement. The individual events are described in Table 4.2.

Figure 4-1 Sequence of Events Following Initial Warning Sign



Alluvial diagram showing the sequence of events following initial warning signs identified in the medical records of women who experienced severe complications or who died. The grey vertical bar on the left represents all 220 warning signs. The orange pathways represent warning signs that did not progress beyond each stage of the clinical recognition-escalation-response process: no documented recognition; recognition without escalation; escalation without a timely clinical response; response without investigation or treatment where indicated. The height of each vertical bar is proportional to the number of warning signs at each stage. Rec. recognition; esc. escalation; resp. response; ix investigation; tx treatment; NAD indicates that no treatment was indicated.

Figure 4-2 Process Diagram Showing Pathways from Warning Signal to Outcome



EWS Early warning score. 'Other signal' denotes a clinical abnormality that was not an EWS, including abnormalities of individual vital signs, symptoms, or clinical signs.

1. Missed signal: EWS or other sign unacknowledged without documentation or response.
2. Partial set of vital signs only.
3. Erroneous documentation: EWS not calculated, EWS mis-calculated, vital signs mis-plotted, or informally documented on paper without using a chart, proforma, or formal documentation.
4. Omitted vital signs: vital signs not measured in response to new warning sign.
5. Unacknowledged abnormalities: lack of documented awareness of concern without subsequent action.
6. Abnormalities not escalated: abnormality acknowledged but dismissed without escalation or subsequent action.
7. Documented decision to re-measure observations but planned re-measurement delayed/did not occur.
8. Escalation occurred but doctor not available: attempt to escalate abandoned/escalation to more junior doctor.
9. Successful escalation with delay in response.
10. Successful escalation leading to telephone advice but not a clinical review.
11. Clinical review triggered that did not lead to appropriate investigation or treatment.
12. Treatment planned but delayed.

Table 4-2 Summary of early warning events from the maternal medical records

Domain	Behaviour	Woman's ID
Integration of EWS	EWS not calculated	1.1.1, 4.1.1 (nausea and vomiting in early pregnancy); 1.3.1 (suspected wound problem); 3.1.1 (SATs 95%); 7.1.4 (PPH); 8.3.1 (wheeze); 35.1.2 (severe hypertension); 36.1.1 (bleeding in early pregnancy); 8.1.1, 8.2.1 (bleeding with low-lying placenta); 11.1.1 (attendance with suspected PPROM); 11.2.1 (suspected PE); 11.4.1 (confirmed PE returning to maternity triage); 11.5.1 (abdominal pain with PE); 12.1.1 (new pyrexia in previous sepsis); 12.1.16; 28.1.3; 16.x.x (11 episodes of hypertension or severe hypertension); 31.6.1-5 (tachycardia and hypertension)
	Escalation tools left blank	17.1.1; 25.1.1
	Triage form incomplete	16.3.1; 16.4.1
Pre-hospital	Delays	24.2.2 (delay in blue-light ambulance); 30.2.1 (delay in ambulance for pain in early pregnancy due to miscategorisation of call); 32.2.1 (delayed extrication); 33.1.5 (delayed extrication)
	Lack of pre-alert	32.2.1; 28.2.2
	Patient chose not to attend	33.1.1, 35.6.1
	Patient escalation dismissed	33.1.2
	Clinical signs potentially unrecognised	31.7.1 (cough, haemoptysis, abnormal chest x-ray – seen by GP); 35.5.1 (dyspnoea, dizziness and vomiting ascribed to viral illness – seen by PA)
Measurement	Large cuff unavailable	31.1.1
	Partial observations	3.1.1; 4.2.2; 4.3.1; 8.2.1; 8.3.1; 11.1.1; 11.4.1; 11.5.1; 7.3.1; 25.1.1; 25.4.1; 25.5.1
	No observations performed when new clinical sign	4.3.4 (haematemesis); 7.1.9 (bilateral leg swelling); 17.3.1 (suspected DKA); 17.3.3-4, 17.4.2-3 (hyperglycaemia); 17.4.1; 18.1.1 (hypoglycaemia); 21.2.4 (loss of consciousness)
	Planned observations not performed/delayed as too busy	1.2.1; 21.2.1 (documented apology for delay in assessment due to lone working in assessment area)
Recognition	No acknowledgement of abnormal vital sign/EWS	1.1.1 (low grade fever); 1.3.1, 4.3.1, 12.1.8, 12.1.13, 21.2.11-12, 31.6.1-3, 31.6.6-13; 36.1.1, 31.2.10 (tachycardia); 1.3.1, 12.1.5, 12.1.15, 18.1.1, 18.2.3-5, 35.8.1 (tachypnoea); 1.1.1, 3.1.1, 24.1.1 (hypotension); 1.2.1 (significant increase from booking BP); 1.3.1, 15.1.1-

Domain	Behaviour	Woman's ID
		2, 16.5.1, 31.6.1 & 4 & 5, 32.1.1, 35.7.1 (hypertension); 4.1.1, 20.1.7 (desaturation), 5.1.1-2 (bradycardia), 1.1.1, 4.2.2, 4.3.1, 17.4.4 (hypothermia)
	No acknowledgement of other signs	1.1.1 (nephrotic range PCR in early pregnancy, alkalaemia, elevated lactate); 1.3.1 (abnormal clotting); 12.1.2 (type 1 respiratory failure); 32.1.1 (signs of undiagnosed pregnancy, oedema); 35.1.2 (ECG abnormality); 7.1.1 (intraoperative haemorrhage); 17.3.1 (delayed recognition of diabetic ketoacidosis)
	No recognition of trends	2.1.1 (upward heart rate trend with normal EWS); 20.1.8 (hypotension only recognised at SBP <60)
	Abnormalities dismissed	7.1.6 (heavy chest pain dismissed as musculoskeletal); 35.2.1 (presyncope due to "v. muggy weather"; 35.2.1 (presyncope and hypertension due to "bad news"); 12.1.3 (tachypnoea due to normal abdominal pain); 12.1.25 (tachycardia due to walking); 19.1.2 (distension with hypotension due to "big dinner"); 19.1.4 (distension with hypotension and pain due to immediate post-op ileus); 20.1.6 (hypotension due to device error); 25.6.2 (tachycardia due to "feeling tired ++"); 28.1.1 (hypertension due to arm position); 15.1.3 (hypertension due to being "stressed and overwhelmed").
	Abnormalities not linked to previous information	8.2.1 (hypertension not connected to proteinuria and oedema); 31.7.1 (cardiac signs not connected to hypertension); 12.1.11-12 (vital sign abnormalities not connected to preceding severe chest pain); 7.1.6 (chest pain not connected to previous severe tachypnoea); 25.4.1 (medical review did not identify current known DVT)
	Abnormalities potentially misreported	1.3.1 (RR 30 misplotted at 22 and reported as stable); 38.1.3-26 (severe tachypnoea with covid pneumonia reported only as stable); 12.1.8 (tachycardia reported only as stable); 12.1.10 (tachypnoea reported only as stable); 7.1.5 (severe tachypnoea reported only as stable)
	Illegible chart	4.2.1 (inconsistent symbols and overlapping), 6.1.2 (overlapping), 38.1.1(illegible handwriting)
	Vital sign or EWS errors	12.1.6, 12.1.8, 12.1.10 (summary totals too low); 19.1.7 (BP of 100/99).
	Vital signs not plotted	12.1.9, 24.1.1
	Vital signs plotted across multiple charts simultaneously	12.1.14

Domain	Behaviour	Woman's ID
	Normal NEWS vs abnormal MEWS	11.2.1
Escalation	No escalation of abnormal vital sign/EWS	31.6.14, 16.2.1 (hypertension); 16.7.2 (severe hypertension – plan to recheck only but not rechecked); 12.1.7-8 & 21 &24 (mild tachycardia); 7.1.5; 12.1.14 (moderate tachycardia); 12.1.4, 12.1.17-20 & 22 (severe tachypnoea); 12.1.6 (pyrexia on background of sepsis); 19.1.2, 19.1.4 (hypotension with pain and distension); 19.1.13 (hypotension, unable to stand); 19.1.6 (hypotension); 20.1.3-7 (hypotension); 21.2.2 (hypotension, nausea/sweats); 28.1.3-4 (persistent post-op hypotension); 16.7.4 (no re-attempt at escalation for hypertension)
	No escalation of other signs	7.1.5 (severe pain requiring opioids); 12.1.11 (chest pain); 21.2.3-4 (vomiting and loss of consciousness); 21.2.9 ("looks unwell"); 25.2.1 (new varicosities in suspected DVT); 25.7.1 (patient-reported collapse); 27.1.1, 27.2.1, 27.3.1 (multiple episodes of reported and witnessed frequent seizures); 31.5.3 (new oedema with known hypertension); 16.7.4 (persistent headache with known hypertension)
	Delayed escalation	12.1.12 (pyrexia, tachycardia, severe tachypnoea not escalated - reviewed at 1 hour 40 minutes on ward round); 17.4.6 (prolonged hypoglycaemia); 24.2.2 (ambulance call for transfer made 10 minutes after documented recognition of severe complication); 8.1.1 (bleeding with low lying placenta); 16.6.1 (severe hypertension escalated after 45 minutes); 16.7.3 (hypertension escalated after 3 hours); 16.7.8 (plan to repeat blood pressure hourly when hypertensive instead of escalation); 16.7.9 (request for 'stat' antihypertensive from less-experienced clinician rather than escalation for review).
	Consultant not involved	1.3.1 (wound complication in emergency department); 37.1.1-3 (EWS up to 9); 38.1.2 (EWS 8); 12.1.2 (tachypnoea, sepsis); 12.1.12 (transfer to labour ward due to acute illness); 6.1.2 (consultant did not attend for return to theatre/acute PPH following escalation); 6.1.3 (did not attend at second escalation following return to theatre); 7.1.1 (intraoperative PPH with severe hypotension); 16.4.1 (severe hypertension with multiple risk factors and admissions seen by FY2 doctor); 17.3.2 (DKA); 17.4.6 (refusing treatment for severe

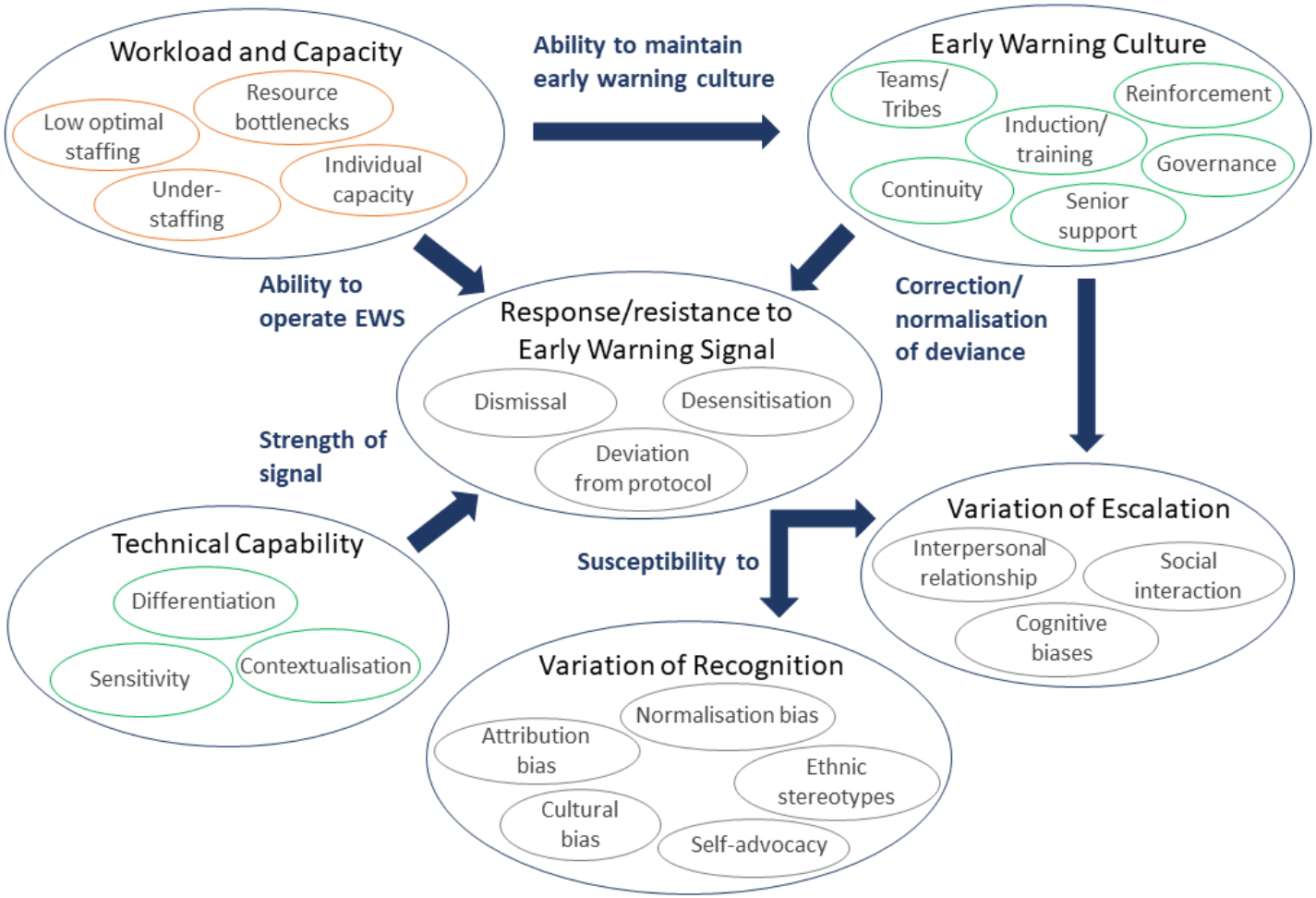
Domain	Behaviour	Woman's ID
		hypoglycaemia); 19.1.14 (severe hypotension); 20.1.2 (no re-escalation to consultant when new concerns after previous decision not to return to theatre); 21.2.5 (persistent hypotension and loss of consciousness not escalated – escalated when shoulder tip pain and confirmed haemoglobin drop); 28.2.4 (septic shock with severely deranged vital signs sequentially seen by several junior and resident doctors); 16.7.10 (first consultant review 7 days after prolonged uncontrolled severe hypertension and preterm caesarean).
	Lack of/delayed escalation into/involvement of maternity service	1.3.1 (wound complication); 35.6.1 (acute asthma); 30.1.1 (vaginal bleeding in early pregnancy)
	Lack of/delayed escalation to/involvement of other teams	12.1.23 (PE untreated for several days until delayed discussion with medical/radiology teams occurred); 7.3.2 (delayed optimal treatment of DKA until discussion with medical/ITU teams occurred).
Response	Absent or delayed response following escalation	4.1.1 ("all busy on [labour ward]"); 4.3.4 (haematemesis); 7.1.7 (senior review >3 hours for abdominal distension following massive haemorrhage) 12.1.1 (new pyrexia and tachypnoea on background of sepsis); 18.2.3 (hypertension – no response – normal on repeat after 1 hour); 19.1.2 (>1 hour following esc for post-op pain and distension); 19.1.4 (registrar review >15 minutes when acutely unwell with severe hypotension); 21.1.1 (>1.5 hours, chest pain radiating to back); 20.1.2 (ongoing 30-minute observations after delay in review by registrar for hypotension) 21.2.5 (>2 hours, registrar for persistent hypotension and collapse with loss of consciousness); 31.4.2 (>2.5 hours for hypertension); 31.5.1 (>4 hours for severe tachycardia and tachypnoea); 8.1.1 (>4 hours for vaginal bleeding and known low-lying placenta); 16.1.1 (>1 hour severe hypertension); 16.2.1 (>3 hours, severe hypertension); 16.6.1 (>1 hour for severe hypertension); 16.7.3 (declined to review postnatally until prolonged period of blood pressure monitoring); 16.7.4 (persistent hypertension for 14 hours without response); 16.7.7 (no response to esc of hypertension). **Covid-related escalation responses** 37.x.x and 38.x.x – extensive number of delays, including delays over 1 hour for EWSs of 9 and 11, delays in review following multiple episodes of desaturation and failed trials of continuous positive airway pressure.

Domain	Behaviour	Woman's ID
Treatment	Delay in response led to delay in urgent investigation or treatment	12.1.15 (oxygen and fluids for sepsis); 12.1.17 (investigation of severe tachypnoea deferred until ward round); 13.1.1 (treatment of PE delayed by 5 hours for a subsequently normal Doppler study); 19.1.4 (investigation and treatment deferred until ward round); 20.1.2 (no treatment after delayed review for hypotension, feeling unwell); 35.3.2 (no change of dose for hypertension); 35.4.1 (no treatment or admission for severe hypertension);
	Delayed appropriate treatment due to delayed involvement of consultant	6.1.4; 12.1.1; 19.1.1; 20.1.12; 37.1.3;
	Delay in treatment due to capacity issues	21.2.8 (>4 hour delay for return to theatre for intra-abdominal haemorrhage due to "urgent/emergency" cases)
	Other delays in treatment	28.2.4 (>1 hour to administer antibiotics for septic shock); 16.3.1 (delay in treatment of severe hypertension); 16.7.1 (delay in treatment of severe hypertension); 28.2.6 (delay as patient did not wish to proceed with treatment); 31.4.2 (no treatment commenced for hypertension); 31.5.1 (no investigation for severe tachycardia or tachypnoea)

4.4.3 Thematic findings – why are EWSs not used as intended?

A model of early warning-related care is shown in Figure 4.3, incorporating six themes: Workload and Capacity (theme 1); Early Warning Culture (theme 2); Capability of EWSs (theme 3); Resistance to Early Warning Signals (theme 4); Variability of Recognition (theme 5); and Variability of Escalation (theme 6).

Figure 4-3 Thematic Analysis of Maternity Documentation and Interviews of Healthcare Workers



The conceptual relationship between themes is shown. Themes 1-3 (Workload and Capacity; Early Warning Culture; Technical Capability) represent the potentially modifiable inputs into the EWS system whereas Themes 3-6 (Resistant to Early Warning Signals; Variation of Recognition; Variation of Escalation) represent the downstream behavioural products of these inputs. Of the modifiable inputs, components that are within the scope of a programme of work to develop and implement an EWS are shown in green and those that are outside of this scope are shown in orange.

Theme 1: workload and capacity

HCWs indicated workload was the major reason for deviation in the early warning pathway with a mismatch between "the staffing and the balance of the workload to support the escalation" (DR 10). This was supported by examples of reasons for delay in the medical records. HCWs described a maternity service under pressure, "within a very depleted health service" (MW 5), and an inability to provide early warning, which "demands a level of staffing and capacity that simply doesn't exist in a lot of hospitals" (DR 7). Under-staffing (planned level of staffing not met), inadequate optimal staffing (planned level of staffing met but perceived to be insufficient), and fluctuations in acuity affected early warning practice. Many midwifery support workers and midwives recognised the benefits of having time and staff to provide individualised care to recognise changes and explore symptoms. Many HCWs stated that improving staffing would improve the quality of early warning. Workload impacted measurement:

> *What staff will do is rush and not do it properly […] through purely trying to juggle too much. So they will skip things like respiratory rate - I'll see that quite often […] it becomes a tick-box instead of your holistic assessment* (MW 10);

the ability to recognise changes:

> *When you work on a ward that is at capacity and you've got staff moving from different areas, there is a lack of appreciation of when people become more and more unwell* (MW 3);

the decision to escalate, "it's not normal but she's not dying, so I won't escalate it because haven't got time" (MW 7); the chance of successful escalation:

> *So you escalate your concerns, the bleep goes off, the registrar [doctor] is in theatre, okay, let's bleep the gynae registrar. The gynae registrar is in gynae theatre, okay, let's bleep the consultant… and actually they're also busy doing an instrumental. Then, so, what then?* (MW 2);

and treatment:

> *Sometimes you don't have that room to [discuss the plan with someone senior]; otherwise, you would have 20 people in the waiting room waiting to be re-reviewed […] and then it blocks up beds […] you just have to make those decisions and just kind of hope that […] I've made the right sensible decision and I just have to keep it moving.* (DR 12)

Doctors recognised the challenge of "properly assess[ing] that patient, particularly if you have to do it remotely" (DR 9) when busy and that "if you're covering multiple clinical areas of patients it can be difficult" (DR 1) or even "overwhelming with the number of calls" when "covering labour ward with triage and postnatal work" (DR 13).

Staffing the delivery suite was a priority whereas postnatal care was regarded as an area of "neglect" that is "always understaffed" to which "the most junior medical staff" are sent (DR 7). "There's a feeling that they don't have the capacity […] to repeat observations as frequently" (DR 6) and that, when vital signs are abnormal "that figure has more importance [on the delivery suite] than it might do on a postnatal ward" (MW 1):

> *The MEOWS score might say, 'get a registrar review within X amount of time' but actually, that rarely happens on the wards outside of delivery.* (MW 3)

Theme 2: early warning culture

Early warning culture represented the practices, norms, and behaviours at the level of the maternity service itself. These patterns were observed across the whole of a maternity service, in women's medical records, or were described as being properties of the systems themselves, by HCWs, rather than the behaviours of individuals. HCWs sometimes highlighted how the constraints on their clinical time, shown in Theme 1, were connected to changes in a service's culture. Culture could therefore be conceptualised as playing an intermediary role, a system behaviour, between the 'input' of clinical time and the output of intervention but there were also a wide range of other aspects of culture that were not wholly dependent on workload and capacity. Some women's medical records showed that EWSs were not measured, vital signs were omitted, and there was no

acknowledgement or escalation of abnormalities, shown in Table 4.2. For many women, this pattern repeated across multiple different attendances and admissions, during which they were cared for by different healthcare professionals within the same service. Across many women's medical documentation, EWSs were "like a language that isn't being used" (DR 6). Two women's records showed well-integrated EWS practice, with regularly recorded and complete vital signs referenced across midwifery notes, handovers, medical reviews, and ward rounds.

Most HCWs perceived that not following protocols was either necessary, tolerable, or the norm. HCWs explained that "people don't necessarily get reviewed according to the [...] escalation policy" (MW 5). Individual examples of deviation apparently became persistent patterns of care: "they're also so busy they're letting these thing slide" (DR 7). This weakens early warning culture "if they see other people not doing it or if they're not used to doing it" (MW 7):

> *It's okay to be tachycardic, it's okay to be tachycardic, it's okay to be tachycardic. We're just going to ignore the yellow* [intermediate level of warning between normal (green) and severe (red)] *or the resps* [respiratory rate] *because we've decided that it's normal even though we know it's not* (DR 7)

Some HCWs described an adversarial relationship between areas: "very 'them and us', even in units: postnatal, antenatal, delivery suite", without a "collective sense of escalation" (MW 3) focussed on the needs of the woman. HCWs being "pulled" from their usual areas due to short staffing was disruptive and could also weaken early warning processes. HCWs who were reliably assigned to a specific role regarded this as a positive factor because "they know exactly how the system works" (MSW 1).

In terms of efforts to maintain early warning practice, one hospital had a systematic programme of EWS audit and feedback whereas others only reviewed early warning-related behaviours during

reviews of adverse events. Multidisciplinary training and 'obstetric drills' training were viewed positively and were opportunities to embed recognition and escalation training. However, several HCWs from all groups had experienced approaches to training that did not meet their needs:

> *Band 5s are being trained by band 5s […] you've not got the really experienced midwives who have lived through these women getting sick to explain why something's important* (MW 10)

> *I wasn't taught how to [measure the blood pressure] properly you know when you have to put the artery signs on, you know, on the inside part of your arm…* (MSW 4)

> *When junior doctors who are rotating start, they will get a very […] rushed induction where there will be thrown lots of facts […] and then you're asked to go and work and be on-call.* (DR 3)

A few HCWs also highlighted how staffing could also impact the ability to conduct both formal training and the day-to-day transfer of knowledge and skills:

> *A lot of our anaesthetic colleagues are brilliant at loads of human factors stuff but we don't have the time to maybe use their expertise for training* (MW 2)

The relationship between the maternity service and wider hospital was deemed important by several HCWs who felt this influenced the use of maternity-specific EWSs on medical wards and emergency areas. Challenges to inter-specialty communication included the baseline health of their populations, i.e. "a lot of [the non-maternity medical team's] patients are scoring that [EWS] on the daily anyway" (MW 7), and the degree of alignment between escalation protocols between specialties but HCWs believed good inter-specialty relationships supported access to medical input when required.

Theme 3: Capability of early warning scores

The capability of early warning scores focusses on the value of the information that they provide to HCWs as well as what kind of response that EWS can reasonably trigger. This was underpinned by what tools actually do at the technical level but also how clinical context may modify their perceived

value in practice. There was often no acknowledgement or action recorded after an abnormal EWS, shown in Table 4.2, and many HCWs relayed the challenge of knowing which scores to act on:

> *It's a fine line […] between knowing […] what is a small deviation and what is […] going to creep up to something more serious* (MW 4);
>
> *You're going to have to filter through a lot of people [with] elevated scores [who] haven't got any disease. I suppose we're talking about predictive values […]* (DR 10)

Many HCWs felt the purpose of EWSs related to early warning, to "notice something [...] at an earlier stage":

> *They're supposed to help you crystallise that decision point - 'now it's a problem' - but they don't work perfectly in the real world.* (DR 7)

Whereas others felt the purpose was to "escalate a deteriorating patient" (DR 3), at a later stage:

> *[P]eople, when they're at capacity and you're on a busy unit, will use it as, you know, 'I want to know is this person alright or are they really sick?'* (MW 3)

Tachycardia and tachypnoea were commonly not escalated, e.g. "obs satisfactory as per [EWS] except resps" (12.1.4). Many HCWs reported EWSs were most helpful for the recognition of sepsis and hypertension, when the abnormality may be related to a diagnosis and course of action: "temperature you can't really excuse – that's why people wait for it" (MW 10). Many HCWs were aware that respiratory rate may be an early indicator of deterioration but some said they were unsure how to act on it.

Doctors reported the importance of knowing the individual parameters that constitute a score, which informs the diagnosis, urgency, immediate actions, delegation, and prioritisation over other women:

> *[T]he value of the score is more in the first responder trying to prioritise when to respond or which person to respond to or who to send to that response*. (DR 10)

Conversely, some midwives could feel “dismissed” (MW 9) when escalation did not lead to a clinical review.

Although EWSs often triggered a medical review, the first-responder may not understand the maternity-specific implication of the abnormality, which is the limit of EWSs’ capability. A few HCWs emphasised that the purpose of EWSs is to get someone to the bedside who can make clinical decisions, not replace that decision-making process.

Recognising early warning signs may be even more challenging in a “generally younger, generally fitter” population (DR 11) among whom EWSs may not “pick up the nuances” because they “compensate physiologically” (DR 8; i.e. that the typical woman in the maternity service is healthy and her body is able to compensate for abnormalities up until the point where they become severe). However, even severe abnormalities were dismissed despite escalation. Conversely, several HCWs believed EWSs are too sensitive in some contexts, e.g. postoperatively or intrapartum:

> *[T]here has got to be a better way of filtering out those women who are genuinely unwell, […] to those women who have maybe been pushing for two hours so yes, they are a bit tachycardic[…]* (MW 4)

and did not account for women’s individual baseline: “the patient is actually fine and that is just their resting vital signs” (DR 13). Several women had relevant risk factors, previous severe symptoms, and complications that HCWs did not acknowledge and that EWSs do not use.

Several HCWs also questioned the reliability of vital signs entered into EWSs, namely respiratory rate, which did not always match women’s respiratory rates on examination. The respiratory is “variable and practitioner-dependent” (DR 2), socially awkward, and time-consuming so may be estimated or omitted, potentially because they “[don’t] understand the significance of it” (MW 10):

> *I do them all the time but [midwives] only expect me to do resp. rate when someone's complaining of a headache or their pulse is high.* (MSW 4)

Theme 4: resistance to early warning signals

Resistance described the tendency of HCWs not to act on signals. Resistance to early warning signals did not necessarily lead to harm and, in light of the constraint of clinical time shown in Theme 1, may represent necessary adaptations to select which women required escalation. However, many HCWs described how resistance to signals may also represent a more systemic lack of confidence in the value of the early warning process, potentially conditioned on clinical time (Theme 1), early warning culture (Theme 2), and the capability of the early warning score (Theme 3).

Inaction or conservative management was common at all stages of the EWS process. Abnormalities may be ignored because:

> *the majority of patients that score at a lower level, they'll probably resolve. They won't have some underlying cause […] whether you get used to that or the balance of probability that you won't have to do anything and maybe people won't see that as a necessarily good use of their limited time[…]* (DR 11)

which may desensitise HCWs:

> *if you get someone who's scoring, like, a three, that's borderline and I think some people kind of think, 'oh, it's only a three, that's quite common now*'. (MW 7)

There were many examples of abnormalities being simplistically ascribed to non-medical causes, e.g. "feeling tired ++", or emotional condition, e.g. "stressed and overwhelmed", and including signs of severe complications, such as abdominal distension with hypotension to "having a big dinner", as shown in Table 4.2. Abnormal vital signs were often repeated as opposed to being acted on. HCWs confirmed "it's quite easy [to say] 'oh but that's because she's in pain'", "she's anxious", "she probably hasn't drunk enough", "recount them" (all MW 1). "It's not automatically like 'yes this is abnormal'" (DR 9).

Resistance to early warning signals extended to the response to escalation. A potentially limited degree of clinical decision making could be applied:

> *Could it be that [the cause of tachycardia is] pain and then I would advise for them to use some pain relief and then call me back? Or if it's that I think it's the temperature, use some antipyretic and call me back? […] if it's that they're tachycardic and their blood pressure is dropping, then obviously I want to go up [...]" (*DR 13*)*

More experienced doctors explained that investigations were not a routine part of understanding potential warning signs further:

> *Thinking about doing an ECG [for tachycardia] and then finding somebody that can do, physically do, an ECG and then interpret an ECG can sometimes be an issue [which changes] your management* [...] *it is almost minimised and managed conservatively because what you actually want to do is not possible […] and kind of crossing fingers and hoping that when you check it again it will be better.* (DR 9)

Most women at the early warning stage will be escalated to the 'SHO' level, who may be "managing unwell people without realising that there's a need to escalate" (DR 2) yet these scores may be the most challenging to interpret as "[i]t takes more mental load, more work, more thought, more time" (DR 9) to respond early on:

> *When they come in with these vague symptoms and you're just like, 'Is this pregnancy related? Is this something I should be worried about?' Is this something that is, you know, is a 'take some paracetamol and go home?'* (DR 12)

Consultants were typically only involved after a severe complication had occurred. Some midwives believed abnormalities should be ameliorated using paracetamol, fluids, or environmental modifications prior to escalation. Several midwives with a shorter length of service felt unprepared to manage medically complex women, highlighting that midwifery training focussed on "empowerment and normality" and was "not […] balanced enough for those really sick women" (MW 10) whereas several midwives with longer service drew attention to differences between midwives who had previous training in nursing ("dual-trained") and those who had not ("direct entry"), highlighting that traditional nursing skills may be perceived as beneficial when

understanding early warning signs. A wide range of examples of multidisciplinary training, high-dependency unit (HDU) training, and clinical assessment skills certification processes for midwives and MSWs were viewed positively.

Theme 5: Variability of Recognition

Whilst the resistance to EWSs appeared to affect the approach to all women, as shown in Theme 4, it was also apparent that recognition of signals could vary between women, including based on their ethnic group. Many HCWs believed EWSs standardised care: "if in doubt, do a full set of obs" (MW 2) but sometimes the characteristics of a specific group was used to disregard a concern, including ethnicity but also women with repeat admissions and women who used drugs. Warning signs were sometimes dismissed because they were deemed normal for a group:

> *I've heard some people say 'oh it's because we look after Bengali women. Their heart rate is a bit higher and that is normal for them'.* (DR 6)
>
> *Sometimes when you do like Afro-Caribbean people, their blood pressure sits a bit high but they always say that's normal because from booking it's always been the same* (MSW 1)

The spectrum of ethnicity-related behaviours included stereotypes, reported by many HCWs, especially in relation to 'pain thresholds':

> *There's a general thing, obviously, women of a South Asian background tend to have a lower pain threshold [...] is it because […] they feel that if they don't say they're in pain they're not going to get a certain level of care [...]?* (DR 8)

Some beliefs could affect women positively or negatively; for example, *"*[Black women] do become pre-eclamptic more quickly" (MW 4), or "have more issues that relate to blood pressure" (MW 10). A few HCWs perceived their service provided proactive care based on ethnicity, "to make sure we're not missing anything" to reduce health inequalities (DR 12).

Several HCWs suspected conscious biases. One MSW related how a Black woman was repeatedly denied pain relief but was then found to be in the second stage of labour:

> *I don't know if it's conscious or subconscious [racism]. It's – I don't know – they might think it's subconscious but I – from looking at it – [differences in the interpretation of expressions of pain] looks a bit conscious because you're treating the same – I don't know – people come in with a lot of pain, you [should] treat them the same as other people. (MSW 4)*

Several midwives identified how a combination of characteristics such as ethnicity, age and perceived socioeconomic position, may influence how a woman's pain is interpreted:

> *If you're a White, middle-aged, well-to-do woman saying 'I'm experiencing severe pain here and I feel that I need x, y, and z' compared to a woman screaming out in pain… and the biases - 'oh that's how that particular group of women express their pain so that's normal'* (MW 3)

Some HCWs perceived racism, including differences in the interpretation of self-advocacy:

> *If the Black woman advocates for themself, you start to get the 'oh they're being really difficult'* (MW 9)

Many HCWs mentioned skin colour as a potential challenge when recognising skin changes (jaundice, petechiae, cellulitis, cyanosis, and oedema) but there were no examples of an effect on care.

Many HCWs identified language as a barrier to recognising problems and several felt the recognition of problems involves communication and care that may not readily occur for women with language barriers:

> *Ask her how she is in herself. I think talking to her, seeing how she actually feels. Does she feel unwell? What's her normal ranges? What's been going on?* (MSW 3)

Several HCWs highlighted that the time to seek and use a translator was the underlying problem and that they may "ask the easy questions" or "point at things" but defer more complicated interactions (MW 9). Rapid communication through bedside devices that "get through to [a translator] in

seconds" (MSW 1) addressed this barrier in one service. Another service had in-house translators who were believed to enhance both the access to and quality of medical translation.

Theme 6: Variability of Escalation

After it was recognised that a signal was abnormal and required action, the nature of the subsequent escalation process could also vary in different ways to the variability of recognition. The decision to escalate appeared to be informed by the social context of escalation rather than medical need alone, particularly to a consultant. This could depend on the individual woman's clinical situation, her ability to self-advocate, system-level pressures, and the individual HCWs involved in the potential escalation interaction. HCWs described a nuanced decision-making process:

> *[I]f everywhere is busy, busy, busy, busy then you're thinking, '[…] her blood pressure has scored a red* [a severe abnormality]*; I told the registrar - he said he'd come back to me; she's still scoring a red an hour later [...] At what point does it become serious enough that I need to get the consultant involved?' I think making that judgement call is quite difficult because you can get people who will push you back.* (MW 1)

Attempting escalation "depends on how approachable [the consultant is] and that's the honest truth" (DR 12), echoed by almost all resident doctors. Some consultants reportedly responded positively, reinforced the need to escalate to them directly if needed, and provided training at escalation but others did not. One doctor stated they would rather ask a patient to wait for a registrar or send them home rather than call a consultant (DR 12). Another said:

> *If I'm worried about a patient, I still do it anyways, because I feel like it's better I take the brunt.* (DR 13)

Several doctors felt that escalation to a consultant may affect their perceived competence - "that fear of 'what is the consultant going to think?'" (DR 5) - and described uncertainty when escalating to a consultant whom they did not know well. Conversely, one HCW characterised the challenge of understanding who is genuinely at risk when a large volume of women may be escalated as "the boy who cried wolf" (DR 4). Several midwives recalled examples of 'pushback' (MW 1) from a consultant, although individual midwives reported that this experience was uncommon. However, several

midwives used an EWS to facilitate escalation to a consultant as this provided "justification for calling" (MW 1). Positive team behaviours may also strengthen early warning culture: an "open approach to listening to that person even if they might be very junior" and "the relationship between obstetricians and midwives" (both MW 3) may impact the threshold at which escalate occurs.

Overall, doctors trusted the clinical judgement of midwives and recognised their status as autonomous practitioners but several recognised their reliance on midwives to present the "whole picture" (DR 8) and their reliance on the midwife to perceive and convey the appropriate level of concern. The clinical narrative that accompanies escalation after an EWS, although informative, also has the potential to introduce cognitive biases, including stereotypes based on ethnicity, "under-presenting or over-presenting certain signs" (DR 5).

An automated escalation process not reliant on the HCW was in use in one service, and, separately, automated or otherwise mandatory escalation was perceived by other HCWs to be potentially beneficial:

> *If someone scores 2 or above you definitely need to escalate. There is no 'oh she's a tall, high BMI, Afro-Caribbean known to us - she will have high blood pressure'* (DR 13)

Other proposed solutions included ward-based screens displaying EWSs or EWS dashboards for remote review.

4.4.4 Thematic findings – summary of potential improvements

Potential technical improvements collected from examples within the medical records and provided by HCWs (either as positive features of their workplace experiences or negatively referenced as omissions) to strengthen early warning are summarised in Box 1. Potential organisational improvements identified by either needs or positive examples from the medical records and provided by healthcare workers are similarly summarised in Box 2.

Box 1: Potential technical improvements for early warning tools

Individualisation

- Recognise when variation is in keeping with or deviates from an individual's baseline (MW 9, MSW 3)
- Recognise whether and when variation is expected in specific contexts or stages of a maternity (MW 9, DR 8, DR 10, DR 14)
- Incorporation of additional clinical signs (8.11; 19.1.13; 28.1.3-4)

Pattern recognition

- Recognising progressive changes that may not meet alert thresholds (2.1.1; 20.1.8)
- Memory of previous abnormalities that HCWs may not know, access, or recall (8.2.1; 31.7.1; 12.1.11-12; 7.1.6; 25.4.1)
- Account for the response to treatment and recognition of new complications (19.1.2, 19.1.4)
- Ensure trends in vital signs are easily accessible and easily visualisable in electronic systems or paper charts (MW 4, DR 9; 4.2.1; 6.1.2; 38.1.1; 12.1.9; 12.1.14; 24.1.1)

Clinical decision support and automation

- Provision of prompts for investigations (DR 14)
- Generation of an EWS (MW 7)
- Escalation to team members (DR 14; 12.1.12; 16.6.1; 16.7.3; 16.7.8; 16.7.9), including senior escalation (1.3.1; 7.1.1; 12.1.2; 12.1.12; 16.4.1; 16.7.10; 17.3.2; 17.4.6; 20.1.2; 21.2.5; 28.2.4)
- Immediate means of acknowledging response to escalation (MW 2)
- Prompt to select correct EWS (MW 6) or automatic selection of correct EWS (DR 14)

Box 2: Potential organisational improvements for early warning

- Induction that incorporates training on maternal early warning scores (DR 3)
- Training on the measurement of the vital signs (MW 3, MSW 4), interpretation of clinical signs (DR 3, MW 5), A-E assessments (DR 10), performing basic medical investigations (DR 9, MSW 2), clinical deterioration (MW 3, DR 14)
- Training and relationships with teams outside of the maternity footprint, including early pregnancy nursing teams (DR 4) and medical wards (MW 6, DR 10, DR 14)
- Support from senior clinical and executive staff, including role-modelling the use of tools (DR 7), supporting and being receptive to escalation (MW 3, DR 4)
- Systematic audit and feedback (DR 14)
- Dashboard showing vital signs (DR 1) or whether vital signs have been completed (DR 14)

4.5 Discussion

HCWs were near-universally positive about the use of EWSs conceptually but their use in practice appeared more complicated and to involve compromise, compared with their ideal use. EWSs, as well as other early warning signals, were commonly not acted on at an early stage. Many HCWs saw value in the EWSs as alarms that signify deterioration but not alerts to consider early warning signals so long as a woman appeared to be well. HCWs described a range of behaviours that filtered out early warning signals at all stages of the early warning pathway, often without clear clinical reasoning or investigation. The main reason for these behaviours appeared to be that maternity services did not have sufficient capacity to support the optimal use of EWSs for the early identification of problems. The level of investigation and escalation appeared to be either unfeasible or unacceptable to HCWs. *Early* warning signals were predominantly interpreted by midwives, who may feel they do not have the nursing-associated skills to undertake comprehensive assessment, and then by doctors who may have limited experience of maternity care but who are tasked with the

greater challenge of interpreting these weaker signals. Medical investigations that may support diagnosis were reserved for women who were already demonstrably unwell unless laboratory investigations were part of protocolised pathways, such as for sepsis. Consultants were not typically involved in the interpretation of potential early warning signs, rather involved once severe complications had already been diagnosed.

EWS processes appeared highly variable, reliant on the beliefs and practices of individual HCWs. The normalisation of deviating from protocols appeared to increase the potential for ethnic biases. Many forms of ethnic bias appeared to be specific examples of the general resistance to early warning signals but not all were. Participants from all ethnic groups were aware of potential biases related to the recognition of clinical signs among women with different skin colours although no participants had experience of this affecting the care of women. Participants appeared to emphasise physical differences whereas fewer participants consciously identified more complex ways in which ethnic biases might affect care; however, several patterns were evident. First, participants from all ethnic groups had observed, experienced, or were aware of ethnic stereotypes, namely regarding a woman's evaluation and communication of her pain. Second, the understanding of why there may be systemic (perceived) differences in either the vital signs or the rate of complications between ethnic groups varied. This included the possibility that abnormalities could be tolerated within some groups because it appeared to be 'normal' for that group. Third, there were also individual examples of cultural biases in the documentation and from individual interview participants, which related to perceptions of the style of communication or norms of communication among women from different ethnic groups. Relatedly, women with language difficulties may be affected by the speed but also the depth of communication regarding the recognition of warning signs. The provision of appropriate care for these women appeared to be particularly sensitive to the workload of HCWs.

In this work, the major determinant of EWS function was workload. The negative impact of workload on EWS processes has been identified previously, including the deficiency of postnatal care(333) as well as in non-maternity settings(334-336). In this work, workload and staffing appeared to modify the EWS-related behaviours of HCWs. Similar issues have been identified in other early warning-related studies outside of maternity(334, 337); in brief, that resources and culture interact to produce behaviours that affect how HCWs perform tasks, reflected in the conceptual model developed by Ghaferi et al.(338). From a behavioural perspective, variability in escalation may be influenced by an individual's attitude as well as team factors, emphasised in the framework developed by Flenady et al.(334), which, in the context of the work presented here, may be considered as partially resource-dependent contributions to EWS function. This work focussed on the clinical effect of the predominant behaviour, which was the resistance to early warning signals because a woman looked well. The main influence on this pattern of response appeared to be individual workload and the interaction of workload with the meaning of the signal itself. HCWs identified that both low staffing levels and staffing shortages impacted their work. In studies outside of maternity, lower staffing has been associated with both missing observations and mortality; Griffiths et al. conceived of the quality of measurement of the vital signs as a potential mediator between staffing and mortality(339). The need for fast access to high-quality translation services has previously and consistently been recognised as essential(318, 340) although there was wide variation in the approaches to and accessibility of clinical translation in this study, supported by a recent study based on Freedom of Information requests by McLellan et al(341). The present study provided further characterisation of how the workload of the HCW can impact when and how they use translation services and the length and quality of the communication they can afford to offer women whose first language is not English. HCWs need time to provide quality communication, particularly in the presence of potentially-related issues, such as differences in health literacy. A qualitative synthesis by Smith et al. identified potential positive impacts of EWS tools on workload but these this focussed on the efficiency with which specific tasks could be completed(342). For

example, in one ethnographic study on the implementation of a maternal EWS, Mackintosh et al. highlighted how a chart-based EWS made the retrieval of information easier but equally highlighted that HCWs questioned the benefit of postnatal EWSs given the increase in workload(21). In the present study, which considered the holistic EWS process, no HCWs felt that it assisted with their workload and many indicated a negative impact on their workload. In contrast to the very low use of EWSs in Mackintosh et al. at the time of implementation, here EWSs were clearly embedded into care but in keeping with Mackintosh et al.(21), HCWs still exercised discretion except that this had shifted to the interpretation and escalation of abnormal EWSs. EWSs were being performed but there were concerns with the quality, timeliness, interpretation, and capacity to act on abnormalities.

An abnormal EWS is very common; for example, during the development of the national MEWS, 44% of all EWSs measured were abnormal (greater than zero)(15). EWSs are high throughput data that busy HCWs have to action quickly. Therefore, it was not surprising that HCWs described having to filter out some warning signals, which is a complex process of reasoning that may not be reproducible. In a cognitive task analysis involving nurses by Ede et al., the clinical evaluation, synthesis of information, and decision to escalate was characterised as difficult(343). In the present study, clinical evaluation and synthesis could be over-simplified with crude explanations for abnormality, potentially reflective of the same cognitive challenge. Elmufdi et al. described how HCWs preferred 'simpler' explanations, simpler treatments, and tolerated abnormality due to cognitive biases, including optimism and confirmation biases(344). In the present study, the potential contributors to these simplified clinical behaviours were also identified; midwives and doctors were concerned about omissions of appropriate clinical evaluation and reasoning both prior to and following escalation due to the availability of staff and time as well as a perceived lack of skills and physical resources. For midwives, level 1 competencies that may inform an acute clinical assessment include pulse strength/volume/character, capillary refill time, skin turgor, and

recognition of altered fluid status(345), some of which some midwives referred to as skills in decline. Several midwives felt that initial midwifery training did not prepare them to care for acutely unwell women. Similarly, once a medical response had been elicited, early – and sometimes late – warning signs were not always recognised, investigated, or further escalated by doctors. Even consultant obstetricians did not always recognise or act on severe abnormalities of the vital signs. HCWs did not ascribe a perceived decline in skills to the EWS itself, as they have elsewhere(336) but did underscore the need for appropriate induction of all staff types, regular multidisciplinary training or skills assessment, and supportive cultures that embed knowledge sharing. Ede et al. found that 35% of escalation interactions were protocol-driven, so-called "informative escalation", where the actual clinical concern was low. The authors highlight that this form of escalation is a potential target to reduce escalations(346). Determining the balance between escalation driven by clinical need and driven by protocol is a balance between caution, the ability to provide genuine early warning, including at levels HCWs would themselves not recognise, and resources, in maternity services that do not have the resources to escalate or investigate every woman according to their protocols. An advanced EWS has the potential to support an appropriate balance if it can reduce the number of women for whom alarms are generated who are truly at very low risk whilst ensuring that there is still a robust, universal, early warning safeguard in place to protect women who are at risk at an early stage.

Overall, maternity systems appeared less equipped to respond to weak warning signals that may be commoner but whose clinical implication is less clear. This shifts the function of the EWS system from an early warning oriented to an alarm oriented system. Similarly, Lamé et al. described how the escalation of fetal concerns may be less consistent when considering "not obviously pathological [cardiotocographic] traces" that require "complex interpretations and judgements"(347). Connor et al. recognised that inaction can also be viewed as a mindful decision to collect more information or allow intermittent abnormalities to resolve(348); however, better individualisation of risk

assessment could support early windows for intervention that HCWs may not be able to recognise. Therefore, tools need to be able to support HCWs to use subtler warning signs in a healthy population so that there is more certainty within the early window for intervention and less need to wait for more severe signs to develop.

Escalation is a human interaction that relies on the communication of objective data and development of a shared clinical narrative to lead to a consensus on the explanation for abnormalities, guided by "clinical scrutiny"(320). Jeffery et al. recognised the concept of "negotiated escalation" where escalation deviates from set thresholds and had to be negotiated between midwives and doctors, which created "conflict"(333). In the present study, which involved staff from across the maternity service and documented evidence, filtering out warning signs was not a process unique to the escalation interaction but happened across the whole EWS pathway. However, workload may create tension between professional groups as HCWs committed to reallocating time from one task to another (both escalating or responding to escalation) based on their own and/or others' clinical reasoning and judgement. Therefore, negotiation may be considered a vital and positive function in the context of resource limitation. Flin et al. described escalation as a two-way form of communication(349) in which HCWs must interact, or negotiate, to reach a shared understanding of the clinical status of a woman. Its interactive nature is likely to be more important when in-person clinical responses cannot be provided for all EWS abnormalities. Flin et al. further detailed how time pressures for the interaction itself and subsequent action could produce "interference between the rational and emotional levels of communication"(349), potentially increasing the chance of miscommunication and negatively impact interprofessional relationships. Structured communication tools exist to standardise communication during escalation interactions. One example is 'SBAR' (Situation, Background, Assessment, Recommendation), where information is delivered in subsections detailing the clinical 'situation', the patient's 'background', the 'assessment' performed, and the 'recommendation' to or request asked of the person being escalated to(350).

Some HCWs highlighted that SBAR may not be used but could support more effective communication, as shown by de Meester et al. in the general adult setting(351). SBAR may also improve the perception of teamwork, safety, job satisfaction, and working conditions in the context of maternity(352). Therefore, embedding a structured communication tool for escalation interactions may support safe and appropriate communication by mitigating the workload pressures that may negatively impact interprofessional communication.

The broader social context of escalation has been identified across various studies, and it has been shown to be influenced by hierarchy, confidence, experience, and the anticipation of a negative response(333, 334, 353), highlighting the vulnerability of this interaction to non-clinical factors. This present work situated the social nature of escalation in the broader EWS process and identified its potential influences. It is also through the narrative interaction between HCWs that cognitive biases may be introduced that places less weight on clinical information. This could involve explicitly referring to ethnicity-based stereotypes, e.g. when communicating pain, or implicit prejudices whereby communication, behaviour, or clinical signs are interpreted differently based on ethnicity, e.g. interpreting self-advocacy as aggression. Morgan et al. found that HCWs were much more likely to identify the ethnicity of Aboriginal Australian patients in clinical interactions without a documented reason but less likely to identify patients from the UK or Republic of Ireland(354), suggesting that HCWs may use ethnic labels to convey social context that may introduce prejudices. Further, Wesevich et al. found that the presentation of biased information, more generally, during HCW-HCW interactions decreased the information recalled(355). EWSs should not be weakened by linking them to ethnic stereotypes; ethnicity should only be communicated when it positively supports the provision of culturally-appropriate care, as shown by Knight et al.(11). In the present study, HCWs demonstrated different interpretations of the relevance of ethnicity in the context of warning signs, highlighting that communicating ethnicity during clinical interactions may have

unintended effects on how information is received. It would be better to communicate cultural needs directly and clearly, where they enhance care.

4.5.1 Strengths and limitations

The strengths of this work include the detailed analysis of individual early warning signals (scores, symptoms, signs) from the routine clinical documentation of a heterogeneous and diverse group of women who experienced severe complications, including both their 'background' care from periods of pregnancy without medical concerns and 'acute' care at the time that complications arose. This provided information from a wide range of HCWs per woman to build a picture of organisational-level care. Prospectively-collected and time-stamped data was used to understand HCW's subjective concerns alongside objective clinical data and clinical actions without the influence of direct clinical observation. These data informed the exploration of patterns through interviews from across the breadth of the multidisciplinary maternity team and from across the breadth of the recognition-escalation-response clinical process. The analysis included care received in the pre-hospital and non-maternity settings to understand clinical interactions and referrals into the maternity service that affected acute care, reflecting women's actual clinical pathways. Similarly, the inclusion of a wide range of different HCWs within different maternity services increased the confidence in and transferability of the findings. Triangulation of the findings from the two sources of data was used to increase the validity of the analysis, as well as enabling the study to answer the complementary questions of what happens in clinical practice and why it happens.

Regarding the limitations of this work, the use of routine clinical documentation posed the potential limitation of not capturing clinical actions; however, a clear escalation response was always accompanied by formal documentation that escalation had occurred, indicating that documentation was reliable. It is also unlikely that early warning signals important enough to trigger escalation would not be documented. Professional guidance sets out the standards of record keeping, which

includes the need to document new findings and the steps taken to manage concerns(356) and to document clinical findings(357). Nevertheless, it is possible that milder warning signals other than vital signs may not have been documented. Despite this, there was representation of a wide range of mild to severe abnormalities. Documentation and HCW experiences related to separate sets of events, which meant that the specific reasons for variation in the documented evidence could not be directly explored. Another challenge conducting this work was the recruitment of participants. This largely relied on HCWs donating their own time to participate. Due to the difficulty of recruiting MSWs, compensation for their time was introduced. This meant there was a systematic difference in recruitment between groups of participants; however, this approach meant that the views of all groups were represented.

Additionally, the positionality of the researcher was both a strength and potential weakness. Maternity care has its own discourse, comprised of jargon and phrases, patterns of speech, and euphemisms, as well as its own ideologies, including cultural or medicolegal approaches to care. A shared understanding meant that interview time focussed on more nuanced aspects of early warning rather than an explanation of maternity care itself. The researcher was able to demonstrate an understanding of the situations that HCWs related. Prior experience of how HCWs from different professional backgrounds typically discuss patient care in the workplace meant that the style was potentially more 'natural' rather than 'academic'. The limitations were related to how participants might choose to discuss the topic with a doctor. Participants may have assumed that the researcher was aware of 'best practice' so HCWs from other professional groups may have been wary of disclosing deviation from protocols. Participants may also have been wary of criticising HCWs of the same type and grade as the researcher. In practice, participants did not appear to have any reserve when expressing critical opinions, although there was some potential discordance between the positivity towards the concept of EWSs but not the practice of EWSs, which may have been genuine or due to social desirability bias. Questions relating to racism and conscious or unconscious ethnic

biases were initially broad to elicit the genuine experiences of participants. In some interviews, HCWs appeared hesitant to talk about their own perceptions of racism; for example, explaining that they did not "want to make it all about race". HCWs were encouraged to voice their views but the ethnicity of the researcher may have had an effect. To reassure HCWs that their perspectives were valuable, self-disclosure (of observations or experiences) was used, which could be potentially leading. To address this, any identical examples following self-disclosure were disregarded but novel examples that self-disclosure prompted were taken into account.

4.6 Conclusion

The findings characterised how HCWs adapt early warning systems based on contextual factors and how EWSs may not be used as intended. There was a clear potential for early warning to vary based on a woman's ethnic group. HCWs often resisted early warning signals and deferred action until late alarm signals were apparent. A major determinant of this practice was the workload of HCWs and their capacity to support a system that provides true early warning balanced with uncertainty regarding the clinical relevance of abnormal EWSs. The same pressure can weaken early warning culture such that deviation from protocols is not corrected. In this context, the recognition and escalation of warning signals can be highly subjective, which may encourage a range of ethnic biases.

This description of how early warning signs are recognised in clinical practice and how they are acted on (thesis objective 3) has provided insight into how sources of variation in responses could be managed. This research has also confirmed the potential for variation to introduce or exacerbate ethnic biases (thesis objective 4). Although the clinical justification for variation was diverse, the underlying meaning of the EWS to HCWs can be addressed and the underlying workload and staffing pressures could be accounted for in the design of an advanced EWS. In order to understand the balance between workload and the perceived benefit of EWSs that HCWs described, the rate of

abnormal EWSs and the 'yield' in terms of 'true alarms vs false alarms' was considered using a range of measures in Chapter 6, in relation to thesis objective 6. This work identified that the recognition of early warning signs may vary between ethnic groups and because of ethnic biases, not only clinical manifestations of complications. These ethnic biases may be addressed at both the development stage of an advanced EWS but, importantly, could also inform the training and implementation of an advanced EWS. Further, to understand how the perceptions of HCWs that care may differ based on ethnicity, a measure of clinical response will be developed in Chapter 6 to measure potential health inequalities in terms of the downstream clinical response to EWSs across ethnic groups.

The research in this chapter was based on HCWs experiences, stories, and documentation, which provided different facets of early warning practice all from 'within' maternity services. In the next stage of this work, early warning symptoms were considered from women's perspectives (thesis objective 5). This may identify ways to strengthen early warning that HCWs themselves have not observed or experienced. The patterns of early warning recognition identified in the present chapter informed how early warning processes were conceptualised and how the data from women who experienced severe complications were analysed. In the later stage of this work, the national MEWS was validated within individual ethnic groups. Preliminary ways of addressing any difference in performance were explored (thesis objective 7) and these were informed by the findings in this qualitative work. Better individualisation and contextualisation of the clinical situation in which vital sign abnormalities occur are potential approaches to understanding how to improve the performance of EWSs between ethnic groups, as reported by HCWs. This would appear to better align a potential tool with how HCWs think and how they believe EWSs should work.

5 Chapter V: Women's Experiences of Recognising and Seeking Help for Symptoms of Severe Complications of Pregnancy

5.1 Introduction

Existing EWSs are based on measurement of the vital signs at discrete points in time. They do not incorporate symptoms, risk factors, or formally support the monitoring of trajectories of symptoms or signs(15). In the previous chapter, a map of medical early warning pathways and a model of early warning practice was developed to identify and explain variation (thesis objective 3), including how variation may contribute to ethnic biases (thesis objective 4). However, the formal timing, organisation, and measurement of physiology may contrast with women's experience of pregnancy and its complications. Therefore, this chapter will describe how women themselves recognised and responded to potential problems in pregnancy (thesis objective 5).

In maternity systems, objective medical data may be prioritised over the subjective experiences of women(358-360) and the "local, individualised, and patient initiated elements"(361). EWSs transform the complexity of the maternal health status into a simple score that makes summary, communication, and comparison of the acute physiological status more efficient. This summarisation complements the clinical narrative and translates women's embodied(362) experiences into a medical discourse but, in isolation, removes the subjective experience of the woman(363, 364). The warning symptoms that women experience and recognise may precede or occur independently of the formal measurement and medical interpretation of the vital signs(42). In order to improve early warning, these early experiential data could potentially be included in EWSs or new ways of

incorporating women's experiences into early warning tools could be identified. In the previous chapter, HCW's narratives and their documentation were used to identify institutional, technical, and interpersonal factors that influenced the recognition of early warning signals. The perspectives of women who use the service may provide different insight. In the analysis of medical records, many women presented to hospital with life-threatening complications and so could not benefit from early warning scores that were measured in-person. In this chapter, a woman-centred approach, based on women's experiences of the natural course of complications, will be taken instead of a medical 'early warning signal-centred' approach. Understanding the perspectives of women who experienced life-threatening complications of pregnancy could identify opportunities to improve a new EWS or improve the protocols that determine how one is used. The aim of the work presented in this chapter was to describe how women themselves recognised their potential complications and to understand how they experienced the recognition of early warning signals by HCWs. The research questions were:

1. How did women themselves first recognise their potential warning signals?
2. How did women experience the recognition of potential warning signals by HCWs?
3. How do women's needs and experiences in relation to life-threatening complications align with the capabilities of early warning tools?

The rationale was that understanding how warning signals were recognised according to women who experienced life-threatening complications of pregnancy, and how those women experienced care in relation to potential problems during or following pregnancy (thesis objective 5), may identify unmet needs that can be addressed in the development of an advanced EWS.

5.2 Methodology

The work within this chapter aligns with the ontological realism and the relativist epistemology outlined in Chapter 1(31). The stories that women told about their experiences were considered to be highly contextual and to offer only one perspective on the phenomenon of clinical recognition(31). Women's experiences could only be accessed and interpreted through retrospective narratives, shaped by the framing of the interview, the mediating role of language, and conditioned by the assumptions of the interviewer and then analyst(365). The underlying philosophical principle was that a thematic analysis of women's accounts of their experiences, symptoms, and the care they received could be developed that reflects aspects of a shared reality and that this analysis could inform improvements to maternal safety systems.

5.3 Methods

This study was a secondary analysis of the transcripts of 36 semi-structured interviews presented as a 'Healthtalk' series on life-threatening complications of pregnancy(366).

5.3.1 The interview dataset

The interviews were carried out as part of a mixed methods programme of research into life-threatening complications of pregnancy ('near miss maternal morbidity'). The objectives of this programme included both providing an educational resource and improving the quality of maternity care. This educational resource was developed into a 'Healthtalk' topic that included information, excerpts and videos of the interview for the public(366). The research questions for the interviews were about experiences of life-threatening complications of pregnancy; the impact on social and family relationships; and views on positive or negative aspects of care(367). Interview participants were women who had experienced severe pregnancy complications and their partners. Women (and

secondarily their partners) were sampled for participation using maximum variation sampling based on their experience of conditions that represented causes of direct maternal deaths in the UK, their ethnicity, and socioeconomic background(367). Women and partners were recruited through support groups, the National Childbirth Trust, social network forums, newspaper advertisements and word of mouth(367). Participant information was translated into Bengali and distributed in an East London hospital. The interviews used an open-ended narrative section and then a semi-structured section to revisit issues not covered in the narrative(367). Interviews were audio- or video-recorded and fully transcribed.

There were 47 interview participants across 36 transcripts in total, including 36 women and 11 partners. The majority of participants (42/47) defined their ethnicity as White British, as well as 3 participants who were of other White ethnicities, 1 who was British Pakistani and 1 who was British Somali. The most common occupational background was 'professional' (21/47), followed by 'other non-manual' (13/47), skilled manual (4/47), unskilled manual (2/47) or no employment (7/47). Most women were aged 30-39 years when they gave birth (23/36) and a minority were either under 30 years (8/36) or 40 years or over (5/36).

5.3.2 Ethical considerations

Ethical approval for the original study was provided by the Berkshire Ethics Committee (09/H0505/66) and written consent was obtained for the inclusion of these data in research publications. Approval for use of the data for this secondary analysis was provided by the Primary Care Hosted Research Datasets Independent Scientific Committee ('PrimDISC'), Nuffield Department of Primary Care Health Sciences, University of Oxford, who provided independent review. The secondary use of the data was approved on 5th September 2024. This secondary use is for the same purpose that the data were originally collected, which is to understand experiences of life-threatening complications to improve the quality of maternity care. Information relating to specific sequences of events particular to an individual woman, partner, or individual healthcare services

were removed from transcripts by the researcher before analysis as not all data originally collected were made publicly available.

5.3.3 Thematic analysis

Thematic analysis was used to identify and describe processes of recognition of early warning symptoms and signs(327). The analysis was informed by the principles of reflexivity(34, 328), acknowledging the active role of the researcher in developing themes through engagement with the data and reflection on the assumptions of the participant, interviewer, and researcher. An initial list of descriptive codes was developed. These included key information to label the women's experiences (type of severe complication) and, informed by the findings of Chapter 4, parent codes related to the timeline of events (recognition, escalation, treatment). Other than this outline, the transcripts were coded inductively in order to provide flexibility to respond to the wide range of information they contained(368). This meant that women's perspectives could be coded and analysed appropriately even if they focussed on different aspects of recognition or escalation. Descriptive, contextual, and conceptual codes were applied using NVivo software and annotations added to engage with the transcripts when re-reading(327, 331). Sections of transcripts that did not include any information relating to early warning symptoms or signs, interactions with HCWs or maternity systems, or the experience of complications were coded descriptively and summarily. Video excerpts from interviews on the Healthtalk website were also reviewed. This deepened understanding of participants' perspectives by providing audio-visual context not present in the text; for example, into emotions that participants were expressing or the certainty with which responses were voiced. Themes were developed to describe how potentially life-threatening medical problems were recognised and how women and their partners experienced the process of recognition and escalation by HCWs(34). Differences between the perspectives of mothers and partners were considered. The themes were supported by illustrative quotes labelled according participant type (mother, M, or partner, P) and interview number.

5.3.4 Reflexivity

I adopted the same broad approach as described in Chapter 4 but consciously considered my reactions towards both the interviewer's and participant's responses to one another. Naturally, I felt that I was an outside observer of this interaction and that the information I would have liked to know was influenced by my professional background. For example, I wanted more context to understand whether the experiences that a participant felt were positive were 'actually' medically appropriate or not. I was careful to base my interpretation on the participants' experiences, staying close to the text, and not to infill context not present in the text with my professional experiences. For example, I avoided over-interpreting implicit cues as to why HCWs may not have recognised warning signs. Participants' responses reflected their own priorities and experiences of care, uninfluenced or led by medically-focussed questions that I might have chosen to ask. The participants' stories were nevertheless conditioned by the cues and the social interaction with the actual interviewer. I respected the integrity of the interview as representing the way in which the participant chose to describe their experiences for the purpose of the interview and its aim of understanding women's experiences of life-threatening complications and how it affected them and their families. I was careful to map the story out in note form when reading the transcripts so that I had a summary record to refer to, including, for example, key events and quotes. This helped me to avoid taking individual aspects of the story out of context and helped with immersion in the narrative, which is more challenging given that I did not collect the data myself. I also felt it was important to select illustrative quotes carefully to ensure that they were not taken out of context. I used my clinical knowledge to determine whether the symptoms and signs (e.g. blood pressure measurements) represented early warning signals of potential complications or represented severe complications.

5.4 Results

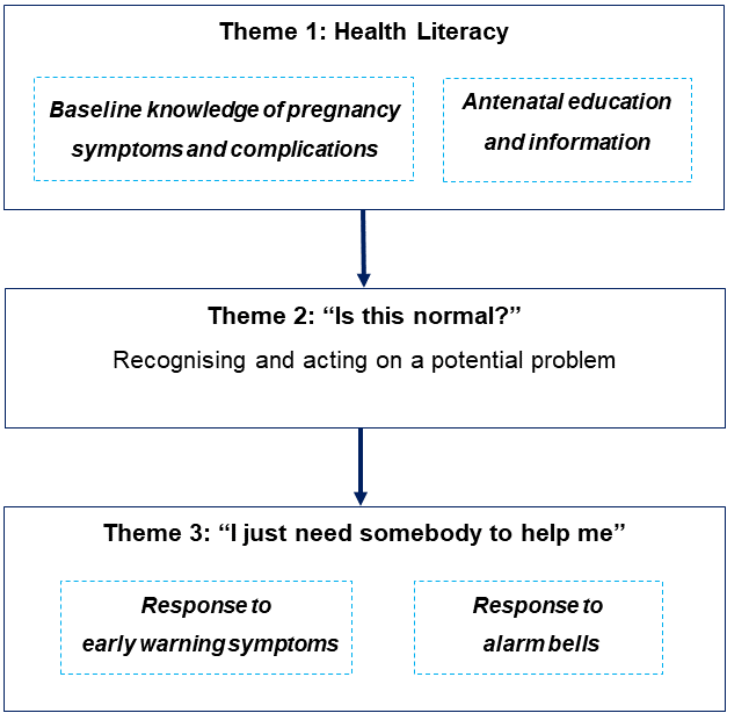
5.4.1 Thematic analysis

Three themes were developed. ‘Health Literacy’ (theme 1) related to the information that women and their partners had at the beginning and then throughout pregnancy. Theme 1 contained the subthemes ‘Baseline knowledge of pregnancy symptoms and complications’, which reflected women’s knowledge at the beginning of pregnancy, and ‘Antenatal education and information’, relating to how and from where women sought pregnancy-related information that developed their baseline understanding. ‘”Is this Normal?”’ (theme 2), represented how women weighed up their symptoms and the threshold at which they decided to seek help. “I just need somebody to help me” (theme 3) related to the reaction or inaction of HCWs who were presented with warning signs. This contained two subthemes: ‘Response to early warning signs’ covering early attempts to get help and ‘Response to alarm bells’ where a severe complication appeared to have occurred and urgent investigation or treatment was required. These themes and subthemes are shown in Figure 5.1.

Differences between Mothers and Partners

Mothers and partners did not demonstrate different attitudes or experiences of recognising early warning signs themselves. The recognition of early warning signs was predominantly described in the narratives of mothers with partners providing complementary supporting evidence. However, partners did not appear to be involved in seeking additional information independently or did not describe their information seeking behaviours in the interviews. Partners’ experiences of severe complications themselves, as observers, did differ but this was not the focus of this work.

Figure 5-1 Thematic Analysis of Women's Perspectives on Recognising their Warning Symptoms



'Health Literacy' (Theme 1) may be influenced by 'Baseline knowledge of pregnancy symptoms and complications' and 'Antenatal education and information' (subthemes). 'Health Literacy' informed a woman's assessment of 'Is this normal?' (Theme 2) in relation to her potential warning symptoms. If a woman decided to seek help, the abnormality had to be communicated to and accepted by a healthcare worker, 'I just need somebody to help me' (Theme 3), which could either relate to the 'Response to early warning symptoms' or the 'Response to alarm bells', where there was a clearer indication that a woman may be severely unwell (subthemes).

Theme 1: Health Literacy

Subtheme: Baseline understanding of pregnancy symptoms and complications

Knowledge about normal or abnormal symptoms of pregnancy varied, meaning that women and their partners did not all have the skills to recognise and act on potential warning signs:

> *I didn't react because I thought 'well occasionally you're going to get spotting'. Now that was my ignorance here because I didn't know anything hardly at all. What could go wrong?* (P, 22)

> *I'm not very medical at all but a lot of these [manifestations of pre-eclampsia] sort of sounded quite normal* (P, 11)

Background health literacy may also affect how advice from HCWs was interpreted. For example, a woman or partner's assessment of what constitutes a "very serious" episode of bleeding could depend on their previous experiences and health education:

> *I'd had these little bouts of bleeding and when I called the midwife to explain this, she said, "Okay it could be normal but because women do bleed after even, you know, six weeks after…" And I said-*

> *And she said, "But if it's very serious", she said, "Call 999, didn't she?"* (M & P, 42)

Several participants were not aware that potential severe complications existed at all:

> *I suppose what was wrong with me [...] was slightly intangible [...] It was, you know, high blood pressure and pre-eclampsia and unless you know what it is, I suppose it doesn't feel like something that's very serious.* (M, 16, on communicating her diagnosis to her employer)

> *I hadn't heard of [pulmonary embolisms]. I wasn't aware of what they were.* (M, 9)

One woman was unaware that chest pain on the right could represent a life-threatening complication:

> *And that certainly had never occurred to me - that it was a life or death type situation [...] I remember saying at the time, if the pain had been on the other side [...] I'd have been convinced it was a heart attack […] but it was on the wrong side so I just thought 'no, there is something muscular going on or something like that'.* (M, 41)

Experience of pregnancy also informed baseline pregnancy-related health knowledge:

> *Having gone through it once before I didn't worry about, you know, the odd sort of twinge here and there because I'd done it before and I knew what felt normal and probably what didn't feel normal* (M, 27).

Whereas one woman highlighted the challenge of recognising new warning signs without a previous experience of birth:

> *I just got all these horrendous lights coming in front of me and my head and I thought someone had hit me over the head, this severe pain, so I thought 'ooh I don't feel very well' and felt very sick and I thought 'ooh I've gone into labour' because obviously I've never had a baby before.* (M, 26)

Some women therefore benefited from their previous experiences whereas others could not.

HCWs may overestimate women's general knowledge about pregnancy and early warning signs, particularly first-time mothers. In one example, a HCW assumed that a woman would know it was important to be able to describe the colour of her amniotic fluid:

> *I didn't call them as soon as my waters broke so they had a bit of a go at me when I phoned up because I couldn't tell them if they were coloured or- I was like, "Well it was on the loo, it was 2 o'clock in the morning and I didn't have the light on."* (M, 17)

Subtheme: Antenatal education and information

From these different baseline levels of knowledge, women accessed new information in different ways and to different levels of depth during or sometimes following pregnancy. Many women perceived deficiencies in the information that was provided to them by HCWs and maternity services and highlighted how they had to proactively seek additional information. Sources of information included written information from maternity books (M, 28), NHS websites (M, 41), patient

information leaflets (M, 25) and social networks (M, 21), antenatal classes (M, 22), or unspecified online research (M, 23; M, 28):

> *Obviously as a result of the liver issue - the [liver function tests] - I've looked on websites around how the liver function works and the test and this, that and the other, and really to try and find out what's normal, what's not normal [...] what the implications are.* (M, 28)

Some women explained the limitations of sources of information, including antenatal classes:

> *short and not very informative and really the message that come out during this whole thing was if you see bleeding call this number* (M, 22);

which potentially contributed to later delays seeking care:

> *I feel that if I'd had more information [whilst discussing antenatal classes] I would have acted quicker when we had the emergency* (P, 22).

Similarly, an information pamphlet on vaginal birth after caesarean was not considered sufficient or relevant to the real experience of uterine rupture:

> *I think the vast majority of information I had, I did gather myself [...] [T]here's not an awful lot of information about just how deadly [uterine rupture] is. Just how badly things can go wrong. Yes, I knew I could rupture, but it actually said, I'm sure [...] on the pamphlet, that was a chance in two hundred chance of rupture, but when noticed early enough there would be no further complications from this. So it made it sound like [...] this can happen but it's okay we can fix it; whereas actually, you know, a lot of the time they can't fix it because things can get so bad and it can happen so quickly and they don't recognize the signs very quickly.* (M, 25)

Several women had proactively filled in gaps in the information they received from HCWs:

> *Basically, from my own research on the internet, while I was actually sat in hospital [...] it was complete placenta praevia and from [what] I read up on all the websites, it was serious. It was, you can haemorrhage, you can die, early labour […] I was just wondering why me midwife had never […] said to me […] 'rush to the hospital'. A little bleed can become a big bleed, you know, I just thought 'I'll be alright'.* (M, 23)

In some cases, finding the right information was related to an element of chance. One woman felt "lucky" she had a family member who had been a patient with the same complication to talk to (M, 27) whereas another recognised her warning signs only coincidentally:

> *I think I was able to find enough information but had I not known or read myself around the symptoms that I had and the condition that I had, the hospital wouldn't have given me that at all… and it was literally just by a standard maternity book. It was one of the conditions in the back and I was just reading them one day as you do and I came across it and I just thought 'hmm, seems quite similar to what I've got'.* (M, 28)

Some women did recall advice on specific warning signs. In one example, chest pain caused by a pulmonary embolism (a blood clot that usually forms in and travels from a vein in the leg) was not thought to be concerning because it did not occur in association with the typical warning sign:

> *I was told to watch out for one leg swelling or a painful spot on your leg that was really tender to the touch but this didn't tick any of the triggers for me with any of the information that I'd been given about what a clot might feel like. I think there was a big focus on a deep vein thrombosis being in your leg and that would be the most likely place it would occur.* (M, 41, who had a pulmonary embolism)

Theme 2: "Is this normal?"

A woman or her partner's general health literacy, dependent on her background, and the knowledge they gained in pregnancy through access to resources, therefore produced a body of knowledge with which they could inform their decision making. The most important decision from the perspective of early warning symptoms was whether to seek help or not. Differentiation between symptoms that are normal or abnormal was challenging for many participants. Some participants conducted targeted research to inform this decision making process. Both women's ability to recognise new problems and the urgency with which help was sought varied. Those whose problems arose in the community commonly described the evolution of symptoms, sometimes over days or weeks. Many problems were initially indistinguishable from every-day complaints; for example, itching from obstetric cholestasis was ascribed to the temperature (M, 28), nausea and dizziness in the context of acute fatty liver of pregnancy were ascribed to not having eaten (M, 43), or "blips" of hypertension were ascribed to "stress" (M 21). Some women did not recognise combinations of acute symptoms that indicated immediate concern for serious pathology:

> *I woke up at night with pains between my ribs […] it was quite hard to breathe […] but I didn't even mention it to the midwife, because I assumed it was indigestion.* (M, 12, with pre-eclampsia)

> *[I]t just really felt like I'd slept wrong and you know, if you pull a muscle or something like that [...] and I remember going out into the garden at one stage [...] and just saying, "Oh I just needed to come out for some fresh air" and "it's just really stuffy indoors."* (M, 41, with a pulmonary embolism)

Another woman found it difficult to interpret her pain in the context of a caesarean section, which she had not experienced before:

> *I know that when me appendix started going to all these tummy things I kept thinking 'is this normal? Is this associated with the caesarean?' I had absolutely no idea because we weren't told anything about things like that.* (M, 26, with acute appendicitis).

By contrast, sudden, severe, or unfamiliar symptoms usually prompted women and their partners to immediate action:

> *We didn't even phone up did we? Just literally drove, and you sort of drove at breakneck speed, but I was, I was - I just can't even describe the pain [...] I felt like if you were ever to imagine what it was like to be stabbed"* (M, 7)

Women reported using a range of resources to inform their decision making process. Several women received explicit advice from family members to seek help:

> *We decided that one night when I was in a lot of pain to go to hospital didn't we? Because my Mother in law had said, "Just go to hospital because we don't know what it is. Just go."* (M, 42)

In one example, familial support was the trigger to seek medical care after previous symptoms had been overlooked by HCWs:

> *[…] and at the end of that week you clearly were not very well. Dad said, "This has been on too long, you really need to get back to the GP again."* (P, 36)

Advice from family members played a complicated role in the decision-making process and did not always lead to seeking immediate care. In one example, a participant's mother-in-law believed her pain on inspiration could be due to a chest infection (M, 41) and she did not seek immediate medical

care. Despite differences in baseline pregnancy knowledge and prospective pregnancy information seeking behaviours prior to warning symptoms, seeking help for new symptoms could be informed by targeted research after symptoms had been recognised. Whereas one woman relied on "instinct" to initiate care (M, 21), another woman "got [her] books out and rang the hospital" to support the recognition of symptoms of pre-eclampsia, which led to investigation, (M, 26).

Some women undertook their own structured assessment, which could form an additional step in the pathway to care:

> *[…] I went down the check list of pre-eclampsia and I thought well, general feeling of being unwell, swelling, and I thought well that's a couple of things ticked off.* (M, 12)

Theme 3: I just need somebody to help me

Subtheme: Response to early warning symptoms

Initial engagement with HCWs in response to early warning symptoms was not always successful. Where HCWs did not recognise or respond to warning signs, some women waited before escalating further:

> *So I texted the midwife, and I said, "I don't feel very well. Feeling slightly swollen. Possible pre-eclampsia?" And she didn't reply for four days [...] So I text the other midwife that I had a number for and she texted me back the next day. I didn't want to call them because it was about 8 o'clock at night and I thought well, I'll just sleep it off you know.* (M, 12)

> *I'd mentioned foot swelling to my midwife before but she kind of seemed to think it was very normal so we didn't really worry too much but when I couldn't walk on it I decided to go and get it checked.* (M, 42)

Whereas some women who recognised the urgency of their symptoms decided to seek a higher level of care directly, based on their own initiative:

> *And [the out of hours service] suggested I could wait till the surgery opened or they said I could maybe go up to [...] the hospital and then maybe get referred and I thought actually, if I've possibly got a blood clot, I'm not hanging around here so [...] I went to the A&E* [Emergency Department]. (M, 27)

Even when women themselves had made the assessment that they required evaluation by a HCW, warning signs were not always recognised. These included breathlessness (M, 9), pain (M, 3; M, 10), gastrointestinal symptoms (M, 28), as well as fetal signs of maternal complications that were noted but not recognised as warning signs (M, 5), hypertension (M, 21), and biochemical abnormalities (M, 26).

A few women described multiple healthcare appointments where warning signs were missed. For example, one woman related making contact with various HCWs over several weeks:

> *I started to notice the change in my stools, and my urine became very, very dark [...] and I didn't think it was normal but when I went every time to the hospital and they did the urine check it came up as yellow, when it was clear, and they assumed that it was a fine colour even though I thought it was very strange [...] I started to have symptoms of diarrhoea and it was very strange.* (M, 28)

> *I went to the doctors on a number of occasions. They did say to me that there was a bug going round, so I just dealt with it […]* (M, 28)

The potentially delayed recognition of hypertensive disease in particular was a feature of several women's experiences. Some symptoms did not appear to have been considered or taken seriously by HCWs. For example, a lack of concern for hypertension with symptoms of pre-eclampsia:

> *I developed oedema and it was really quite bad, and [...] my mobility was quite profoundly affected. I was given support tights but no one flagged it up as an issue really because my blood pressure was elevated slightly, but not enough to be a worry* (M, 21)

Several women reported that HCWs took an incautious approach to pre-eclampsia with signs of severe complications. One woman appeared to have the severity of her condition under-recognised and was advised to stay at home over the weekend despite abnormal liver function tests and epigastric pain:

> *[T]his tight pain kind of here, right under my boobs and [...] whether that was my liver being quite up high and that was the pain, and that's what I thought it was[...]* (M, 10)

This woman was advised that "nothing's going to happen over a weekend. Why bother putting you in hospital […]?" (M, 10). Another woman who had pre-eclampsia with a severe headache, nausea and an abnormal blood test was informed she had a "borderline" pre-eclampsia that could be managed by the community midwife at home. When she then developed visual disturbance and facial oedema two days later, she was admitted but discharged before returning again with severe hypertension, only then receiving definitive treatment (M 26).

Problems with the recognition of potential warning signs persisted in the inpatient setting. Some HCWs did not seem able to complete a holistic assessment of potential early warning signs. One woman related how the maternity service did not appear equipped to assess her symptoms or needs:

> *There was a real shortage of staff. Massive shortage of staff [...] "Look I can't get anybody, they're all really busy. There's an emergency down the corridor." So we were left to it [...] One woman really had a go at us, and said, "Look, you may not have noticed but it's headless chicken time, round here, and you're obviously not in labour, so you're not high priority. I'm very sorry but that's it" and she went.* (M, 3)

This experience was echoed elsewhere:

> *All the midwives who are trying to look after you have got other commitments to the women who are labouring in the delivery suite and it all just seems so incredibly sort of wrong really*. (M, 7)

Subtheme: Response to alarm bells

There were also examples of late warning signs that indicated a severe complication had already occurred but were not recognised. These were 'alarm bells' that provided clear indication that urgent treatment was required and therefore did not require HCWs to make a potentially challenging or individualised risk assessment. For example, HCWs ascribed epigastric tenderness to indigestion; severe, continuous pain and fever to the normal latent phase of labour; breathlessness to influenza; and chest pain to a normal postnatal course. The reasons for a lack of recognition

differed, including not being listened to (M, 7) or the belief that the signs of severe complications were normal symptoms of pregnancy (M, 40). In other examples, the reason that HCWs rejected clear evidence of complications was unclear:

> *I have a blood pressure monitor [...] and it was extremely high. It was 191/113 [...] I took my partner's blood pressure and that was fine. So I took mine again and it was still the same high reading and on the NHS Direct site it had also said high blood pressure. So I called NHS Direct and [...] they said, "You should call the hospital." [...] and I told the midwife exactly how I was feeling and I told her the reading on my blood pressure monitor and she said, "Well it must be faulty." So I said, "I'm really sorry. I feel really stupid. Sorry to have bothered you."* (M, 12, with severe hypertension);

Similarly, the information gathered from a physical examination may be ascribed to a simpler cause, even if incongruent with the symptoms and signs:

> *The first thing I noticed really [...] was when the consultant checked sort of the fundus and measurements and just as he touched me sort of there I just winced and I sat up [...] I was in so much pain [...] He said that it was just the third trimester sickness and it was a bit of indigestion*. (M34, with acute fatty liver of pregnancy)

In cases when a woman's concern was acknowledged and acted on by healthcare workers, many participants described challenges with having the urgency of their care recognised:

> *[T]he doctor couldn't come out so they spoke to me on the phone and [...] said, "Well it could be either that I had a clot or a chest infection." But I was outside of the prime ten days after the Caesarean operation, so to leave it 24 hours and if it hurt that much, I still had the drugs that they'd given me when I was discharged from hospital for the Caesarean, just to take the drugs."* (M, 41)

Some women were relied on to make their own health assessments whilst they were unwell:

> *[T]hey said, "Do you think it's serious enough to call an ambulance?" And I was like "Yes" - at this point I was like 'I just need somebody to help me'.* (M, 40, with sepsis)

Several respondents also perceived ambulance transfer to hospital to have lacked urgency:

> *[B]y this stage, it was agonising, continuous pain [...] The ambulance seemed to take forever to get to the hospital [...] So we trundled along and eventually got there [...] the paramedics hadn't put their siren on or the lights on so I just thought 'Oh, this is just a routine journey'.* (M, 21).

Whereas it was assumed that another woman understood the urgency of her condition and the need for ambulance transport:

> *The hospital called me on the way and said, you know, "Are you on your way?" I said, "Yes, I'm just trying to find money for the parking meter." And they said, "Well can't the driver sort that out? You need to come up here." And I was like, "Well no, I drove myself in." "You should have got an ambulance." "Oh well you didn't tell me that."* (M, 24)

The delay in recognition of a severe complication could be prolonged and involve multiple interactions with HCWs. One woman communicated her pain with various 'red flag' signs to her midwife following admission to hospital. The woman was offered benzodiazepine to help her sleep instead of a medical assessment, which impaired her ability to escalate her care:

> *And if I'd have been with it enough to recognize that something didn't feel right, I could have raised the alarm earlier.* (M, 7)

She was then prescribed paracetamol for a fever and severe pain without a medical review (M, 7), then triggered belated recognition of her uterine rupture through her own escalation:

> *"I literally just couldn't move for pain. And [...] I said [...] "Don't press the buzzer, go and get someone right this minute because something isn't right." And [...] that was the first time in a few hours that we'd seen the midwife.* (M, 7, uterine rupture and stillbirth)

But she still did not receive urgent treatment:

> *And two hours passed before anything happened. So from the time of discovering there was a problem to actually being wheeled into theatre*. (M, 7)

Another woman described a slow response to a postpartum haemorrhage on the postnatal ward after alerting a midwife, followed by sequential escalation through several HCWs, before receiving definitive treatment for a traumatic postpartum haemorrhage only several hours later:

> *I said to the midwife, "You know, I'm bleeding quite a lot." And the trouble is [...] the postnatal ward is quite busy, so she said "Okay, I'll come and see you in a minute. I'll come and see it." And went off and did a few other things and eventually came back, and was like, "Oh yes, you are bleeding quite a lot" sort of thing. It just seemed to be, it seemed she wasn't particularly bothered or interested.* (M, 46)

There were also numerous examples where women believed their severe complications were recognised quickly, both in situations of clear acute pathology and also in situations where the symptoms were proactively elicited:

> *And as it happened there was a midwife in there and she said, "Did you have chest pain?" And I said, "Yes, you know, it's probably, it's probably just you know, from where I was lying or something." I didn't really think it was something really serious and she said, "Oh I'll go and tell the doctor." And the doctors came back and said, "We need to send you for a scan."* (M, 43, with pulmonary embolism)

5.5 Discussion

This analysis of women's experiences of severe complications of pregnancy identified that, prior to the use of an EWS or other formal risk assessment tool, a wide range of routes into maternity care existed. Most women initially described a process of identifying and understanding their symptoms. This period was characterised by the initial interpretation of new symptoms and with subsequent recognition of an abnormality leading to a decision to either wait longer or to escalate their symptom to a HCW. The interpretation of new symptoms was informed by baseline health literacy, by the information sought and education received prospectively in pregnancy, and by specific research into the significance of symptoms as they arose. Some women presented to hospital directly whereas some women engaged remotely in the first instance. Once a woman had decided to ask for help, in several cases appropriate advice was given or action taken. However, advice that warning signs amounted only to normal/harmless symptoms of pregnancy without further investigation was common. Additionally, there were examples of apparent severe complications being dismissed without an explanation. There were also examples of individual women who presented with progressive symptoms to multiple HCWs both acutely and non-acutely whose complications were not recognised and whose clinical condition deteriorated. Some examples involved maternity systems that were not equipped to provide timely and attentive care so that symptoms could be recognised, evaluated, and treated.

5.5.1 Relation to evidence from healthcare workers

These findings complement the findings from the documentation and interviews of HCWs from the Chapter 4. Participants did not detail the use of EWSs although many described, implicitly and sometimes explicitly, recognition and escalation processes. The narratives highlighted how the previously-identified acuity and workload of HCWs and maternity services impacted care and was experienced by women themselves as being dismissed, not listened to, and for one woman, scolded. It was also apparent in these narratives that some systems did not provide robust early warning processes and cultures in which women's concerns were recognised, believed, and acted on. This was as apparent in women's narratives as it was in the accounts of HCWs. What this work adds is women's experiences prior to engagement with HCWs and systems as well as triangulation of the phenomenon of resistance to warning symptoms and signs after engagement with maternity services.

5.5.2 Relation to evidence from the previous literature

The first implication of this work is that, alongside a new EWS, women need to be provided with a basic, consistent, easily accessible, and reliable source of information regarding warning signs that require communication with a HCW. This emphasises the importance of organisational health literacy(369) to facilitate equitable individual access and use of information. In a survey by Simpson et al., 19% of British adults reported difficulty reading and understanding health information, which differed by social deprivation, education, and ethnicity whereas 35% reported difficulty 'making sure healthcare providers understood their problems properly', which differed by deprivation and education but not ethnicity (when grouped as Asian, Black, and other ethnicities combined vs. White)(370). Perceived deficiencies in the quality of antenatal information were also identified by Mackintosh et al., amid a procedural rather than an individualised focus of antenatal care(371). The potential benefit of thorough and consistent counselling was highlighted by Ray et al.(372). Without

providing all women with reliable and easily-accessible information, women with lower personal health literacy(369) or who are less able or inclined to seek additional information will be disadvantaged and may be less likely to ever receive a midwifery or medical assessment into which an EWS is incorporated. Further, Fagan et al. found that understanding of warning symptoms of life-threatening complications differed by ethnic group(373). Knowledge of pre-eclampsia has been identified as problematic, with a majority of women being unaware of symptoms prior to diagnosis in one (predominantly USA-based) study by Bijl et al.(374). A qualitative analysis of the same data set by Shree et al. found that women desired more information about a wide range of aspects of hypertensive disease and believed this would have enabled them to recognise symptoms, self-advocate, and seek earlier treatment(375). In Baker's conceptual model, health outcomes, contingent on individual capacity, may be modifiable by optimising written and oral communication(376). An advanced EWS may improve the quality of acute care for women who present to maternity services but there were examples of women who did not know they were experiencing symptoms of life-threatening complications who would not have benefit from any EWS. Potentially overlooked 'red flag' symptoms have been systematically identified over the course of successive confidential enquiries into maternal deaths in the UK(377). These have been developed into recommendations for HCWs and for women in the form of lay summaries, organised by disease process(378). These 'red flag' symptoms could be consolidated into a single patient-facing digital or paper-based resource and reoriented towards a symptom-based tool which could be provided to women at the onset of antenatal care, similar to the approach by the USA's CDC(379). Randomised evidence from You et al. identified the potential to improve symptom recognition using a graphical, co-designed tool(380). However, there was an apparent lack of clinical impact from health-literacy oriented interventions focussing on women from minority ethnic groups and disadvantaged backgrounds found in one scoping review(381) and therefore such a process should be carefully informed by the views of stakeholders and ideally piloted. A co-design workshop analysis by Maclellan et al. showed that developing resources following the principles of accessible information

may support understanding among women who face challenges accessing healthcare, and used these principles to develop both written and audiovisual resources on postnatal warning signs(382).

The second implication is that EWSs should be made robust to HCWs who decide to dismiss early warning signs without a comprehensive assessment, especially when potentially brief, unstructured or poorly-documented advice may be provided by text message or telephone. Women with the same symptoms should receive the same structured risk assessment and same advice and investigation, incorporating an EWS when appropriate. In the UK, the Health Services Safety and Investigations Body (HSSIB) investigations have identified differences in triage administrative processes(383) and both HSSIB and the Care Quality Commission(383, 384) have identified concerns with the evaluation of clinical urgency and the training and skills of HCWs who provide telephone advice. Telephone triage processes, including the degree of structure in the assessment, were found to vary in an Australian study by Bailey et al.(385). Further, Engeltjes et al. showed that women may not necessary recall the symptoms-based advice received during telephone triage conversations(386). In the present study, the concerns of women often differed to the perspectives of HCWs, representing a potential hierarchy of "professional over embodied knowledge" where women may either be disempowered to act on their concerns or, on the other hand, may need to employ "strategies […] to secure clinical help", as described by Mackintosh et al.(371). In the present study, women had different ways of negotiating resistance from HCWs, including inaction, waiting, repeating, or bypassing the HCW/process. Solutions could include strengthening protocols for remote assessment and communication. The RCOG recommends continuous audit of triage processes(387). The use of electronic rather than paper-based telephone triage interactions may increase accountability for verbal advice and facilitate audit and feedback if HCWs have to document and justify the advice they provided. Electronic systems could also be used to identify actions in response to 'red flag' symptoms that HCWs may otherwise ignore, which could address issues such as recognising symptoms of pre-eclampsia. With additional work, EWSs may even be adapted for

remote use, potentially using patient-reported(388) or remotely-measured symptoms or vital signs(389), symptom severity, and combined with other risk factors. Future research may eventually allow the real-time analysis and inclusion of either documented clinical narratives(390) or verbal narratives(391) into EWSs directly, potentially including a wider range of information(392).

Third, HCWs and systems should understand and be designed to recognise that women have different levels of awareness of symptoms of pregnancy and its complications, of how severe the symptoms they are experiencing may be, and of how urgent their need to access treatment may be. Spiby et al. demonstrated how understanding of aspects of labour and the perceived reliability of telephone triage conversations can differ between women(393). Knowledge of symptoms of complications of pregnancy should not be assumed and women should not be asked to make subjective global judgements on the urgency of their symptoms or care needs without a structured discussion of symptoms facilitated by a HCW. There is a clear potential for women with lower levels of health literacy to be less able to assess the urgency of their symptom. The RCOG recommends that requests to attend hospital should be documented and women informed of the urgency and timeframe for attendance(387). A checklist-based approach to advice or triage conversations could help to structure conversations, including ensuring that measurement of severity (e.g. using visual measures of blood loss) has been conducted, and that advice on urgency, and ongoing action has been communicated and understood.

5.5.3 Strengths and limitations

The strength of this work is that in the original interviews, women were provided the opportunity to tell their story chronologically and to expand on aspects of their story that were important to them. The Healthtalk series was a valuable resource to use because of this, and also because the scale of data collection was greater than would have been otherwise feasible. The first main limitation was that the interviews were conducted between 2010 and 2014 and the experiences of the included

women may not be representative of women's experiences in the present day. In mitigation, although EWSs may have been updated since the interview period, the model of care by which women may self-refer and attend a maternity triage area has not. It is therefore likely that the perspectives expressed in the Healthtalk narratives remain relevant today, and indeed these perspectives complement and align with those of health professionals as described in Chapter 4, which were more recently collected. The second main limitation was that the secondary nature of this analysis, whereby the interview questions did not reflect the current research questions exactly. The main impact this had on the work was that participants were not specifically asked for their suggestions to improve the maternity system they experienced. However, many participants naturally expressed their preferences either directly or indirectly by highlighting negative practices and how they overcame perceived deficiencies in care. Thirdly, the Healthtalk series was limited to women who spoke English and the ethnic diversity of participants was limited. Women whose first language is not English are likely to face this additional barrier in relation to making contact with HCWs, which may interact with barriers relating to health literacy. These barriers to accessing timely and appropriate acute care were recognised by healthcare workers in Chapter 4, including those who worked in acute areas, such as maternity triage areas.

5.6 Conclusion

The recognition of symptoms as warning signals may begin prior to engagement with a maternity service and prior to the measurement of an EWS. This pre-engagement stage was influenced by differing levels of health literacy and information-seeking behaviours, in contrast to the HCW-dependent behaviours, healthcare system-level determinants, and functions of an EWS identified in Chapter 4. In common between the two approaches to understanding early warning processes was the attitudes of individual healthcare workers, which led to variation. This description of how women themselves recognise and act on early warning symptoms (objective 5) provides an

important perspective on how an ideal EWS ought to function. Women who have an early warning symptom should be able to access care that includes an assessment with an EWS. Access to this EWS should not differ based on a woman's background education or social network. Therefore, an EWS could be accompanied with patient-facing information on warning signs and EWSs could potentially be adapted to better support equitable access to maternity care. Additionally, and in line with the findings of Chapter 4, systems should be designed that are robust to the contextual influences on HCWs, such as their workload. EWSs should be based around women's experiences of early warning symptoms and signs wherever and whenever these may arise and not restricted to particular periods of pregnancy or of acute care. In the longer term, the development of an advanced EWS could potentially be adapted to incorporate warning signs for women who are at home, based on either symptoms themselves or remotely measurable vital signs.

6 Chapter VI: Validation of the National Maternity Early Warning Score within Ethnic Groups

6.1 Introduction

Systematic biases differentially affect the baseline health status of women according to their ethnic group(7). These health inequalities with respect to SMM were identified in the systematic review of prognostic factors for severe outcomes (thesis objective 2). Acquired differences in health status may be worsened when HCWs do not recognise or act on risk factors or early warning signs, as identified in the analysis of documentation of and interviews with HCWs (thesis objective 4). Early warning tools have the potential to mitigate acquired differences in health and to reduce health inequalities but only if they perform well within individual ethnic groups. Performing validation of new tools within individual groups, or any groups of interest, is a recognised stage of model validation(394) and validation within ethnic groups is particularly relevant when designing tools to reduce health inequalities. In this chapter, the preliminary consensus definition of SMM (thesis objective 1) and prognostic factors (thesis objective 2) was used to validate the English, physiology-based, maternal early warning score (MEWS)(15). The perspectives of HCWs and how EWSs are used in practice (thesis objective 3) informed the selection of additional prognostic factors to understand the impact on performance. Evidence on the variation of clinical recognition based on ethnicity (thesis objective 4) informed how potential differences in early warning processes were measured. Differences in the performance of the MEWS between ethnic groups was explored by modification of the MEWS with additional prognostic factors, understanding statistical interaction between the MEWS and other risk factors, as well as adjustment for sources of confounding.

The English MEWS was based on prospectively-collected data on the vital signs of healthy pregnant women(15). These vital signs are the respiratory rate (RR), oxygen saturation (%, SpO_2), temperature (T), heart rate (HR), systolic blood pressure (SBP) and diastolic blood pressure (DBP). This MEWS is currently being rolled out nationally(395). In order to understand how implementation of a new tool may affect the care of women from different ethnic groups, it is necessary to measure the ability of the MEWS to predict SMM within ethnic groups and then to understand how the modification of the MEWS with validated prognostic factors previously identified (chapter 3) may impact performance within ethnic groups. The rationale for this research was that EWSs may perform differently among individual ethnic groups because of differences in the rate of SMM between groups (identified in Chapter 3), differences in either the distribution or strength of risk factors within ethnic groups (identified in Chapter 3), or differences in the downstream early warning process after an EWS-based alert has been generated (identified in Chapter 4). Identifying the potential reason for differences means that an advanced EWS may be developed to handle these reasons equitably by specifying a clinical prediction model that maximises performance across all ethnic groups and embedding it within an early warning process that minimises ethnic biases.

6.2 Methods

6.2.1 Source of data

Routinely-collected data were extracted from electronic pregnancy records and linked to routinely-generated administrative maternity and discharge data of women who received care from one NHS Trust comprised of one acute general hospital, two district general hospitals, as well as community-based outpatient settings. Prospectively-collected data from the electronic pregnancy record included demographic information, medical history, obstetric history, electronic vital signs data, and clinical diagnoses and events collected through structured fields and proformas. Administrative data included International Classification of Diseases (10^{th} edition) clinical diagnostic codes(43). These

data were submitted by the relevant NHS services into the Thames Valley and Surrey Secure Data Environment (SDE) and accessed and analysed within the SDE. Patient identifiers were removed and linkage of these data was achieved within the SDE using a hashed NHS number (a pseudonymised unique identifier derived from the NHS number using a one-way hashing algorithm) prior to access to the data. Research Ethics Committee (reference 24/SC/0132) approval was obtained through the DREaMED study, granted on 12th June 2024. Confidentiality Advisory Group (reference 24/CAG/0060) approval was also obtained through the DREaMED study that allowed access to confidential electronic medical records without specific written consent (Section 251 support), granted on 29th July 2024.

6.2.2 Sample

Eligible maternity episodes were those of women who were 16 years of age or above who received care at any point between 20 weeks of gestational age and 6 weeks postpartum. Maternity episodes were excluded if they did not have at least one full set of electronically-recorded vital signs (HR, RR, SpO_2, T, SBP, DBP) recorded at the same point in time.

6.2.3 Outcome

The outcome of severe maternal morbidity is shown in Table 6-1. This definition was based on the systematic review conducted in chapter 2, informed by the application of the World Health Organisation (WHO)(80) definition of SMM applied to administrative data in high-income settings. Components for which there was not a high consensus across the existing literature but which appeared to map to aspects of the WHO definition were discussed with a multidisciplinary panel of experts, including an anaesthetist, intensivist, midwife, obstetric physician, obstetrician, and epidemiologist to determine inclusion or exclusion based on the specific features of the potential phenotype in the electronic health record. Where these data were not reliably recorded, clinical

measures were replaced with diagnostic codes in conjunction with a reliably-recorded and time-stamped clinical event that indicated the onset of a severe complication. Acute renal failure was not included because it was not possible to reliably distinguish between transient acute kidney injury and severe disease due to data quality concerns with renal function tests. However, severe renal disease is more likely to occur in combination with another component of the definition; for example, women with severe pre-eclampsia, severe haemorrhage, sepsis are likely to be included through these indicators(396).

6.2.4 Process Measures

Maternal medical review within 2 hours was defined as any documented electronic medical review by a doctor of any grade or specialty that was not produced as part of planned care (i.e. only unscheduled medical reviews were considered) that occurred within 2 hours of an EWS being measured. Two hours allowed time for repeat measurement as indicated by the local escalation policy, escalation, a medical response, and the documentation of the response. This form of documentation was the way in which medical care and its findings were recorded according to the local policy and training on use of the electronic maternity health record. Neither the exact trigger for a medical review nor the content of the medical documentation were extracted or reviewed.

Table 6-1 Definition of Severe Maternal Morbidity

Component	Clinical	ICD-10	Basis for Inclusion
Haemorrhage	Documented blood loss of 2,000 mls or ≥30% of weight-based circulating blood volume.		Systematic review
Sepsis	Diagnostic code or surgical intervention (return to theatre, laparotomy, drainage of collection) + 2 or more of: T <36^{o}c or >38^{o}c (x2, >4 hours apart); HR >100 BPM (x2, >4 hours apart); RR >20 RPM (x2, >4 hours apart); WCC <4 or >17 x10^9/L	In addition to O85	Systematic review
Disseminated intravascular coagulation	Fibrinogen <2g/L		Systematic review
Cardiac arrest		I460	Systematic review
Myocardial infarction		I211, I213, I214, I219, I249	Systematic review
Pulmonary oedema		J81	Systematic review
Eclampsia		O15	Systematic review
Pulmonary embolism		O882, I26	Systematic review
Acute respiratory distress syndrome		J80	Systematic review
Coma		R402, G936	Systematic review
Stroke		I60, I61, I62, I63, I64	Systematic review
Respiratory failure		J960	Expert review, informed by WHO definition
Acute Liver Failure		K711, K720, K763	Expert review, informed by WHO definition
Status asthmaticus		J46	Expert review, informed by WHO definition
Diabetic ketoacidosis		E10, E11	Expert review, informed by WHO definition
Peritonitis		K650, N733	Expert review
Severe hypertension with end-organ injury	SBP ≥160 or DBP ≥110 with protein:creatinine ratio ≥30 mg/mmol or creatinine ≥90 umol/L or ALT or AST ≥40 IU/L or platelets <150,000 uL or bilirubin ≥20 umol/L		Expert review

HR heart rate, BMP beats per minute, RR respiratory rate, RPM respirations per minute, WCC white cell count, SBP systolic blood pressure, DBP diastolic blood pressure, ALT alanine aminotransferase, AST aspartate aminotransferase.

6.2.5 Exposures

Maternal ethnicity was self-described at the booking appointment and recorded in the electronic pregnancy record. For this analysis, ethnic groups were categorised into higher-level groups based on the Office for National Statistics classification(397). These were:

- Asian/Asian British (Bangladeshi, Chinese, Indian, Pakistani, any other Asian background)
- Black/African/Caribbean/Black British (African, Caribbean, any other Black/African/Caribbean background)
- Mixed/Multiple ethnic groups (White and Black Caribbean, White and Black African, White and Asian, any other Mixed/Multiple ethnic backgrounds)
- White (English/Welsh/Scottish/Northern Irish/British, Irish, Gypsy or Irish Traveller, any other White background)
- Other ethnic groups (including Arabic or other ethnic groups).

6.2.6 Covariables

Prognostic factors were selected based on the systematic review conducted in chapter 3. These included maternal age (continuous), Index of Multiple Deprivation score (continuous), parity (discrete), number of previous caesarean sections (discrete), multiple pregnancy (binary), body mass index (continuous), and pre-existing conditions, which were all collected at the booking appointment, as well as the gestational age at which the booking appointment occurred (continuous, measured in discrete days). Pre-existing conditions included any pre-pregnancy hypertension, diabetes, renal disease, sickle cell disease or haemoglobinopathies, and substance dependency or misuse (all individual binary measures), which were replicated prognostic factors for which there was strong evidence. Cardiac disease and liver disease as recorded in the early pregnancy risk assessment proformas were highly heterogeneous groups that included unrelated conditions and were not included. Gestational age at MEWS measurement (continuous, measured in

discrete days) and whether a woman had given birth at the point of vital sign measurement (binary) were collected from the electronic record of the vital signs and from the electronic birth record.

6.2.7 Statistical analysis

The characteristics of participants were described overall and according to ethnicity using means and standard deviations, counts and percentages, or medians and interquartile ranges as appropriate. Marginal mean values for the vital signs that comprise the national MEWS were described with 95% confidence intervals using linear regression with clustered standard errors to account for the clustering of vital signs within maternities. Mean vital signs were compared across groups using the global cluster-robust Wald test. Complete sets of vital signs were converted into a single summary score using the matrix of the national MEWS(15).

Performance was described at the level of the clinical risk categories according to the MEWS protocol (low risk, low-medium risk, medium risk, high risk) using positive predictive values (PPV). Due to the repeat measurement of the vital signs, validation was then conducted at the level of the individual MEWS or the set of vital sign observations using a wider range of measures. Each MEWS was included in the evaluation only if the last included MEWS was more than six hours previous. This was to reduce clustering within latent periods of acute illness/care, to reduce noise from repeat identical scores with the same outcome, and to reduce over-estimation of the performance of the MEWS. Logistic regression was used to model the composite outcome of SMM on the MEWS. The MEWS was included as a continuous, linear score based on an exploration of the functional form of the MEWS on the log-odds scale, which is the appropriate scale for logistic regression, using fractional polynomials. Although the association was linear on the log-odds scale, this corresponds with a non-linear relationship on the probability scale. Each observation (row) represented a single measured MEWS with an associated binary indicator as to whether an event occurred within the specified number of hours (referred to as the ‘time horizon’). This approach represented a form of

discrete-time time-dependent covariate modelling(398). The occurrence of SMM within 12 hours, 24 hours, and 48 hours was evaluated(30) using separate models for each outcome. Additionally, to reduce the influence of extreme scores at the time a severe complication may have either occurred or may have been unpreventable, or at the time a woman was already in receipt of acute or critical care, MEWS that were measured in the 2 hours prior to a severe complication were removed from the analysis data set(30).

All measures of MEWS performance were evaluated within individual ethnic groups (Asian, Black, Mixed, 'Other' groups, White). The effect of adding additional prognostic factors for SMM to the performance within individual ethnic groups was tested. These prognostic factors were selected based on the findings from the systematic review of prognostic factors reported in Chapter 3 (thesis objective 2). Prognostic factors that were generalisable for which there was strong evidence were included: maternal age, parity, Index of Multiple Deprivation score(399), previous caesarean section, pre-existing conditions, multiple pregnancy, as well as gestational age at MEWS measurement. These prognostic factors also reflected those whose prevalence was observed to differ between ethnic groups in Chapter 3. Additionally, gestation at booking (the first antenatal appointment with a midwife) was included on the basis that the strength of its association with SMM differed by ethnic group in two independent studies, as reported in Chapter 3. Whether a woman was antenatal or postnatal was also included, in response to HCWs perspectives on this aspect of clinical context, in Chapter 4. The functional form of other continuous variables was also explored using fractional polynomials. The baseline model contained only the MEWS. Additional prognostic factors were all added to the model individually and then in combination. Statistical interaction was tested if effect modification was suspected, including for gestational age and MEWS, parity and MEWS, and ethnicity and MEWS. The additional prognostic factors, including interaction terms, were then combined into one model referred to as the 'modified MEWS'. The modified MEWS model was compared with and without ethnicity. Interaction between ethnicity and MEWS

was additionally considered on the additive scale using the relative excess risk due to interaction (RERI)(400). Inclusion of location of vital sign measurement was not considered desirable as this conditions prediction on local context and means that an advanced EWS would not be generalizable. It would be expected that including location in a prediction model would improve performance because it reduces heterogeneity. Nevertheless, to understand the potential impact of population structure on ethnic inequalities, the adjustment for location was explored as an addition to the modified MEWS and the interaction analysis.

All models included all ethnic groups and the general model was then evaluated within individual ethnic groups. Discrimination was estimated using the c-statistic, which represents the probability that, for a pair of observations in which one experienced the outcome and one did not, the model assigns a higher predicted risk to the observation with the outcome(401). Improvement in prognostic performance for individual additional predictors and then the modified MEWS was compared using the percentage change Brier score(402), relative to the MEWS. For the MEWS, the observed probability of a severe complication (y-axis) was plotted against the score values (x-axis). For the modified MEWS models, calibration was quantified using the calibration intercept, slope, and visualisation of moderate calibration for these models, with the risk of SMM (y-axis) plotted against deciles of the continuous predicted probability (x-axis)(403). Net benefit per 10,000 vital signs was calculated to understand the potential clinical impact. This was defined as:

$$\text{Net benefit} = (TP/N) - (FP/N) \times (T/(1 - T))$$

Where TP denoted true positives, FP false positives, N the sample size, and T the decision threshold, whereby net benefit is the number of true positives after penalisation of false positives weighted by the decision threshold(404), compared to a counterfactual policy where no MEWS generates an alert at all. For EWSs, an alert for escalation is typically triggered at a low decision threshold. A higher decision threshold leads to a greater penalisation of false positives, which reflects a higher assumed

clinical cost. Net benefit was calculated based on a range of decision thresholds based on the predicted probabilities that corresponded with the MEWS values. These measures of model performance were compared between the MEWS and the modified MEWS. The 'MEWS' model contained only the summary score for the national MEWS(15) whereas the 'modified MEWS' model included the MEWS and additionally gestational age at MEWS measurement, maternal age, parity, previous caesarean birth, pre-pregnancy hypertension, pre-pregnancy diabetes, pre-pregnancy renal disease, sickle cell disease or haemoglobinopathies, substance dependency or misuse, plurality, gestational age at booking, ethnic group, and interaction terms between MEWS and ethnic group, MEWS and parity, and MEWS and gestational age at measurement. Net benefit was the primary measure of clinical utility.

Separately, to understand the potential mediating effect of treatment based on vital sign abnormalities, the receipt of a medical review within 2 hours of the vital sign measurement was entered into the models. To understand whether biases in the early warning pathways may influence care, the rate ratio ('relative risk') of receipt of a documented medical review within 2 hours of vital sign measurement was estimated using Poisson regression with robust standard errors, given that this was not a rare outcome.

6.2.8 Sensitivity analyses

First, because physiological changes occur at distinct time points in pregnancy and the prevalence of individual complications differs according to the stages of pregnancy, the MEWS was evaluated within the antenatal period and the postnatal period separately. Second, the MEWS-only, MEWS and ethnicity, and full models were refit and the performance tested among an expanded range of ethnic groups, in which 'Black' was divided into 'Black African' and 'Black Caribbean' and in which 'Asian' was divided into 'Bangladeshi', 'Indian', 'Pakistani' to understand whether the performance differed within these higher-level groups.

6.2.9 Missing data

The main results are based on a complete case analysis so that the validation reflects its use in clinical practice rather than the theoretical use of a MEWS at times when it was not measured or used in actual clinical practice. There are a range of clinical situations that may involve measurement of the vital signs outside of a MEWS or that involve the measurement of individual vital signs in the intervening period between MEWS measurements. Secondarily, the performance of the MEWS and modified MEWS was evaluated in situations where a comprehensive physiological assessment was likely desirable or intended. Vital sign measurement points with ≤2 missing vital signs were first imputed with a score of 0 on the basis that this was the information available to the healthcare worker (unmeasured and therefore uninformative) and because healthcare workers may have omitted individual vital signs if they appeared or anticipated the vital sign would be normal. Separately, the same ≤2 missing vital signs were imputed using multiple imputation by chained equations to generate 10 imputed data sets. The vital signs rather than summary scores were entered into the multiple imputation procedure, as well as maternal ethnicity and all covariables from the modified MEWS model, including all outcome-time horizons. Auxiliary variables were selected based on their association with both the known values of a variable with missing data and missingness of the same variable in order to strengthen the missing at random assumption. These included blood loss at delivery, whether a sepsis protocol was triggered, the diagnosis of pregnancy-induced hypertension, gestational diabetes, mode of birth, gestational age at birth, maternal education, and the individual components of the composite outcome. The imputation of up to two missing vital signs ensured there was sufficient data observed at each time point to strengthen the missing at random assumption.

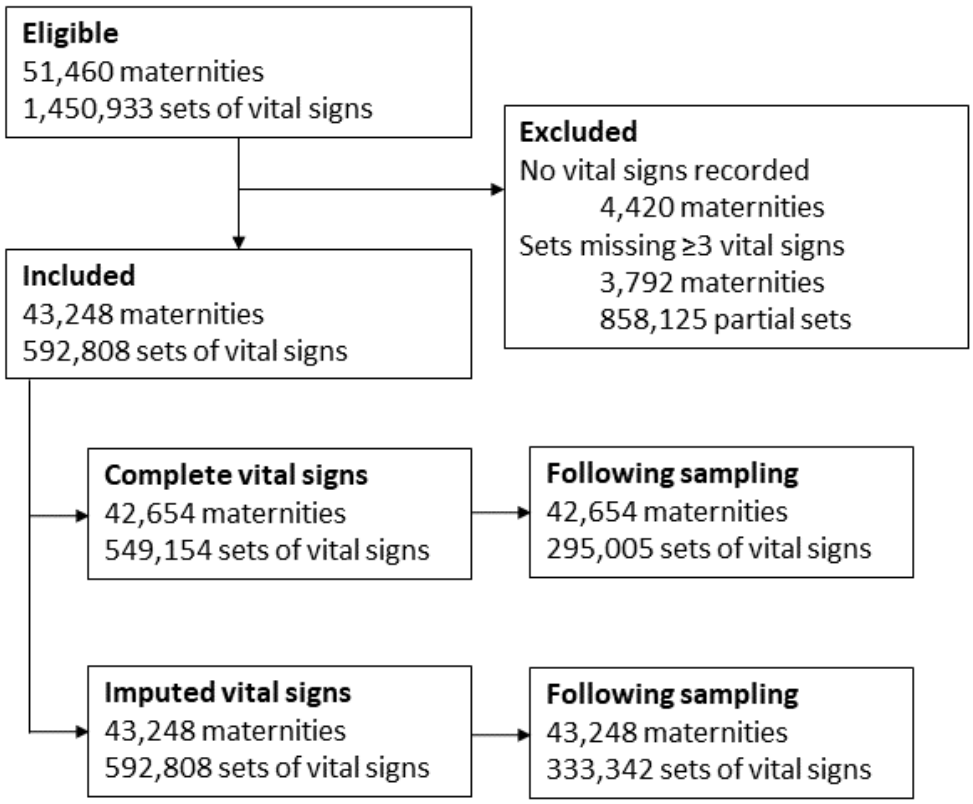
Ethnicity was initially complete for 81.9% of vital signs, which was the level of observation for these analyses. Missing maternal ethnicity was replaced with a baby's ethnicity where available and where a baby was assigned a single ethnic group, leading to complete ethnicity for 93.4% of vital signs in

the primary analysis. Maternal age and previous caesarean section were both missing for 6.0% of vital signs. Therefore, the analyses were repeated following multiple imputation of ethnic group and covariables alongside the vital signs as described above. Analyses were conducted across all imputed data sets and combined using Rubin's rules or else by reporting the mean value across imputed data sets.

6.3 Results

There were 40,202 women who contributed 47,040 maternities. Over the course of these 47,040 maternities, 1,450,933 sets of vital signs were measured, including both individual vital signs or multiple vital signs that were measured at the same time. This represented a median of 23 (IQR 14-38) vital sign measurement events per maternity. Of the 47,040 maternities, 42,654 had at least one documented complete set of vital signs. In total, there were 549,154 complete sets of vital signs (38%, 549,154/1,450,933) from which a MEWS could be measured. This represented a median of 8 (IQR 5-14) complete MEWS per maternity. After the removal of vital signs repeated within 6 hours, there were 295,005 MEWs (54% of all complete sets, 295,005/549,154), representing a median of 3 (IQR 1-7) MEWS per maternity. The flow diagram is shown in Figure 6.1. Among women who had at least one MEWS, the rate of SMM was 1.7% (740/42,654). At the level of the MEWS, 0.10% (309/295,005) MEWS were followed by a severe complication within 12 hours; 0.19% (547/295,005) within 24 hours; and 0.30% (872/295,005) within 48 hours. The rate of SMM at the level of the EWS is shown in Table 6.2.

Figure 6-1 Flow Diagram



More White women resided in the least deprived areas whereas Asian women and women from the 'other' ethnic group resided in the most deprived areas, compared with all other groups. A higher percentage of women who were Black were multiparous and had a previous caesarean birth, compared with all other groups. Mean maternal age and median gestational age at birth were similar across groups. Whilst White women's vital signs were predominantly measured in 'Hospital 1', all other ethnic groups' vital signs were predominantly measured in 'Hospital 2', out of all hospital and community locations for measurement of the vital signs. The starkest difference was for Asian women for whom 20% of the vital signs were measures in 'Hospital 1' and 74% in 'Hospital 2'. The full range of baseline characteristics is shown in Table 6.3. The vital signs were similar across groups with small differences. The highest mean heart rate was among Asian women, 90.3 (90.1-90.5) beats per minute (BPM), and lowest among White women, 88.2 (88.0-88.3) BPM. Systolic blood pressure

was highest among White women, 118 (118-118) mmHg, and lowest among Asian women, 115 (115-115) mmHg, shown in Appendix Table D6.1. The median gestational age of vital sign measurement for Asian women was 38 weeks and 4 days; for Black women was 39 weeks; for women from mixed ethnic backgrounds was 38 weeks and 2 days; for other ethnic groups was 39 weeks; and for White women was 38 weeks and 2 days. The distribution of vital signs over gestational age for each ethnic group is shown in Figure 6.2.

6.3.1 Predictive values

Overall, the positive predictive values for the MEWS were 0.16%, 0.38%, 0.51%, and 2.99% at score thresholds of 1 (non-zero low risk group and above), 2 (low-medium risk and above), 5 (medium risk and above), and 8 (high risk and above), respectively. The positive predictive values were highest for Black women. Some groups had no events within the upper risk categories. These results are shown in Appendix Table D6.2.

Table 6-2 Rate of Severe Maternal Morbidity over 12-hour, 24-hour, and 48-Hour Time Horizons per 10,000 Sets of Vital Signs

	Overall	**Asian**	**Black**	**Mixed**	**Other**	**White**
SMM-12 hours						
n/N	309/295,005	97/109,082	42/26,893	5/9,796	15/11,152	139/129,837
Rate per 10,000	10 (9.4-12)	8.8(7.3-11)	16 (12-21)	5.1 (2.1-12)	13 (8.1-22)	11 (9.1-13)
SMM-24 hours						
n/N	547/295,005	176/109,082	76/26,893	7/9,796	24/11,152	246/129,837
Rate per 10,000	19 (17-20)	16 (14-19)	28 (23-35)	7.1 (3.4-15)	22 (14-32)	19 (17-21)
SMM-48 hours						
n/N	872/295,005	283/109,082	116/26,893	9/9,796	35/11,152	400/129,837
Rate per 10,000	30 (28-32)	26 (23-29)	43 (36-52)	9.2 (4.8-18)	31 (23-44)	31 (28-34)

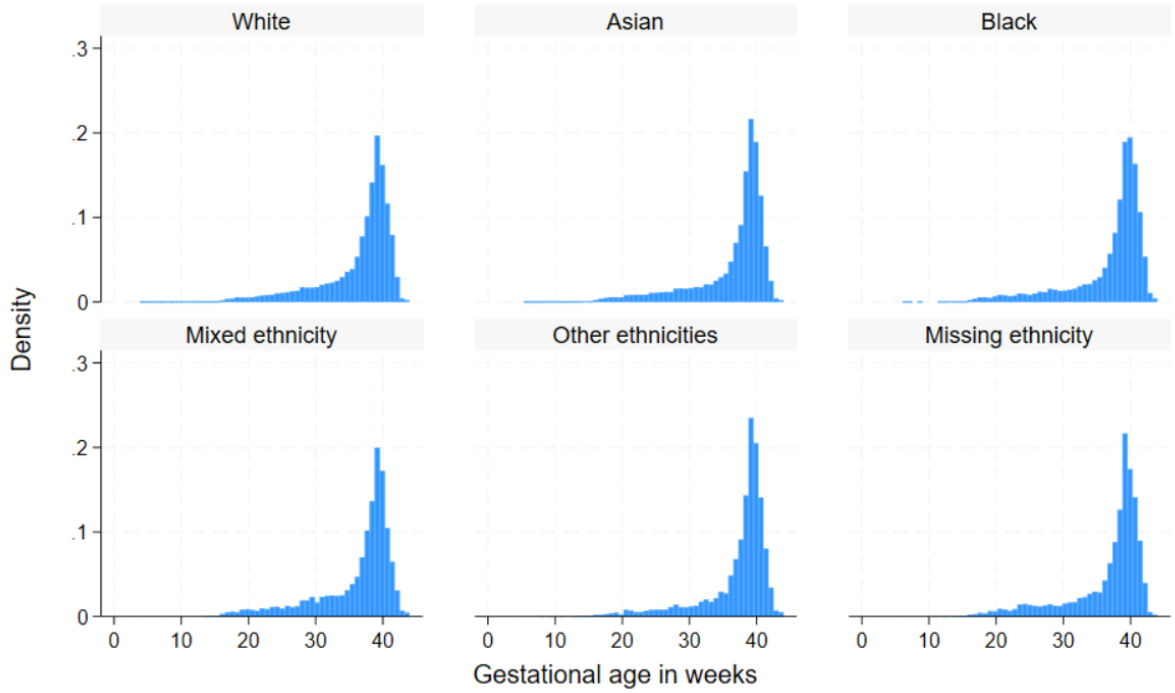
SMM-12, -24, and -48 represent severe maternal morbidity that occurred over 12, 24, and 48 hour time horizons, respectively.

Table 6-3 Baseline Characteristics by Ethnicity at the Level of the MEWS

	Overall	Asian	Black	Mixed	Other	White
Maternal characteristics	295,005 (100%)	109,082 (37%)	26,893 (9.1%)	9,796 (3.3%)	11,152 (3.8%)	129,837 (44%)
Maternal age, mean years (sd)	29.82 (5.8)	30.4 (5.5)	31.2 (5.6)	28.3 (6.0)	29.3 (6.4)	29.2 (5.8)
IMD percentile, median (IQR)	87 (58-94)	90 (76-95)	81 (92-96)	89 (66-95)	91 (77-95)	72 (42-92)
Nulliparous, n (%)	138,152 (47)	51,520 (47)	11,221 (42)	4,831 (49)	4,473 (40)	61,565 (48)
Primiparous, n (%)	78,215 (27)	27,533 (25)	6,456 (24)	2,466 (25)	2,854 (26)	31416 (24)
Multiparous, n (%)	78,638 (27)	30,029 (28)	9,216 (34)	2,499 (26)	3,825 (34)	33,906 (25.6)
Previous CS, n (%)	54,605 (19)	22,969 (21)	5,834 (22)	1,527 (16)	2,259 (20)	20,516 (16)
Gestational age at birth, median weeks (IQR)	39.1 (38.0-40.0)	39.1 (38.0-40.0)	39.3 (38.0-40.4)	39.1 (37.7-39.9)	39.1 (38.1-40.1)	39.0 (37.9-40.0)
Location of vital sign measurement						
Hospital 1, n (%)	77,857 (27)	13,660 (13)	6,264 (23)	3,002 (31)	2,167 (20)	51,235 (40)
Hospital 2, n (%)	138,719 (47)	64,674 (60)	11,708 (44)	3,997 (41)	6,063 (55)	51,235 (40)
Hospital 3, n (%)	33,716 (12)	17,579 (16)	3,802 (14)	1,382 (14)	1,331 (12)	8,580 (7)
Other sites, n (%)	25,507 (8.7)	6,988 (6.4)	988 (3.7)	651 (6.7)	777 (7.0)	14,043 (11)

Maternal age missing for 18,829 observations; gestational age at birth missing for 1,764 observations; location of vital sign measurement missing for 2,772 observations. Maternal ethnicity was missing for 8,245 observations (not shown).

Figure 6-2 Distribution of Vital Sign Measurement by Gestational Age and Ethnicity



6.3.2 Discrimination

Overall, discrimination was moderate across all time horizons, with 12-hour, 24-hour, and 48-hour time horizons for SMM of 0.64 (0.60-0.67), 0.60 (0.58-0.62), and 0.59 (0.57-0.61) for the MEWS. The addition of predictors led to small improvements but the relative gain in c-statistic when predictors were added was greater for 24- and 48-hour SMM, compared with 12-hour SMM. The addition of interaction terms MEWS and gestational age, MEWS and ethnicity, and MEWS and parity did not lead to substantial improvement in model discrimination. The largest improvement was for the fully-adjusted models that included ethnicity itself, for 12-, 24-, and 48- hour time horizons: 0.70 (0.67-0.73), 0.68 (0.66-0.70), and 0.65 (0.64-0.67), respectively. Discrimination was consistently higher for Black women, which remained in the 'good' range for 12- and 24-hour time horizons and moderate for the 48-hour time horizon. Improved discrimination was also found among women of mixed ethnicity. A summary of the discriminative performance for the MEWS and modified MEWS model

across time horizons is shown in Table 6.3. The full results are shown in Appendix Tables D6.3 to D6.5 and summarised in Table 6.4.

Table 6-4 Summary of Discriminative Performance

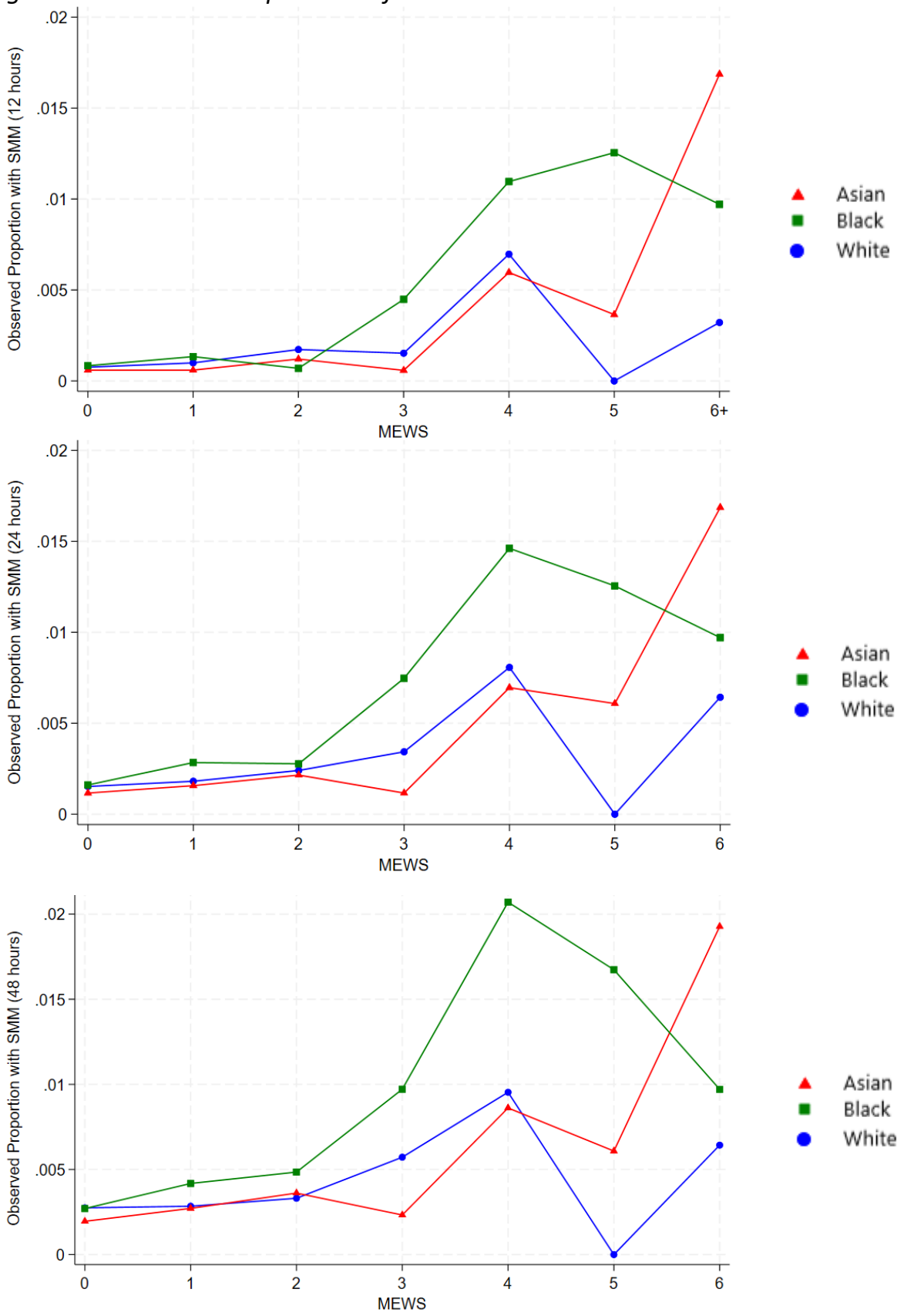
	Overall	**Asian**	**Black**	**Mixed**	**Other**	**White**
SMM-12	c-statistic	c-statistic	c-statistic	c-statistic	c-statistic	c-statistic
	(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)	(95% CI)
MEWS	0.64	0.64	0.71	0.71	0.57	0.61
	(0.60-0.67)	(0.59-0.70)	(0.63-0.79)	(0.38-1.00)	(0.44-0.70)	(0.57-0.66)
Modified MEWS	0.70	0.70	0.76	0.73	0.54	0.66
	(0.67-0.73)	(0.65-0.76)	(0.69-0.84)	(0.40-1.00)	(0.39-0.69)	(0.62-0.71)
SMM-24						
MEWS	0.60	0.61	0.67	0.73	0.56	0.57
	(0.58-0.62)	(0.57-0.65)	(0.61-0.73)	(0.50-0.96)	(0.45-0.66)	(0.54-0.61)
Modified MEWS	0.68	0.71	0.70	0.74	0.59	0.63
	(0.66-0.70)	(0.67-0.75)	(0.64-0.76)	(0.53-0.95)	(0.47-0.71)	(0.60-0.66)
SMM-48						
MEWS	0.58	0.59	0.64	0.71	0.56	0.55
	(0.56-0.60)	(0.56-0.63)	(0.59-0.70)	(0.50-0.92)	(0.46-0.65)	(0.52-0.57)
Modified MEWS	0.65	0.69	0.66	0.72	0.63	0.60
	(0.64-0.67)	(0.66-0.72)	(0.60-0.71)	(0.54-0.90)	(0.53-0.72)	(0.57-0.62)

SMM-12, -24, and -48 represent severe maternal morbidity that occurred over 12, 24, and 48 hour time horizons, respectively. A c-statistic <0.60 was considered to be poor, 0.60-0.69 moderate, and ≥0.70 good(405). MEWS maternal early warning score; Modified MEWS denotes the model that includes the MEWS with additional predictors (gestational age, maternal age, parity, previous caesarean, pre-existing conditions, plurality, gestational age at booking, ethnicity, and interaction terms between the MEWS and ethnicity, the MEWS and parity, and the MEWS and gestational age).

6.3.3 Calibration

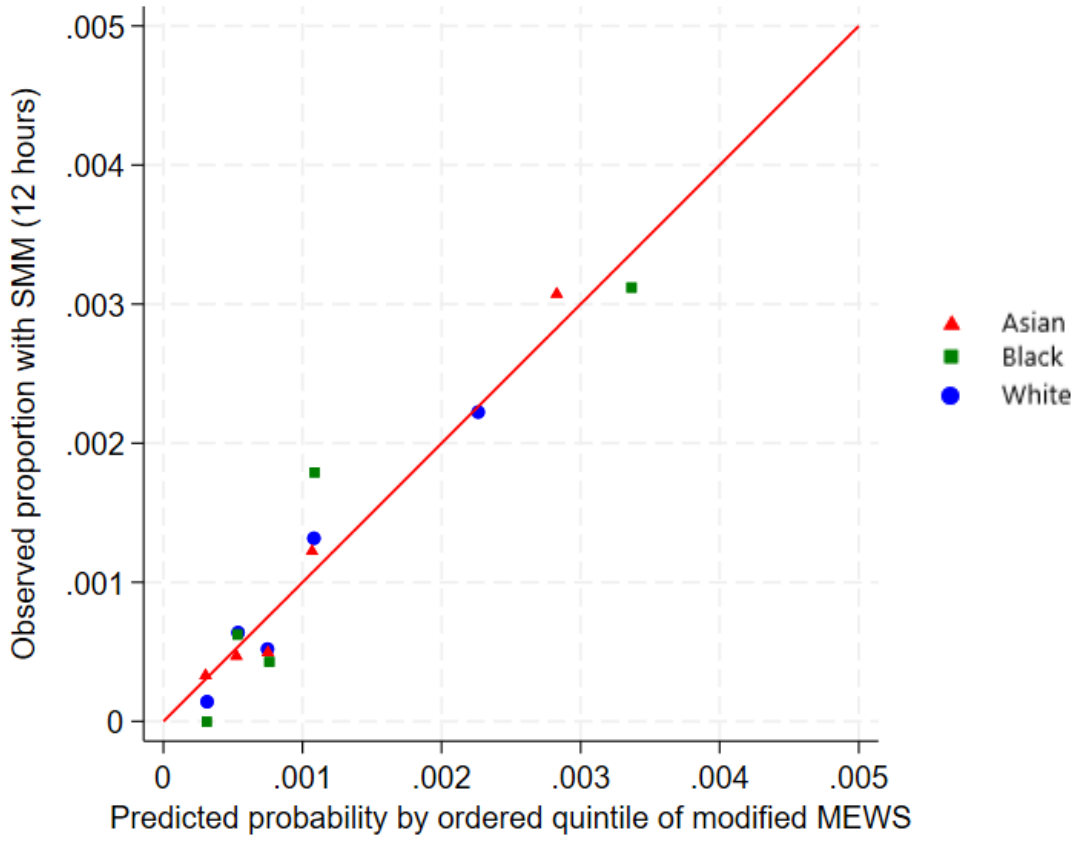
For the MEWS, the scatter plots comparing the observed probabilities of SMM over MEWS values (concatenated at 6 or above) identified a higher risk of SMM among Black women over a MEWS of 3-5, compared with Asian or White women but a higher risk of SMM among Asian women at the highest scores. This was the same over all three time horizons, shown in Figure 6.3. For the modified MEWS, calibration plots of observed probabilities of SMM over ordered quintiles of the predictive score from the model reflected the limited predictive range, which increased with time horizon. There was evidence of under-prediction among Black women across all time horizons, shown in Figure 6.4 to 6.6. The effect of adding individual prognostic factors to the MEWS differed according to ethnic group. For SMM over 12 hours, the scaled Brier scores indicated that all prognostic factors together without ethnicity worsened prognostic performance whereas the addition of ethnicity to all prognostic factors led to an improvement, compared to the MEWS. The addition of interaction terms (MEWS and gestational age, MEWS and ethnicity, and MEWS and parity) did not meaningfully enhance prediction. A similar pattern was true for both SMM over 24- and 48-hours except that all prognostic factors without ethnicity demonstrated improvement and the addition of ethnicity or interaction terms made no difference over either time horizon. The percentage change in Brier scores are shown in Appendix Tables D6.6 to D6.8.

Figure 6-3 Observed Proportions of Women with SMM over MEWS Values



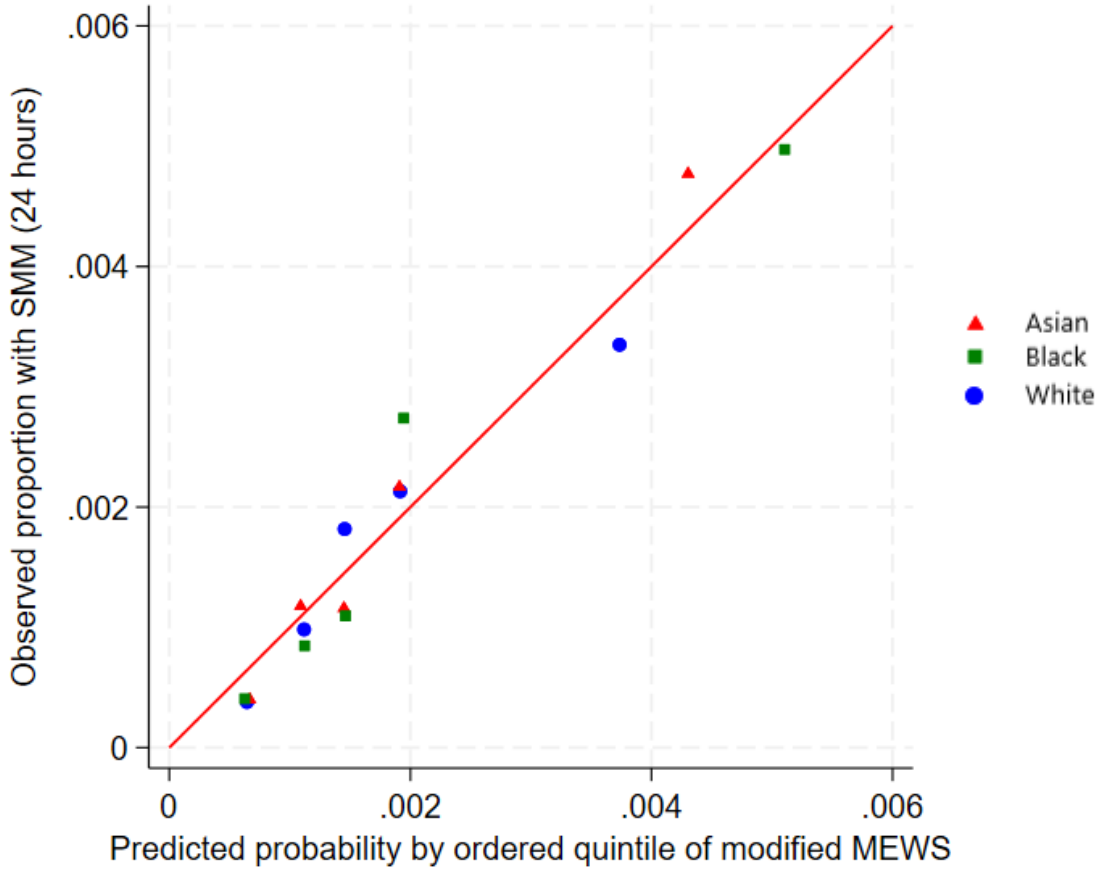
SMM severe maternal morbidity, MEWS maternal early warning score

Figure 6-4 Observed Proportions of Women with SMM (12 Hours) over Ordered Quintiles of the Modified MEWS



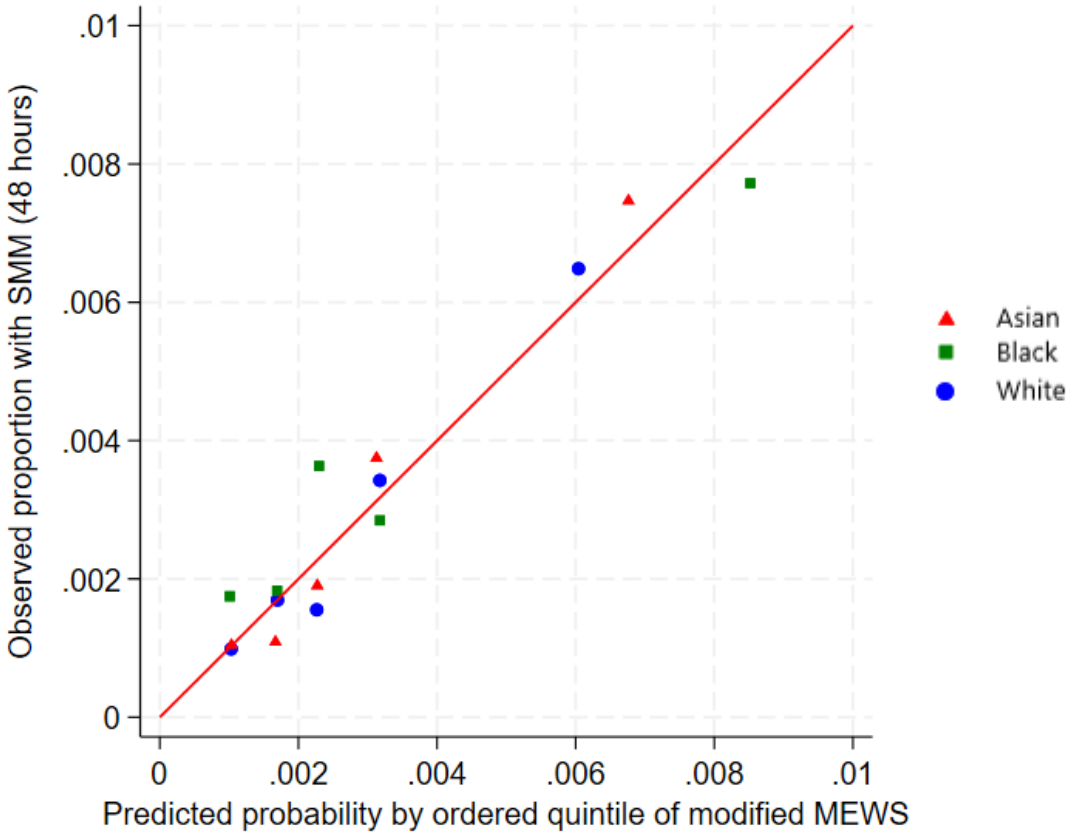
SMM severe maternal morbidity, MEWS maternal early warning score.
Calibration plots show the relationship between predicted and observed probabilities of SMM. Predicted probability of severe maternal morbidity (SMM) is shown on the x-axis, within quintiles of the risk score from the modified maternal early warning score (MEWS). The observed rate of SMM for each quintile is shown on the y-axis. Plotted values represent the mean predicted probability within each quintile for Asian, Black, and White women separately.

Figure 6-5 Observed Proportions of Women with SMM (24 Hours) over Ordered Quintiles of the Modified MEWS



SMM severe maternal morbidity, MEWS maternal early warning score.
Calibration plots show the relationship between predicted and observed probabilities of SMM. Predicted probability of severe maternal morbidity (SMM) is shown on the x-axis, within quintiles of the risk score from the modified maternal early warning score (MEWS). The observed rate of SMM for each quintile is shown on the y-axis. Plotted values represent the mean predicted probability within each quintile for Asian, Black, and White women separately.

Figure 6-6 Observed Proportions of Women with SMM (48 Hours) over Ordered Quintiles of the Modified MEWS



SMM severe maternal morbidity, MEWS maternal early warning score.
Calibration plots show the relationship between predicted and observed probabilities of SMM. Predicted probability of severe maternal morbidity (SMM) is shown on the x-axis, within quintiles of the risk score from the modified maternal early warning score (MEWS). The observed rate of SMM for each quintile is shown on the y-axis. Plotted values represent the mean predicted probability within each quintile for Asian, Black, and White women separately.

6.3.4 Net benefit

For SMM-12 overall, the MEWS demonstrated a net benefit equivalent to 1.6 true positives per 10,000 MEWS at a score of 1 and 0.92 true positives per 10,000 at a score of 2, compared to no alert system being in place. For SMM-24, net benefit was 1.5 and -0.045 per 10,000, at a MEWS of 1 or 2, respectively, and for SMM-48 the same figures were 1.5 and -0.71, respectively. Net benefit differed by ethnic group. At a MEWS of 2, at which clinical escalation is indicated, net benefit for SMM-12 ranged from 5.3 among Black women to 0.91 for White women, per 10,000 MEWS, for SMM-24 ranged from 6.5 among Black women to -0.070 to the women from other ethnic groups, and for SMM-48 ranged from 9.0 among Black women to -0.22 for Asian women.

The modified MEWS for SMM-12 demonstrated an improved net benefit of 3.8 and 2.2 per 10,000 MEWS at a score of 1 and 2, respectively. For SMM-24, 3.2 and 2.2, respectively, and for SMM-48, 8.4 and 5.4, respectively. There was positive net benefit among all ethnic groups for all time horizons at a MEWS score of 1 or 2. At a MEWS of 2, net benefit for SMM-12 ranged from 5.6 for Black women to 1.6 for White women. For SMM-24, the range was 7.6 for Black women and 0.66 for women from 'other ethnic groups'. For SMM-48, 12 for Black women and 0.055 for women of mixed ethnicity. The full results for net benefit are shown in Tables 6.5 to 6.7.

6.3.5 Effect modification

There was evidence of both statistical (multiplicative) and additive interaction between ethnic group and MEWS for all time horizons without adjustment and for 12- and 48-hours with adjustment. The baseline risk of SMM was lower among Asian women compared with White (all time horizons) whereas no difference was observed between Black women compared with White. For SMM over 12 hours after adjustment, the ORs per 1-unit increase in the MEWS for Asian, Black, and White women were 1.75 (95% CI 1.56-1.96), 1.89 (95% CI 1.60-2.24), and 1.56 (95% CI 1.39-1.75), respectively. For

SMM over 48 hours after adjustment, the same ORs were 1.43 (95% CI 1.32-1.56), 1.63 (95% CI 1.45-1.83), and 1.30 (95% CI 1.19-1.41) respectively, with the ORs for SMM over 24 hours lying between the two. The relative excess risks due to interaction, after adjustment, were not significant for Asian women over any time horizon and were significant for all time horizons for Black women without adjustment and significant for SMM over 24 and 48 hours after adjustment, shown in Appendix Table D6.9 (unadjusted) and Table 6.8 (adjusted). Additional adjustment for location did not meaningfully alter the estimates and the findings regarding additive interaction were unchanged.

Table 6-5 Net benefit per 10,000 MEWS by ethnicity (12-hour time horizon)

Probability threshold (corresponding MEWS value)	**Overall**	**Asian**	**Black**	**Mixed**	**Other**	**White**
MEWS						
0.0010 (MEWS = 1)	1.6	1.1	6.2	-0.90	3.8	2.0
0.0016 (MEWS = 2)	0.92	2.3	5.3	1.9	1.3	0.91
0.0024 (MEWS = 3)	0.13	1.3	3.4	2.3	-0.99	0.59
0.0038 (MEWS = 4)	-1.6	0.036	0.50	-0.29	-0.65	-0.57
0.0059 (MEWS = 5)	-2.8	-0.44	-0.033	-0.45	-1.0	-0.94
Modified MEWS						
0.00097 (MEWS = 1)	3.8	3.4	7.3	2.0	4.3	3.4
0.0014 (MEWS = 2)	2.2	2.2	5.6	1.9	4.1	1.6
0.0023 (MEWS = 3)	1.3	1.7	4.0	0.83	1.3	0.71
0.0039 (MEWS = 4)	0.28	0.66	2.7	0.59	-0.10	-0.31
0.0071 (MEWS = 5)	-0.73	0.025	-0.12	-1.9	-0.062	-1.2

MEWS maternal early warning score; Modified MEWS denotes the model that includes the MEWS with additional predictors (gestational age, maternal age, parity, previous caesarean, pre-existing conditions, plurality, gestational age at booking, ethnicity, and interaction terms between the MEWS and ethnicity, the MEWS and parity, and the MEWS and gestational age). Threshold denotes various levels at which a MEWS may be programmed to trigger an alert. Figures rounded to two significant figures

Table 6-6 Net benefit per 10,000 MEWS by ethnicity (24-hour time horizon)

Probability threshold (corresponding MEWS value)	Overall	Asian	Black	Mixed	Other	White
MEWS						
0.0019 (MEWS = 1)	1.5	1.1	10	-2.2	3.6	2.0
0.0026 (MEWS = 2)	-0.045	0.063	6.5	-0.62	-0.070	0.65
0.0037 (MEWs = 3)	-0.93	0.54	3.3	1.9	-0.89	0.045
0.0053 (MEWs = 4)	-3.1	-0.92	-0.57	-0.40	-1.3	-1.3
0.0074 (MEWs = 5)	-4.4	-1.6	-1.9	-0.17	-1.3	-1.4
Modified MEWS						
0.0018 (MEWS = 1)	3.2	3.1	9.6	0.89	0.73	2.2
0.0026 (MEWS = 2)	2.2	2.0	7.6	0.85	0.66	1.5
0.0039 (MEWs = 3)	1.4	1.4	5.3	0.72	-0.19	0.81
0.0060 (MEWs = 4)	0.21	0.54	2.7	0.31	-0.97	-0.36
0.0096 (MEWs = 5)	-1.0	-0.22	-<0.01	-2.4	-1.2	-1.5

MEWS maternal early warning score; Modified MEWS denotes the model that includes the MEWS with additional predictors (gestational age, maternal age, parity, previous caesarean, pre-existing conditions, plurality, gestational age at booking, ethnicity, and interaction terms between the MEWS and ethnicity, the MEWS and parity, and the MEWS and gestational age). Threshold denotes various levels at which a MEWS may be programmed to trigger an alert. Figures rounded to two significant figures

Table 6-7 Net benefit per 10,000 MEWS by ethnicity (48-hour time horizon)

Probability threshold (corresponding MEWS value)	Overall	Asian	Black	Mixed	Other	White
MEWS						
0.0030 (MEWS = 1)	1.5	1.8	11	-0.29	1.8	2.0
0.0040 (MEWS = 2)	-0.71	-0.22	9.0	0.48	-0.15	0.25
0.0052 (MEWS = 3)	-1.7	0.10	4.4	1.4	0.17	-0.37
0.0069 (MEWS = 4)	-4.1	-1.4	-0.82	-0.52	-1.7	-1.7
0.0090 (MEWs = 5)	-5.6	-2.3	-1.7	-0.69	-2.2	-2.3
Modified MEWS						
0.0030 (MEWS = 1)	8.4	7.8	16	2.2	4.5	8.5
0.0041 (MEWS = 2)	5.4	5.5	12	0.055	5.0	4.9
0.0057 (MEWS = 3)	3.0	3.9	8.9	-0.20	1.3	2.0
0.0081 (MEWS = 4)	1.3	2.1	5.2	-1.5	0.59	0.69
0.011 (MEWs = 5)	-0.51	0.80	1.7	-3.2	-2.0	-1.2

MEWS maternal early warning score; Modified MEWS denotes the model that includes the MEWS with additional predictors (gestational age, maternal age, parity, previous caesarean, pre-existing conditions, plurality, gestational age at booking, ethnicity, and interaction terms between the MEWS and ethnicity, the MEWS and parity, and the MEWS and gestational age). Threshold denotes various levels at which a MEWS may be programmed to trigger an alert. Figures rounded to two significant figures.

Table 6-8 Effect modification of MEWS by ethnic group with adjustment

	MEWS 0		**MEWS >0**		
	N with/without SMM	**OR (95% CI)**	**N with/without SMM**	**OR (95% CI) per 1-unit**	**OR (95% CI) per 1-unit within-strata**
SMM-12h					
Asian	38/64,486	0.68 (0.48-0.98)	59/47,587	1.75 (1.56-1.96)	1.81 (1.59-2.06)
Black	13/15,521	0.97 (0.58-1.62)	29/12,088	1.89 (1.60-2.24)	1.80 (1.47-2.20)
White	60/79,340	1.00	79/52,987	1.56 (1.39-1.75)	1.59 (1.39-1.82)
SMM-24h					
Asian	75/64,486	0.77 (0.59-0.99)	101/47,587	1.56 (1.41-1.71)	1.62 (1.45-1.80)
Black	25/15,521	1.04 (0.72-1.50)	51/12,088	1.71 (1.50-1.96)	1.69 (1.44-2.00)
White	121/79,340	1.00	125/52,987	1.42 (1.29-1.57)	1.45 (1.30-1.62)
SMM-48h					
Asian	126/64,486	0.76 (0.63-0.93)	157/47,587	1.43 (1.32-1.56)	1.44 (1.31-1.59)
Black	42/15,521	0.96 (0.72-1.29)	74/12,088	1.63 (1.45-1.83)	1.65 (1.44-1.88)
White	218/79,340	1.00	182/52,987	1.30 (1.19-1.41)	1.32 (1.20-1.45)

SMM-12, -24, and -48 represent severe maternal morbidity that occurred over 12, 24, and 48 hour time horizons, respectively.

SMM-12 hour: RERI for Asian vs. White -0.049 (-0.22, 0.12), Black vs. White 0.31 (-0.014, 0.63)
SMM-24 hour: RERI for Asian vs. White 0.0012 (-0.13, 0.13), Black vs. White 0.32 (0.096, 0.54)
SMM-48 hour: RERI for Asian vs. White 0.036 (-0.068, 0.14), Black vs. White 0.31 (0.15, 0.47)

6.3.6 Medical review

The rate ratio for receipt of a medical review within two hours was lower for Black women, compared with White, as well as Asian women once the healthcare site was adjusted for. After adjustment for the MEWS itself and healthcare site, only Black women had a lower chance of medical review, RR 0.92 (0.89-0.96), compared with White. After adjustment for all prognostic factors, including those that may influence interpretation of the MEWS (smoking and body mass index), Black women were less likely to receive a medical review within 2 hours, RR 0.95 (0.90-1.00; p-value 0.032), compared with White women, shown in Table 6.9. There was a positive association between receiving a medical review within two hours of a MEWS and SMM over all time horizons, shown in Appendix Table D6.10. The relative risk of SMM following a medical review did not differ according to ethnic group.

Table 6-9 Association between ethnic group and the receipt of a medical review within two hours of a MEWS

	Asian	**Black**	**Mixed**	**Other**	**White**
Review <2 hours	*RR (95% CI)*	*RR (95% CI)*	*RR (95% CI)*	*RR (95% CI)*	
Unadjusted (all scores)	0.99 (0.96-1.01)	0.93 (0.89-0.96)	1.03 (0.97-1.09)	1.01 (0.95-1.06)	*Ref*
+ location	0.95 (0.93-0.97)	0.93 (0.89-0.96)	1.00 (0.94-1.06)	0.97 (0.92-1.02)	*Ref*
Adjusted for score	0.99 (0.97-1.01)	0.93 (0.89-0.96)	1.01 (0.95-1.07)	1.00 (0.94-1.05)	*Ref*
+ location	0.95 (0.92-0.97)	0.92 (0.89-0.96)	1.00 (0.94-1.06)	0.97 (0.91-1.02)	*Ref*
Adjusted	1.02 (0.99-1.05)	0.94 (0.90-0.99)	1.01 (0.94-1.08)	1.08 (1.01-1.16)	*Ref*
+ location	0.98 (0.96-1.01)	0.94 (0.90-0.99)	1.00 (0.93-1.07)	1.06 (0.99-1.13)	*Ref*
Adjusted +BMI and smoking	1.04 (1.01-1.07)	0.95 (0.90-1.00)*	1.01 (0.94-1.09)	1.10 (1.02-1.17)	*Ref*
+ location	1.00 (0.97-1.03)	0.95 (0.90-1.00)*	1.00 (0.93-1.08)	1.07 (1.00-1.15)	*Ref*

*p-values 0.032.

6.3.7 Sensitivity analyses

When the MEWS was tested among antenatal and postnatal vital signs separately, there was a similar positive net benefit among both groups. Net benefit decreased as the time horizon increased among postnatal women, shown in Appendix Table D6.11. When exploring differences between ethnic groups in more detail, there was a broadly positive net benefit among Indian, Pakistani, Black African and Black Caribbean women, shown in Appendix Table D6.12. There was more variation in the net benefit for Bangladeshi women, which was the smallest group. Performance was best among Black Caribbean women and there was no clear pattern of differential performance within the higher level ethnic groups of Asian or Black.

6.4 Missing data

Of the 1,450,933 times points at which any vital signs were collected, no HR was measured at 14% (201,263/1,450,933); no RR at 62% (905,448/1,450,933); no blood pressure (combined, as both systolic and diastolic blood pressures had the same completion) measurement at 31% (451,482/1,450,933), no temperature at 60% (874,265/1,450,933), and no oxygen saturation at 61% (878,808/1,450,933). One vital sign was unmeasured for 2.9% of time points (41,864/1,450,933); two vital signs were unmeasured for 1.7% of time points (25,032/1,450,933); three vital signs were unmeasured for 15% of time points (213,168/1,450,933) and four for 44% of time points (644,951/1,450,933).

Following imputation of up to two missing vital signs with a 'normal' value of zero or following multiple imputation of the same missing vital signs, the number of MEWS for analysis was 333,342. Following either of these procedures, re-evaluation of the MEWS and the modified MEWS did not produce findings that meaningfully differed from the complete case analysis. The findings following the first approach towards imputation are shown in Appendix Tables D6.13 to D6.15.

6.5 Discussion

The performance of the English MEWS varied between ethnic groups. The risk of SMM was higher for Black women and lower for Asian women, compared with White women. Positive predictive values increased as MEWS category increased and Black women had consistently higher positive predictive values compared with other groups. The MEWS demonstrated moderate discrimination overall (poor-good(405) across individual ethnic groups) across all time horizons and discrimination was consistently higher in Black and Mixed ethnic groups. Discrimination decreased as the time horizon increased. The modified MEWS appeared better at ranking vital sign sets (discrimination) but this did not equate to a substantially improved estimation of absolute risk (calibration). The direction and magnitude of change, as scaled Brier scores, differed by both ethnicity and time horizon with the addition of prognostic factors, relative to the MEWS. The MEWS did not demonstrate net benefit at an alert threshold of 2 for 24 or 48 hours, at which clinical escalation is indicated, whereas the modified MEWS did at the equivalent probability threshold, although the differences were small. Black women benefitted most from the MEWS and modified MEWS, across all time horizons. There was evidence that the addition of baseline prognostic factors improved prediction across almost all ethnic groups, alert thresholds, and time horizons although there was some uncertainty among the smallest ethnic groups. There was evidence of additive interaction between MEWS and ethnic group such that an increase in score was associated with a greater absolute risk of SMM among Black women but not Asian women, compared with White women.

The modest net benefit for both the MEWS and modified MEWS is likely to be related to the rarity of the outcome, especially at the level of the individual vital sign. This is because the upper limit of net benefit is the prevalence of the outcome(404). Modification of the MEWS offered limited clinical benefit, as identified in other comparisons of advanced early warning tools(406). Potential reasons for limited improvement include insufficient separation of the risk distributions of women with or

without SMM, regardless of the strength of a prognostic factor(407). It may also be expected that a proximal, contemporaneous, physiological status is more reflective of short term risk compared with early-pregnancy prognostic factors. In the short term, the example modified MEWS led to between 1.6 and 5.6 new net true positives per 10,000 MEWS measurements at the risk threshold corresponding with a MEWS of two or 2.0 and 7.3 per 10,000 at a MEWS threshold of one, across the individual ethnic groups. The same figures over the longest time horizon of 24 hours were between 0.055 and 12 (threshold corresponding with MEWS of 2) or 2.2 and 16 (threshold corresponding with MEWS of 1). Interpretation is complicated by the fact that a local EWS was already in use to recognise and prevent deterioration, representing usual clinical practice. The measured performance therefore represents a minimum benefit when considering the alerts for severe complications not already prevented. The addition of predictors improved the net benefit based on these 'residual' severe complications and appeared to have a greater effect over the longer time horizons. Although recent physiological data appears to be the main determinant of model performance in many contexts(408), the addition of these baseline prognostic factors appeared to support prediction over a longer rather than shorter time horizon, replicating the finding from other clinical contexts(409). The risk among women who did not receive a timely documented medical review was lower across all time horizons, suggesting that clinical risk assessment was informed by clinical prioritisation. It is important to recognise that these metrics reflect the appropriateness of alerts only and not the quality of clinical escalation or response, although the frequency and meaning of alerts is likely to influence the response, as shown in chapter 4.

The risk of SMM was greater for Black women, compared with White women. There was evidence that the association between the MEWS and SMM was modified by ethnicity, including on the additive scale, meaning that the absolute risk among Black women was greater than that captured by either MEWS or ethnicity alone. One implication is that both the intercept (baseline risk) and slope (increase per one-unit increase) may differ between ethnic groups, leading to under-prediction

among Black women. This may be due to unmeasured differences in physiology or clinical status between women who have the same score. It may also be due to contextual factors such as whether or how the score is recognised, escalated, responded to may differ between ethnic groups (chapter 4), as evidenced by the lower rate of medical review among Black women, compared with White. Third, acquired differences in health, due to systemic biases over the life course may mean that the risk of clinical deterioration differs between groups, potentially due to differences in physiological reserve(8) or a higher burden of comorbidities that may manifest in pregnancy(410). The inclusion of additional prognostic factors does not necessarily lead to improved MEWS performance across ethnic groups and the inclusion of both ethnicity and the interaction between MEWS and ethnicity did not improve performance at all over the longer time horizons. The inclusion of ethnicity in the model was a proxy measure to account for unmeasured health status in combination with the exposure to systematic biases. This could be beneficial provided that it leads to early, appropriate clinical review by an appropriate healthcare worker who has the time to conduct an individualised assessment that reduces the risk of progression to SMM. Both the inclusion or exclusion of ethnicity may lead to the exacerbation of health inequalities(411). Whilst there was evidence that net benefit was higher among Black women compared with other groups, the potential benefit depends on the nature and quality of both subsequent clinical action and the potential indirect effects of the tool on care provided, such as potential differential effects of alarm fatigue. A timely, documented medical review appeared to be a scarce resource and there was evidence that clinical judgement overrode escalation protocols, reflective of the findings in chapter 4 and in other contexts of acute care(412).

This work demonstrated how an advanced MEWS could improve the performance of the existing national MEWS as well as offer more equitable prediction across ethnic groups. Performance was most enhanced at the 48 hour time horizon suggesting that prognostic factors may offer greater benefit to provide earlier warning. There are several implications for the development of an advanced MEWS. First, the impact on net benefit was marginal. The extraction and inclusion of

prognostic factors that provide a more comprehensive measure of acute physiological status may be more beneficial than these predominantly baseline predictors. Whilst more comprehensive sets of physiological status have been developed, often the evaluation of these prognostic factors has been limited(413). Second, measures of model performance may be dependent on prevalence (positive predictive value, c-statistic, net benefit) or not (measures of calibration including Brier score-based measures). Therefore, superior performance among Black women for prevalence-dependent measures may be due to a higher prevalence of SMM. This does not mean that it is not clinically beneficial. Interaction between ethnicity and MEWS for SMM was not explained by differences in obstetric history, pre-existing comorbidities or neighbourhood-level deprivation. This highlights how, in addition to an appropriate alert, consideration could be given to ensuring that the subsequent escalation and medical response is appropriate and is not subject to ethnic biases. Third, the inclusion of ethnicity and its interaction with MEWS should potentially be considered over a broader range of maternity settings to understand how differences in baseline risk, the distribution of prognostic factors among ethnic groups, the ethnic composition of maternity populations and their early warning practices may modify its impact. The clinical impact of including ethnicity in an advanced EWS cannot be considered stable across hospitals or services. Finally, there was evidence that a complete set of vital signs was not always measured. Whilst it was not possible to determine the exact reason for incomplete vital sign measurement, 'nearly complete' sets of vital signs were common, which imply the intention was to provide a holistic physiological assessment, which accords with the findings from HCWs (Chapter 4). Therefore, processes to ensure the completion of vital signs, so that an EWS can be produced and acted on, could also increase the benefit from early warning systems.

6.5.1 Strengths and limitations

The strengths of this research are the use of detailed, prospectively-collected clinical data from the electronic medical records for an ethnically diverse cohort of women. An important limitation is that

maternal early warning scores were already implemented, as is the case nationally. It is therefore only possible to compare systems based on SMM that was not prevented by the EWS already in place. The severe complications identified may therefore be 'less preventable'; however, the underlying disease processes are the same and it is likely that there are nevertheless opportunities to intervene or modify clinical behaviour given early warning. A second limitation is that this evaluation is based on several snapshots of how the MEWS or its modified forms perform at specific binary thresholds and over specific time horizons and does not reflect the full spectrum of clinical interventions that may be used in practice or even other ways that EWSs may be used or benefit women or healthcare workers. Relatedly, the initial alert is a necessary but not a sufficient component of the early warning process to prevent clinical deterioration. The subsequent clinical escalation and intervention was measured but was not accounted for when comparing models; however, adjustment or stratification for a documented medical response did not affect the findings. Third, the number of women from a mixed ethnic background and from 'other' ethnicities was low. This was reflected in the broader confidence intervals for these groups and the more erratic changes across the models and metrics. Therefore, there was less certainty with respect to these two groups; however, there was positive net benefit in these groups for the modified MEWS. A final limitation was that the objective of this work was to externally validate the MEWS and to understand the reasons for differences in performance between ethnic groups to inform the development of an advanced EWS. Although the modified MEWS performed better than the MEWS, this may be optimistic given that the modified MEWS was developed and tested in the same sample. If a modified MEWS were to have been intended for actual clinical use, then it would need to be internally validated using techniques to evaluate the degree of optimism in addition to subsequent external validation of the updated model.

6.6 Conclusion

The performance of the MEWS was improved by using additional prognostic factors but the effect on performance differed between ethnic groups and overall benefit was limited. The net benefit was highest for Black women for both the MEWS and modified MEWS. The inclusion of ethnic group in the model did not improve calibration for the purpose of early warning at 24-48 hours but had a small positive effect for warning at 12 hours. There was evidence of additive interaction between ethnic group and MEWS, meaning that the risk among Black women may be under-estimated by the MEWS. Further development of an advanced EWS could incorporate a broader range of measures of acute physiological state alongside the vital signs, such as clinical signs or laboratory values, in addition to baseline prognostic factors and the impact of including ethnicity and its interaction with MEWS should be considered across a range of different services to inform its inclusion or exclusion.

7 Chapter VII: Discussion

7.1 Introduction

The aim of this thesis was to understand the performance of EWSs in maternity and their clinical use, including within individual ethnic groups, to inform the development of an advanced EWS. An advanced EWS is one based on a statistical prediction model that can incorporate additional prognostic information alongside the maternal vital signs. The function of a safety system based on a prediction model is dependent first on how that model is developed, namely how it produces an alert and what that alert represents, and second on how that alert is used and whether it leads to an improvement in outcomes. This chapter will synthesise the findings from across the preceding chapters, focussing on the key concepts from across the various methods that will help to strengthen the development and use of EWSs and systems in maternity services.

7.2 Summary of findings

The systematic review of outcome definitions of SMM in high-income countries included 45 definitions from across 40 studies. Of these, 13 definitions were developed for use with the primary medical record; that is, based on abstracting detailed data from the medical record. The other 32 definitions were developed for use with administrative data, comprised of International Classification of Disease codes and codes of procedures that were performed. There was no existing application of the WHO definition that could be directly applied to data from the electronic health record. Administrative codes did partially map onto the WHO definition and a set of diagnostic codes was identified for which there was high consensus across existing definitions of SMM. Following the subsequent application of the definition to data from the electronic health record and curation that include the input from a multidisciplinary team of experts, the identified components could be used

to validate, and then modify, the national Maternity Early Warning Score (MEWS) (**thesis objective 1**).

The next objective was to understand the strength of evidence for prognostic factors recorded in electronic health records so that differences in the performance of the MEWS across ethnic groups could be understood. There was strong evidence for demographic, socioeconomic, pregnancy history, and obstetric prognostic factors. The evidence for smoking was inconclusive and the evidence for immigration and rurality was highly variable across studies. The strongest prognostic factors were pre-existing conditions and peripartum interventions. Because peripartum interventions may be the result of SMM and because no studies considered the indication for interventions, this group of prognostic factors was not considered suitable for inclusion in a subsequent modified MEWS. There was strong and consistent evidence of ethnic health inequalities across all high-income countries, highest for Black women, compared with White, with RR 1.81 (95% CI 1.68 to 1.94). The prevalence of prognostic factors for SMM differed between ethnic groups where these data were available. Among studies that reported the prevalence of prognostic factors within ethnic groups, demographic, socioeconomic, medical, and obstetric prognostic factors had a higher prevalence among Black women, compared with White. There was insufficient evidence to judge whether the strength of those prognostic factors differed between ethnic groups. The prognostic factors that had strong evidence and that appeared to be generalisable were considered for inclusion in the subsequent modified MEWS (**thesis objective 2**).

The next objectives were to describe how early warning signs were recognised and acted on, including how EWSs were used. Then, to understand the reasons for any variation, including between ethnic groups. First, EWSs were not acted on at an early stage (**thesis objective 3**). This demonstrated a fundamental gap between their intended and actual use. A major reason for this appeared to be the individual workload of HCWs and, at the service level, the capacity to operate an

early warning system as intended (**thesis objective 4**). A key behaviour of healthcare workers was the 'resistance' (not acting on early warning signs or offering potentially simplistic explanations for abnormalities) to early warning signs. There was also evidence of limited medical investigation of potential complications at an early stage and evidence that senior medical staff were not involved or did not respond at an early stage (**thesis objective 4)**. Whether early warning signs were labelled as concerning and whether clinical escalation or actions occurred had the potential to vary based on HCW's individual beliefs about early warning signs and the meaning of EWSs. There were differences in the interpretation of early warning signs between ethnic groups, which included whether abnormalities were seen as normal or abnormal dependent on a woman's ethnic group (**thesis objective 4**). The endorsement or observation of stereotypes about ethnic groups was identified by HCWs, which may affect the recognition of abnormalities within individual ethnic groups and the subsequent clinical actions (**thesis objective 4**). There were also examples of other interpersonal and cultural biases related to ethnic stereotypes.

To complement the findings related to women's medical records and healthcare workers' beliefs, objective 5 related to how women themselves experienced and recognised early warning symptoms. The work in this objective defined a 'pre-EWS' process of recognition and decision making that may be hidden to HCWs. There was wide variation as to whether or when women recognised their early warning symptoms as a problem, influenced by women's' baseline health literacy and the information and resources available to them antenatally (**thesis objective 5**). Once women did recognise their symptoms and decided to seek help, they described challenges to accessing advice or medical treatment (**thesis objective 5**). In women's accounts, HCWs did not always appear to recognise their concerns and did not appear to recognise or proactively investigate signs of potentially severe complications (**thesis objective 5**).

The performance of the national MEWS within individual ethnic groups was then estimated among an ethnically diverse group of women. Women who were Black had a higher rate of SMM and women who were Asian had a lower rate of SMM, compared to women who were White. The positive predictive value, the ability of the score to correctly rank women (discrimination), and the prognostic ability of the model (calibration) varied between ethnic groups. Although the performance across most measures and time horizons appeared best among women who were Black, compared with other ethnic groups, the absolute differences were very small. The c-statistics for Asian, Black, and White women for SMM occurring within 24 hours were 0.61 (95% CI 0.57-0.65), 0.67 (95% CI 0.61-0.73), and 0.57 (0.54-0.61). There was evidence of additive interaction such that an increase in the MEWS value represented a greater increase in risk for women who were Black, compared with White. This interaction may arise for various reasons but there was evidence that Black women were less likely to have a documented medical review within two hours of a MEWS being measured, with RR 0.94 (95% CI 0.90-0.99) after adjustment for confounding and the location of measurement (**thesis objective 6**). The MEWS demonstrated net benefit for the prediction of SMM that occurred within 12 hours of the score when a MEWS score of 2 was the threshold for a clinical alert, as is the case in clinical practice. It did not demonstrate net benefit over a longer time horizon, of 24 or 48 hours, for the same alert threshold (**thesis objective 6**).

The next objective was to understand differences in performance between ethnic groups by modifying the MEWS based on the prognostic factors identified previously and informed by the perspectives of HCWs. The differences between the modified MEWS and the original MEWS were small but discrimination, calibration, and net benefit improved marginally (**thesis objective 7**). The c-statistics for the modified MEWS for Asian, Black, and White women for SMM occurring within 24 hours were 0.71 (95% CI 0.67-0.75), 0.70 (0.64-0.76), and 0.63 (0.60-0.66). Net benefit (in terms of additional true positives identified per 10,000 MEWS) increased from -0.71 to 5.4 overall, from -0.22 to 5.5 for Asian women, from 9.0 to 12 for Black women, and from 0.25 to 4.9 for White women, for

the prediction of SMM occurring within 48 hours when using the modified MEWS compared to the existing MEWS. The addition of baseline prognostic factors improved prediction across almost all ethnic groups, alert thresholds, and time horizons, although there was some uncertainty among the smallest ethnic groups and the additional clinical benefit appeared to be very small. The relative improvement in performance between the MEWS and the modified MEWS was greatest for Asian women, across all time horizons (**thesis objective 7**). With additional prognostic factors, the MEWS could therefore be adapted for better prognostication of future SMM over a longer time horizon.

7.3 Synthesis of findings

The first challenge was to determine an appropriate outcome whose prediction would support early intervention and prevention of further deterioration(1). SMM captures severe complications that may occur over the course of a maternity due to either obstetric or medical causes(80). Several adaptations of the WHO definition of SMM were in use or had informed definitions of SMM for use with either clinical or administrative health data (Chapter 2). Electronic health data sit between these two forms of data in terms of complexity and scalability. There were no examples of how the WHO definition had been reliably mapped to administrative data(414) whereas the degree of clinical detail was too great for the electronic health data obtained using structured fields in the maternity records. Therefore, the principles of the WHO definition were captured as reliably as possible but with some trade-offs to adapt to and leverage the advantages of data from the electronic health record. These included using clinical data to specify an individualised severity threshold for haemorrhage and to develop individual algorithms for severe pre-eclampsia and sepsis. Conversely, severe acute renal failure was omitted due to concerns regarding both the reliability of biochemical investigations and the indication for and provision of dialysis. Despite this, several aetiologies that may be complicated by acute renal failure were included in the composite definition(415). The operationalisation of SMM affects which women a safety system is going to flag as at-risk. A

comprehensive range of obstetric and medical complications were ultimately included based on the electronic health data available.

Prognostic factors that were replicated across multiple studies at low risk of bias were considered to have strong supporting evidence and, additionally, were considered to be generalisable in the presence of low absolute heterogeneity (Chapter 3). These were considered to be theoretically-informed prognostic factors that were used to modify the national MEWS to understand whether individualisation of risk assessment could reduce differences in performance across ethnic groups. A preference for generalisable prognostic factors is important(312), particularly when a model is intended to be used nationally. A model needs to be useful among women with different characteristics and in different maternity services. Generalisability means that the additional prognostic factors would more likely apply in new populations and settings(416). An extremely wide range of associations between prognostic factors and SMM have been investigated. Attempting to consider all of these prognostic factors as candidate variables may impair generalisability, additionally dependent on the way that prognostic factors may be selected for retention in the model(417). Despite the inclusion of generalisable prognostic factors with strong evidence, including both common and strong prognostic factors, the improvement in performance was limited (Chapter 6). Particularly over the shortest time horizon, these baseline prognostic factors appeared to be less important when compared with the acute measure of physiological status provided by the EWS itself (Chapter 6). HCWs also highlighted perceived contextual factors that they believed should modify the interpretation of abnormalities of the vital signs, including whether a woman is in labour or not, whether a woman is antenatal or postnatal, and the mode of birth (Chapter 4). This highlighted how the relationships between the large number of potential prognostic factors also needs to be carefully curated. When modifying the national MEWS, interaction between select baseline prognostic factors and the MEWS were included on the basis of very common prognostic factors used to broadly stratify risk in clinical practice (parity, gestational age), as well as ethnicity but an advanced EWS may

require a more systematic approach to the selection of interaction terms if considering a wider range of prognostic factors.

Evidence from women, their medical records, and from the narratives of HCWs highlighted how EWS use is imperfect in clinical practice (Chapters 4 and 5). This was not simply a case of HCWs not following protocols. Rather, in practice, HCWs may not be able to undertake a comprehensive and holistic assessment. If they do detect abnormalities, HCWs have to weigh up what the early warning protocol dictates, what they believe the actual risk is from the abnormal vital signs, and whether they have the time to communicate an EWS onwards or to respond to an EWS (Chapter 4). Whilst these behaviours meant that EWSs were not used as intended, they were also pragmatic adaptations that meant that the basic function of the system was maintained: the systematic measurement and documentation of the vital signs, the flagging of abnormalities in the first instance, and the prompt that further action was recommended. This adaptability may be regarded as a positive feature of safety systems in alignment with Hollnagel's perspective of 'Safety-II', which, broadly, is an approach to understand "the system's ability to succeed under varying conditions"(325). The same adaptability may be seen in HCW's prioritisation of women at highest risk for medical review following an abnormal EWS (Chapter 6). The most clearly modifiable determinant of early warning practice identified in Chapter 4 was the EWS itself. HCWs require a tool that helps them to differentiate between women who do or do not have complications. A tool must be manageable in terms of its burden on HCWs and alert rate and could be made so by reducing the false alarms it generates through improved prognostication(418). HCWs demonstrated a need to understand the meaning of the alert generated and how to investigate the early warning signs they are presented with(345, 419). The mismatch between staff workload and the demands of early warning is a pathway to non-medical decision making and the introduction of ethnic biases but these products of early warning systems may be modifiable if the tool can better differentiate between well and unwell women(420).

A woman's ethnic group or her perceived cultural identity had the potential to influence whether the early warning signs that she displayed were recognised and how they were acted on (Chapter 4), which is one explanation for the observed difference in the risk of SMM according to ethnicity, both in the validation sample (Chapter 6) as well as across high-income settings (Chapter 3). Black women were at greatest risk of SMM, compared to White women. Further, the same clinical alert threshold for a Black women signified a greater risk of progression to SMM, compared with White women. The difference in medical response following abnormalities of the vital signs between ethnic groups (Chapter 6) represented one pathway by which the risk of SMM may differ based on the same EWS. This difference in clinical response may reflect the ethnic biases described in the qualitative evidence (Chapter 4). Together, this meant that the chance of a problem being recognised, the meaning of the EWS value itself, and potentially the action following the generation of an alert may all vary based on a woman's ethnic group.

The pathways of early warning based on the analysis of medical records (Chapter 4) reflected how clinical signs may be acted on by HCWs but this contrasted with women's experiences outside of early warning systems (Chapter 5). The contrast highlighted how a holistic approach may improve early recognition and intervention; that is, getting women to the point of having an EWS measured should also be considered a part of the EWS system. In the first instance, women need access to the assessment itself for it to be used. Women with early warning symptoms at home face barriers to seeking help or having their concerns acted on (Chapter 5). Additionally, even in inpatient settings, women who had clinical abnormalities may not have their vital signs measured at all (Chapter 4). Women who did have their vital signs measured may not have a complete set measured and therefore may not benefit from an EWS (Chapter 6). Women need to be informed of the warning signs that require further investigation and need clear and reliable pathways that lead to an EWS being measured and an individualised risk assessment, when indicated. Women could be provided with comprehensive but concise information on warning signs in particular so that all women have

the same opportunity to recognise when to seek help, including when a clinical assessment is required. Existing information could be improved, consolidated, and actively disseminated(421). HCWs should measure a full set of vital signs when clinically indicated so that complications can be recognised at the earliest opportunity.

Several of the elements discussed so far may be addressed at the development stage of a new tool. Using a woman's other characteristics along with the vital signs improved the apparent performance of the MEWS. However, modification of the MEWS led to a marginal improvement in performance across ethnic groups, compared with the MEWS alone (Chapter 6). Further development based on other contemporaneous data, such as the results of laboratory investigations or clinical symptoms and signs, may improve prognostication so that the same, or greater, benefit may be derived with a lower number of alerts overall. It is imperative that a safety system can be fully operated so that HCWs are able to consider, escalate, and investigate abnormalities and intervene at an early stage. The second component that may be approached at the development stage is how the clinical relevance and therefore benefit of a tool may be made apparent to HCWs, which HCWs highlighted as a potential barrier to acting on EWSs (Chapter 4). This may involve validating tools and disseminating these findings in clear and interpretable language. It may also involve making the clinical predictions themselves clear and interpretable. Although there are no direct comparisons on the effect of integer-based EWSs vs model-based EWSs on the behaviours of HCWs, the communication of risk scores has the potential to affect clinical practice(422).

These findings provide an understanding of several interlinked processes that constitute early warning in clinical practice, including how and when care is accessed and how and when early warning signals are acted on. Early warning systems do not reflect the deterministic protocols that outline their intended use, sometimes termed "work as prescribed"(423). In practice, the early warning process map was more complicated (Chapter 4); the clinical decisions that healthcare

workers made were complex and informed by social and cultural context (Chapter 4); in response to an early warning score that many healthcare workers did not believe was as meaningful as protocols indicated (Chapter 4). Their use also depends on women being able to access face to face care (Chapter 5). Healthcare workers may not always know what to do or whether action is necessary in response to an abnormal early warning score (Chapter 4). When healthcare workers provided a response, it was an indicator that a woman was at higher risk of a severe complication (Chapter 6), reflective of the allocation of a higher level of care to women based on their perceived clinical need. Together, this work builds a picture of early warning in terms of 'work as done'(325), recognising that early warning systems are series of interactions between healthcare workers who have a range of competing clinical tasks. Whilst the adaptations that healthcare workers may make alter the function of early warning systems, they also maintain the systematic measurement of the vital signs in an under-resourced system. An advanced EWS should be developed with this model of practice in mind to reflect actual use so that the solution is aligned with clinical need and the problems that HCWs face(423). How, when and how often healthcare workers are expected to act in response to EWSs should take into account how maternity care is organised and how acute care is delivered to women in practice.

7.4 Strengths and limitations

The strengths of this work include its holistic approach to the multiple and sequential dimensions of early warning systems. These dimensions included the data and definitions needed to develop a tool, the potential effects of modifying a tool on performance and health inequalities, and the clinical consequences of early warning alerts and how they may differ between ethnic groups. The work was supported by comprehensive and systematic literature reviews that followed best practice, ensuring that conceptual clarity regarding outcome definition may appropriately direct clinical resources as well as supporting generalisability. The qualitative work included healthcare

workers from across the whole range of healthcare roles involved in early warning and from a diverse range of ethnic backgrounds, increasing the chance of including different perspectives on health inequalities. Women's perspectives were included so that early warning systems can be designed around their early recognition of symptoms. The rigor of this work was supported by the use of triangulation between different professional groups and between healthcare workers and the medical records to strengthen the credibility of the findings. Further, the sequential application of these findings to develop initial codes with which to analyse women's narratives supported the credibility of this analysis. The quantitative element used prospectively-collected electronic health data from an ethnically diverse sample of women that enabled detailed typing of SMM.

There were several limitations to acknowledge when evaluating whether the evidence is sufficiently credible to inform the development of new safety systems. Interpretation of the validation of the MEWS and exploration of the modified MEWS is not simple. These were counterfactual alert systems whose performance was compared within a maternity service that already used an EWS. Therefore, these were potential gains above standard clinical practice, representing incremental net benefit. Nevertheless, this approach avoided making an unfair comparison between a tool that did influence outcomes and a modified version that did not influence outcomes.

Thinking about the early warning system holistically, these alerts have to lead to preventative action. There was no evidence that a timely medical review reduced the risk of SMM; rather that a minority of women received a timely documented medical review and that this was associated with a greater risk of progression to SMM. This was potentially reflective of a reliance on clinical judgement to inform medical responses following an abnormal MEWS. It was not possible to estimate the potential downstream effects of the MEWS or modified MEWS using the electronic health data in more detail and it is an assumption that true positives lead to clinical benefit(424). Insight into the downstream clinical process was largely obtained from healthcare workers and women's medical

records. Although some women themselves commented on early warning processes directly, women's accounts focussed on their process of recognising or responding to their symptoms. This provided insight from times when women were not being monitored by HCWs. The ethnic diversity of women who were included in the secondary analysis was low and whilst it was therefore not possible to directly compare the experiences of women between ethnic groups. Findings related to access to information and access to services were concepts likely to be relevant to health inequalities(10) but this could not be evidenced within this work. The positionality of the researcher meant that the accounts of some healthcare workers may have been more familiar. This was handled through a recursive interpretation of the data through the reflexive process. A final general and conceptual limitation to consider is that the focus of this work is on clinical prediction. However, the inclusion of structural prognostic factors in a clinical prediction model must not detract from the need to address those upstream factors(425). Women subject to intersecting biases are not at risk because of their ethnicity and cultural identity but because of ultimately modifiable structural biases.

7.5 Implications of findings

7.5.1 Implications for the development and validation of advanced early warning tools

- A core set of severe complications was identified for which there was high consensus across existing definitions of SMM (Chapter 2). These conditions may form the basis for any future outcome on which an advanced EWS may be based.
- Data from the electronic health record enabled the development of phenotypes for conditions with a wide spectrum of severity, which varied across definitions of SMM for use

with administrative health data (Chapter 2). These included severe haemorrhage, severe pre-eclampsia, and sepsis.

- The prevalence of prognostic factors differed across individual ethnic groups whereas there was insufficient evidence with which to infer that the magnitude of association differed across individual ethnic groups (Chapter 3). Therefore, consideration should be given to including prognostic factors in EWSs whose prevalence differed.
- HCWs perceived the limitations of EWSs to include a lack of context awareness for the clinical circumstances of individual women (Chapter 4). Therefore, an advanced EWS that incorporates additional prognostic factors may be better aligned with the mental model of HCWs who use EWSs.
- Not all women recognised their early warning symptoms at the earliest opportunity, prior to engagement with HCWs (Chapter 5). Therefore, consideration could be given to how women could be provided with information in the pre-EWS setting.
- Not all women who recognised their early warning symptoms and sought help received a proportionate and comprehensive risk assessment by a HCW (Chapter 5). Therefore, consideration could be given to how an advanced EWS could interface with remote assessment and telephone triage services to standardise the response to women's concerns.
- Baseline prognostic factors appeared to offer less benefit for the prediction of SMM over a shorter time horizon but benefit appeared to increase over a longer time horizon (Chapter 6). The inclusion of baseline prognostic factors may therefore support true early warning.
- There was evidence of additive interaction between ethnicity and the MEWS (Chapter 6), which should prompt consideration of the potential mechanisms underpinning a differential association according to ethnic group, including model specification or subsequent clinical response.
- The modification of the national MEWS improved its predictive performance and reduced health inequalities (Chapter 6) when evaluated in the population among whom it was

developed. An advanced EWS may therefore support more equitable recognition of clinical risk.

- Because the impact of modifying the MEWS differed across ethnic groups (Chapter 6), consideration should be given to validating an advanced EWS within ethnic groups prior to implementation.

7.5.2 Implications for clinical practice and governance

- HCWs did not use early warning tools as intended when their workload exceeded their individual capacity (Chapter 4). Therefore, consideration may be given to the feasibility and flexibility of early warning tools in the context of potential resource constraints.
- Abnormal early warning scores did not always prompt clinical escalation or investigation or appropriate senior involvement (Chapter 4). Therefore, consideration should be given to ensuring HCWs have sufficient time, resources and training to act on EWSs or signs.
- HCWs demonstrated cognitive biases that affected or that may affect the equitable recognition of early warning signals among different ethnic groups (Chapter 4). Therefore, consideration should be given both to developing training to reduce cognitive biases or designing an advanced EWS that reduces the conversion of biases into differences in the care provided.
- The documented response to abnormalities of the vital signs differed by ethnic group, including following adjustment for confounding by clinical risk factors or maternity hospital (Chapter 6). Further consideration should be given to the reason for the observed differences and the replication of this finding within other maternity services so that an advanced EWS could be designed to reduce inequalities at the response stage.

7.6 Future research

Future research may involve further developing measures of physiological status that are routinely-documented within electronic health records in order to improve the performance of an advanced EWS. This may include structured electronic health data used across a range of systems such as urine output and level of consciousness status but also laboratory investigations, novel clinical signs, and electronic prescription data. Similarly, better characterisation of the response to early warning signals, including medical or surgical responses, using electronic health data would help to understand the downstream effects and how they could be optimised. Understanding healthcare workers' perceptions of risk in relation to early warning signs quantitatively could inform alert thresholds or foresee barriers to clinical benefit and inform how a future tool could communicate risk to healthcare workers. Finally, the implementation of a future advanced EWS ought to be evaluated to understand its effect on clinical practice, including on the care of women from individual ethnic groups across a range of different maternity services.

7.7 Conclusion

This thesis provides a body of knowledge about how early warning scores perform and how they are used in clinical practice, including how different stages of the early warning process may contribute to ethnic health inequalities. A woman's ability to recognise warning symptoms and to seek care was dependent on her health literacy and the quality of information provided by maternity systems. Once engaged with maternity services, the performance of early warning scores differed across individual ethnic groups. There was evidence that the addition of baseline prognostic factors improved model calibration within all ethnic groups. This meant that the balance of 'true alarms' and 'false alarms' was appropriate and that, with ideal use, a prediction model-based early warning score may lead to clinical benefit if early warning alerts are acted on appropriately. The risk of severe

maternal morbidity increased at a greater rate for Black women as their MEWS score increased, compared to White women, even after accounting for other maternal characteristics. There is a need to better characterise the acute physiological status, either by using additional clinical data alongside the vital signs or better using the information already measured by the vital signs without conversion into a simplified score. Pragmatically, an early warning score needs to be feasible to use within the constraints of an under-staffed maternity service. Healthcare workers need training that equips them to understand the clinical relevance of abnormalities and to know how to investigate or act on it. Training ought to incorporate a more comprehensive and nuanced understanding of ethnic biases that goes beyond the recognition of physical symptoms based on skin colour.

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Appendix A: Chapter 2

Appendix Table A2.1 Search Strategy

Search	Query	Records
9	7 AND 8	6,800
8	"risk factor"[Title/Abstract] OR "determinant"[Title/Abstract] OR “predict*”[Title/Abstract] OR “surveillance” [Title/Abstract] OR “monitor*”[Title/Abstract]	3,465,163
7	1 OR 4 OR 6	32,152
6	5 + 3	12,734
5	"intensive care"[Title/Abstract] OR "ICU"[Title/Abstract] OR "intensive treatment"[Title/Abstract] OR "ITU"[Title/Abstract] OR “cardiac arrest” [Title/Abstract]	273,415
4	2 + 3	118
3	“maternal”[Title/Abstract] OR “pregnan*”[Title/Abstract] OR “obstetric*”[Title/Abstract]	676,536
2	"potentially life threatening complication"[Title/Abstract] OR “PLTC”[Title/Abstract]	1,851
1	"maternal morbidity"[Title/Abstract] OR “maternal near miss”[Title/Abstract] OR "maternal mortality"[Title/Abstract] OR "maternal mortality"[MeSH Terms]	20,773

Appendix B: Chapter 3

Appendix Table B3.1 Search Strategy

Search	Query	Records
9	7 AND 8	6,134
8	"risk factor"[Title/Abstract] OR "determinant"[Title/Abstract] OR “predict*”[Title/Abstract] OR “surveillance” [Title/Abstract] OR “monitor*”[Title/Abstract]	3,191,020
7	1 OR 4 OR 6	29,631
6	5 + 3	11,634
5	"intensive care"[Title/Abstract] OR "ICU"[Title/Abstract] OR "intensive treatment"[Title/Abstract] OR "ITU"[Title/Abstract] OR “cardiac arrest” [Title/Abstract]	250,664
4	2 + 3	110
3	“maternal”[Title/Abstract] OR “pregnan*”[Title/Abstract] OR “obstetric*”[Title/Abstract]	650,796
2	"potentially life threatening complication"[Title/Abstract] OR “PLTC”[Title/Abstract]	1,688
1	"maternal morbidity"[Title/Abstract] OR “maternal near miss”[Title/Abstract] OR "maternal mortality"[Title/Abstract] OR "maternal mortality"[MeSH Terms]	19,224

Appendix Table B3.2 Risk of Bias Assessment

Study	Part.	Att.	Prog.	Out.	Conf.	An./Rep.	RoB	Raw	Outcome
Admon 2018	Low	Low	Mod	Low	Low	Low	Mod		SMM CDC T, NT
Admon 2019	Low	Low	Low	Low	Low	Low	Low		SMM CDC T
Adane 2020	Low	Low	Low	Low	Low	Low	Low		SMM AMMOI T, NT
Alexander 2003	Mod	Low	High	Mod	High	Mod	High		Death
Aoyama 2019	Low	Low	Low	Low	Mod	Mod	High	Low	SMM CPSS NT, Death
Bae 2021	Low	Mod	Mod	Low	Mod	Mod	Mod		Death
Balayla 2020	Low	Low	Mod	Low	High	Mod	High	Mod	Death
Balki 2017	Low	Low	Mod	Low	Mod	Low	Mod		Cardiac arrest
Bateman 2012	Low	Mod	Low	Low	Mod	Low	Mod		Death
Belanoff 2016	Low	Low	Low	Low	Mod	High	High	Low	SMM CDC T
Ben-Ayoun 2023	Low	Low	Mod	Low	High	High	High	Mod	ITU
Black 2021	Mod	Mod	Mod	Low	Mod	High	High	Mod	SMM CDC T
Boulet 2020	Low	Low	Low	Low	Low	Low	Low		SMM CDC T, NT
Brown 2017	Low	Low	Low	Low	Mod	Low	Mod	Low	SMM Other NT
Brown 2011	Mod	Low	Mod	Low	Mod	Low	Mod		SMM Other RT
Brown 2020	Low	Low	Low	Low	High	High	High	Low	SMM CDC T, NT
Brown, C 2021	Low	Low	Mod	Low	Mod	Low	Mod		SMM CDC T, NT
Brown, H 2021	Low	Low	Low	Low	Low	Low	Low		SMM CPSS T
Campbell 2013	Low	Low	Mod	Low	High	Mod	High	Mod	Death
Carr 2022	Low	Low	Mod	Low	High	High	High	Mod	SMM BC NT, ITU
Chen 2019	Low	Low	Mod	Low	Mod	Low	Mod		SMM BC NT
Chen 2021	Mod	Low	Mod	Low	Mod	Low	Mod		SMM CDC NT
Clapp 2022	Mod	Low	Mod	Low	High	Low	High	Mod	SMM CDC T
Combier 2020	Low	Low	Mod	Low	High	Mod	High	Mod	Death
Conrey 2019	Low	Low	Low	Low	High	Mod	High	Low	SMM CDC NT
Courchesne 2021	Mod	Low	Mod	Low	High	Mod	High	Mod	SMM CDC T
Creanga 2014	Low	Mod	Mod	Low	Mod	Mod	Mod		SMM CDC T, NT
Cromi 2018	Mod	Low	Mod	Low	Mod	High	High	Mod	SMM WHO PLTC T
Cudjoe 2023	Low	Low	Mod	Low	High	Mod	High	Mod	SMM CDC NT
Dakin 2023	Mod	Low	Mod	Mod	Mod	Mod	Mod		SMM Mantel RT
Dayan 2018	Low	Low	Mod	Low	Mod	Low	Mod		CPSS NT
Dayan 2019	Low	Low	Mod	Low	High	High	High		SMM CPSS T, ITU, Death
Dayan 2021	Low	Low	Mod	Low	Mod	Mod	Mod		SMM Bateman/CPSS NT
Decker 2021	Low	Low	Low	Low	High	High	High	Low	SMM CDC T
Dinsmoor 2022	Mod	Mod	High	Low	High	Mod	High		SMM Other NT
Diop 2022	Low	Low	Mod	Low	Low	Low	Mod		SMM CDC NT

Study	Part.	Att.	Prog.	Out.	Conf.	An./Rep.	RoB	Raw	Outcome
Donoso 2003	Mod	Mod	Mod	Low	Mod	Mod	Mod		Death
Donoso 2014	Mod	Low	Low	Mod	Mod	Mod	Mod		Death
Du 2023	Mod	Mod	Mod	Low	High	Low	High	Mod	SMM CDC T, NT
Dzakpasu 2020	Low	Low	Mod	Low	Mod	Mod	Mod		SMM CPSS T
Early 2023	Low	Low	Mod	Low	Mod	Mod	Mod		SMM CDC NT
Eslier 2022	Low	Low	Low	Low	Mod	Low	Mod	Low	SMM Precare T
Fernandez 2011	Mod	Low	Low	Low	High	High	High	Mod	Death
Fitzpatrick 2017	Mod	Mod	Mod	Low	Low	Low	Mod		ITU
Frederiksen 2017	Low	Mod	Low	Low	Mod	Low	Mod		SMM CDC T, NT
Freese 2020a	Low	Low	High	Low	Mod	High	High		SMM T
Freese 2020b	Low	Low	High	Low	Low	Low	High		SMM T
Friedman 2022	Low	Low	Low	Low	Mod	Low	Mod	Low	SMM CDC NT
Garg 2022	Mod	Mod	Mod	Low	High	Low	High	Mod	SMM CDC T, NT
Gibson 2017	Low	Mod	Low	Low	High	High	High	Mod	SMM CDC T, NT
Gleason 2021	Low	Low	Mod	Low	Mod	Low	Mod		Death
Grobman 2014	Low	Low	Mod	Low	High	High	High	Mod	SMM Geller T (>/4u)
Guglielminotti 2019	Low	Mod	Mod	Low	High	High	High	Mod	SMM CDC T, NT
Guignard 2021	Low	Low	Mod	Low	Low	Low	Mod		SMM Epimoms RT (SA NT)
Gyamfi-Bannerman	Mod	Low	Mod	Low	Mod	Mod	Mod		SMM CDC T, NT
Ha 2023	Mod	Low	Low	Low	Low	Low	Mod		SMM T, NT
Hage Diab	Low	Low	Mod	Low	Mod	Low	Mod		SMM CDC NT
Hailu 2022	Low	Low	Low	Low	Low	Low	Low		SMM CDC T, NT
Hansen 2022	Low	Low	Mod	Low	Low	Mod	Mod		SMM CDC T, NT
Harden 2022	Low	Low	Low	Low	High	Low	High	Low	SMM CDC T, NT
Harrison 2021	Low	Low	High	Low	Mod	Mod	High		SMM Novel T
Hayashi 2012	Low	Mod	Mod	Mod	Mod	High	High	Mod	ITU, Death
Hitti 2018	Mod	Low	Low	Low	Mod	Mod	Mod		SMM CDC T
Horner-Johnson 2022	Low	Low	Low	Low	Mod	Mod	High	Low	SMM CDC T, NT
Howell 2016 A	Low	Low	Mod	Low	High	High	High	Mod	SMM CDC T
Howell 2016 B	Low	Low	Low	Low	High	High	High	Low	SMM CDC T
Howell 2017	Low	Low	Low	Low	Low	Mod	Mod	Low	SMM CDC T
Howell 2020	Low	Low	Mod	Low	Mod	Mod	Mod		SMM CDC T, NT
Howland 2019	Low	Mod	Mod	Low	Mod	Mod	Mod		SMM CDC T
Huang 2023	Low	Mod	Mod	Low	Mod	Mod	Mod		SMM CDC T, NT
Huennekens 2020	Low	Low	Mod	Low	High	Mod	High	Mod	SMM CDC NT
Huisman 2013	Low	Low	High	Mod	Mod	Mod	High		Cardiovascular SMM
Jarlenski 2020	Low	Low	Mod	Low	High	Low	High	Mod	SMM CDC T, NT
Jeffers 2023	Low	Low	Low	Low	Low	Low	Low		SMM CDC T, NT
Joseph 2010	Low	Low	Mod	Low	Mod	Mod	Mod		SMM CPSS T

Study	Part.	Att.	Prog.	Out.	Conf.	An./Rep.	RoB	Raw	Outcome
Karamlou 2021	Low	Mod	Low	Low	Mod	Mod	Mod		Death
Kilpatrick 2016	Low	Low	Low	Low	High	High	High	Low	SMM ACOG RT
Knight 2020	Low	Low	Mod	Mod	Mod	Low	Mod		Death
Knight 2009	Mod	Low	Mod	Low	Low	Low	Mod		SMM (direct) NT
Korb 2019	Low	Low	Mod	Low	High	High	High	Mod	SMM Epimoms RT
Kozhimannil 2019	Low	Low	Low	Low	High	High	High	Low	SMM CDC T, NT
Kozhimannil 2020	Low	Low	Mod	Low	Low	Low	Mod		SMM CDC T, NT
Kramer 2023	Low	Low	Mod	Low	Low	Low	Mod		SMM CDC T, NT
Kuklina 2011	Low	Low	Mod	Low	High	High	High	Mod	Cardiac arrest, Death
Lazariu 2017	Low	Mod	Low	Low	High	Mod	High	Mod	SMM CDC+NYS T
Leonard 2019A	Low	Mod	Low	Low	High	High	High	Mod	SMM CDC T, NT
Leonard 2019B	Low	Mod	Mod	Low	High	High	High	Mod	SMM CDC T
Leonard 2020A	Low	Mod	Mod	Low	Low	Low	Mod		SMM CDC T, NT
Leonard 2020B	Low	Low	Mod	Low	Mod	High	High	Mod	SMM CDC T, NT
Leonard 2022	Low	Low	Low	Low	Mod	High	High	Low	SMM CDC T, NT
Le Ray 2019	Low	Low	Mod	Mod	Low	Low	Mod		SMM Epimoms RT
Lewkowitz 2019	Low	Low	Mod	Mod	Mod	High	High	Mod	SMM CDC T, NT
Liese 2019	Low	Low	Mod	Low	Mod	Low	Mod		SMM CDC T
Linard 2018	Low	Low	Low	Low	Low	Low	Low		SMM PreCARE RT
Lindquist 2013	Mod	Low	Mod	Low	Low	Low	Mod		SMM
Lindquist 2015A	Low	Low	Low	Low	Low	Low	Low		SMM AMMOI T
Lindquist 2015B	Mod	Low	Low	Low	Mod	High	High	Mod	SMM Selected (direct) NT
Lipkind 2019	Mod	Mod	High	Low	Mod	High	High		SMM CDC NT
Lisonkova 2017A	Low	Low	Low	Low	Low	Low	Low		SMM CPSS T, ITU
Lisonkova 2014	Low	Mod	Mod	Low	Mod	Low	Mod		SMM CPSS T, death
Lisonkova 2016	Low	Low	Low	Low	Mod	Low	Mod	Low	SMM CPSS T
Lisonkova 2017B	Low	Low	Mod	Low	Low	Low	Mod		SMM CPSS T, ITU, death
Liu 2020	Low	Low	Low	Low	Mod	Low	Mod	Low	SMM CDC T, NT
Liu 2019	Low	Mod	Mod	Low	High	Low	High	Mod	SMM CDC T
Luke 2019	Low	Mod	Low	Mod	Mod	High	High	Mod	ITU
Luke 2020	Low	Low	Mod	Low	Mod	Mod	Mod		SMM CDC T, NT
Lutomski 2012	Low	Low	Mod	Low	High	High	High	Mod	SMM AMMOI T* Select (unadjusted are all mod)
Lyndon 2015	Low	Low	Mod	Low	High	High	High	Mod	SMM CDC T
Lyndon 2012	Low	Low	Mod	Low	High	High	High	Mod	SMM CDC T
MacDonald 2015	Low	Low	Mod	Low	Mod	Mod	Mod		SMM CDC T, Death
Madar 2019	Low	Low	Low	Low	Low	Low	Low		SMM Epimoms RT
Main 2020	Mod	Mod	Mod	Low	Low	Low	Mod		SMM CDC T, NT
Malhamé 2021	Mod	Mod	Mod	Low	Mod	High	High	Mod	SMM cardiovascular NT
Männistö 2013	Low	Low	Mod	Mod	Mod	Mod	Mod		ITU

Study	Part.	Att.	Prog.	Out.	Conf.	An./Rep.	RoB	Raw	Outcome
Martin 2016	Mod	Mod	Mod	Low	Mod	Mod	Mod		SMM CDC T
Masterson 2022	Low	Low	Mod	Low	Mod	Mod	Mod		SMM EMMOI NT, ITU, death
Matas 2021	Low	Low	Low	Low	Mod	Mod	Mod	Low	SMM CDC T only
Matsuo 2022	Low	Mod	Mod	Mod	Mod	High	High	Mod	SMM CDC T, NT
McKinley 2021	Low	Mod	Mod	Low	High	High	High	Mod	SMM CDC NT
Meeker 2021	Low	Low	Mod	Low	High	High	High	Mod	SMM CDC T
Mhyre 2011	Low	Low	Mod	Low	High	High	High	Mod	SMM Mhyre NT
Mhyre 2014	Low	Low	Low	Low	Mod	High	High	Low	Cardiac arrest
Minkauskiene 2006	Mod	Low	Mod	Low	High	High	High	Mod	SMM Waterstone RT
Mitra 2021	Low	Low	Low	Low	Mod	Mod	Mod	Low	SMM CDC T, NT
Mooney 2022	Mod	Low	Low	Low	Mod	Mod	Mod		SMM CDC T
Mujahid 2021	Low	Low	Low	Low	Mod	Low	Mod	Low	SMM CDC T
Mujahid 2023	Low	Low	Low	Low	Mod	Low	Mod	Low	SMM CDC T, NT
Murugappan 2020	Mod	Mod	Mod	Low	Mod	High	High	Mod	SMM CDC T
Montori 2021	Mod	Low	Mod	Mod	Mod	Mod	Mod		ITU
Nagata 2019	Low	Low	Low	Mod	Mod	High	High	Mod	ITU
Nair 2016	Low	Low	Mod	Low	Mod	High	High	Mod	Death
Nair 2014	Mod	Low	Low	Low	Mod	Low	Mod		SMM select direct NT
Nam 2022	Low	Low	Mod	Low	High	High	High	Mod	SMM CDC T, SMM ACOG RT, Zwart SAMM RT, EURONET T
Olive 2005	Low	Mod	Mod	Low	Mod	Mod	Mod		ITU, SMM novel T
Oot 2021	Low	Mod	Mod	Low	High	High	High	Mod	SMM CDC T
Osei-Poku 2023	Low	Low	Low	Low	Low	Low	Low		SMM CDC NT, arrest
Ozimek 2016	Mod	Low	Mod	Low	Mod	Mod	Mod		SMM ACOG RT
Park 2023	Low	Low	Mod	Low	Mod	Mod	Mod		SMM CDC T
Pallasmaa 2008	Low	Low	Mod	Low	High	High	High	Mod	SMM Direct NT
Pallasmaa 2015	Low	Low	Mod	Low	Mod	High	High	Mod	SMM Direct NT
Panelli 2021	Low	Mod	Low	Low	Mod	Mod	Mod		SMM CDC T, NT
Phillips 2023	Mod	Low	Low	Low	High	Low	High	Mod	SMM CDC T, NT
Phillips 2021	Low	Mod	Mod	Low	Mod	Low	Mod		SMM CDC T, NT
Platner 2019	Low	Low	Mod	Low	Low	Low	Mod		SMM CDC T, NT; arrest; death
Platner 2020	Low	Low	Low	Low	Low	Low	Low		SMM CDC T, NT; death
Raineau 2022	Low	Low	Mod	Low	Mod	Mod	Mod		SMM Epimoms antepartum
Ray 2020	High	Low	High	Low	Low	Low	High		SMM T
Ray 2018	Low	Low	Low	Low	High	Low	High	Low	Death
Rezaeiahari 2023	Low	Low	Low	Low	Mod	Low	Mod	Low	SMM CDC T, NT
Rosenbloom 2019	Low	Mod	Mod	Low	Mod	High	High	Mod	SMM CDC T

Study	Part.	Att.	Prog.	Out.	Conf.	An./Rep.	RoB	Raw	Outcome
Rossi 2019	Low	Mod	Low	Low	High	High	High	Mod	ITU
Salahuddin 2020	Mod	Low	Mod	Low	Mod	Mod	Mod		SMM CDC T
Sastow 2021	Low	Low	Low	Low	Mod	High	High	Low	SMM CDC T
Schummers 2015	Low	Low	Mod	Low	Mod	Low	Mod		SMM Novel NT
Selo-Ojeme	Mod	Low	Mod	Low	High	High	High	Mod	ITU
Sheen 2018	Mod	Low	Mod	Low	Low	Low	Mod		SMM CDC T, NT
Siddiqui 2017	Low	Low	Mod	Low	Mod	Mod	Mod		Cardiac arrest, Death
Siddiqui 2019	Low	Low	Mod	Low	Low	Low	Mod		SMM EPIMOMS RT
Siddiqui 2021	Low	Low	Low	Low	Low	Low	Low		SMM CDC T, NT
Snowden 2021	Low	Low	Mod	Low	Mod	Mod	Mod		SMM CDC T
Somerville 2019	Low	Low	Low	Low	Mod	Mod	Mod	Low	SMM CDC NT
Stanhope 2022	Mod	Low	Low	Low	Mod	Low	Mod		SMM CDC T, NT
Sutton 2020	Low	Mod	Low	Low	Mod	Low	Mod		SMM ACOG RT
Tangel 2019	Low	Low	Low	Low	High	High	High	Low	Death
Tangel 2020	Low	Low	Low	Low	High	High	High	Low	SMM CDC T
Thompson 2015	Low	Low	Low	Low	Mod	High	High	Low	SMM Cardiovascular NT, cardiac arrest, death
Ukah 2020	Low	Mod	Mod	Low	Low	Low	Mod		SMM CPSS-CDC T
Urquia 2015	Low	Low	Mod	Mod	Mod	Low	Mod		SMM Wahlberg NT
Urquia 2017	Low	Low	Low	Low	Low	Low	Low		SMM CPSS T
van Dillen 2010	Mod	Low	Low	Mod	High	High	High	Mod	SAMM Zwart RT, death
van Hanegem 2011	Low	Low	Mod	Low	High	Mod	High	Mod	SAMM Zwart RT
Vousden 2021	Mod	High	Low	Low	High	Mod	High		SMM Other NT; ITU
Wagner 2020	Low	Low	Mod	Low	High	High	High	Mod	SMM Other T
Wahlberg 2013	Low	Low	Low	Low	Mod	Low	Mod	Low	SMM Wahlberg NT
Wall-Wieler 2019	Low	Low	Low	Low	Mod	Low	Mod	Low	SMM CDC T, NT; arrest
Wanderer 2013	Low	Low	Low	Low	Mod	Mod	MoL	Low	ITU
Wang 2016	Mod	Mod	Low	Low	High	High	High	Mod	SMM ACOG RT
Wanigaratne 2015	Low	Low	Low	Low	Mod	Mod	Mod	Low	SMM CPSS T
Waterstone 2001	Low	Low	Mod	Low	High	High	High	Mod	SMM Waterstone RT
Zanconato 2012	Low	Low	Mod	Low	High	High	High	Mod	SMM Other RT
Zwart 2008	Low	Low	Mod	Low	High	High	High	Mod	SMM Zwart RT
Zwart 2010	Low	Low	Mod	Low	High	High	High	Mod	ITU
Zwart 2011	Low	Low	Mod	Low	High	High	High	Mod	SMM Zwart RT

Part. Participation; Att. Attrition; Prog. Prognostic factors; Out. Outcome; Conf. Confounding; An./Rep. Analysis and Reporting. RoB Overall risk of bias rating. Raw Sub-rating applicable to raw data only.

Appendix B3.3 Harvest Plot of Prognostic Factors for SMM-T

1	Protective factor in 1 study at high RoB	1	No association in 1 study at high RoB	1	Risk factor in 1 study at high RoB
1	Protective factor in 1 study at mod RoB	1	No association in 1 study at mod RoB	1	Risk factor in 1 study at mod RoB
1	Protective factor in 1 study at low RoB	1	No association in 1 study at low RoB	1	Risk factor in 1 study at low RoB

Prognostic factor	**Unadjusted**			**Adj. distal conf. Age + SEP/educ. Not comorb/lifestyle**			**Adj. distal conf. + Comorb/lifestyle**			**Adj. distal conf/ comorb/lifestyle + Interventions**		
	-	=	+	-	=	+	-	=	+	-	=	+
DEMOGRAPHIC												
Race/ethnicity												
Aboriginal			1						1			
Aboriginal/Torres Strait Islander vs. not			1						1			
African			1						1			
Asian			2 2			1			1			2
Asian/PI		3	4 4 2			2			3 1		2	2
Hawaiian/Pacific Islander			1 1						2		1	
Chinese	1							1				
Filipina			1						1			
Indian	1	1						2				
Japanese | Korean | Vietnamese		1						1				
Black		2	8 23 4			2 4			9 2		1	15

Prognostic factor	Unadjusted									Adj. distal conf. Age + SEP/educ. Not comorb/lifestyle									Adj. distal conf. + Comorb/lifestyle									Adj. distal conf/ comorb/lifestyle + Interventions								
Hispanic/Latina					4		7	17	2					1		1	3						1	1		7	1							3						9
Puerto Rican								1																		1														
Maori/Polynesian							1																	1																
Multi-race							2																				1													
Native American or Alaskan/Native							1	6	1								2									2	1							1					1
White/Caucasian (ref unless specified)																																							
Immigration status																																							
Immigrant, vs. non-migrant		1		4	2			1					1	1*						1			1									2							
Refugee, vs. non-migrant							1										1*																						
Immigrant, long term | insecure							1																																
Immigration status and place of																																							
Legal, non-Sub-Saharan African with EU					1									1																									
Other legal, Sub-Saharan Africa					1													1																					
Undocumented, Sub-Saharan Africa									1									1																					
Europe and Western | South Asia	1									1																													
Caribbean | Sub-Saharan Africa							1									1																							
E Asia, SE Asia, Pacific							1						1																										
Hispanic America | N. Africa and Middle				1									1																										
Mexican | Dominican								1																		1													
Oceania | UK and Ireland | Europe | N.				1																		1																
Middle East vs. AUS	1																			1																			

Prognostic factor	Unadjusted									Adj. distal conf. Age + SEP/educ. Not comorb/lifestyle									Adj. distal conf. + Comorb/lifestyle									Adj. distal conf/ comorb/lifestyle + Interventions								
Maternal age																																						
Advanced age					2		3	2									2							3	3														
U-shaped association							7	17	1								1							1	1	1									1	5		
Advanced age (dichotomous)								5										1					1		2	1						1			3		
Age (continuous, linear)																															1			1				
SOCIOECONOMIC																																						
Marital status																																						
Unmarried				1	1		3	4	1								1					1		2								1					
Unpartnered								1																														
Maternal education																																						
<HSE, vs. HSE				2	2		1	2																		1											
<HSE, vs. any post-HSE level							3	2	1															1	1											2	
HSE, vs. any post-HSE level				1	1		2	2	1															1	1							1					
HSE, or below, vs. any post-HSE level					1		1	2																1													
Some college, vs. college							1		1													1															
Healthcare funding																																						
Public insurance, vs. private					1		6	17	1							1	1					1		1	5	1						2		1	6		
Uninsured/self-pay vs. private							2	6									1								1							2			2		
Income and deprivation																																						

Prognostic factor	Unadjusted	Adj. distal conf. Age + SEP/educ. Not comorb/lifestyle	Adj. distal conf. + Comorb/lifestyle	Adj. distal conf/ comorb/lifestyle + Interventions
Lowest SAHHI quantile vs. highest	2 2	1 1	1 1 1	1 1
Lowest SAHHI vs. higher	1 3		1	1 2
Most deprived quantile vs. least deprived	3		1 1 1	
Employed during pregnancy	1			
Housing tenure				
Private vs. public accommodation	1			
Housing-insecure vs. housing-secure	1		1	
Rurality of residence				
Rural vs. urban	1 3 4	1 1 1	1 1 2	1 1
Large metro	2 1 3		1	1 1
Small-medium/small metro (ref)				
Micropolitan	1 2 1 1		1	1
Rural (noncore)	2 1 3		1	1 2
Major city (ref)				
Inner region	1		1	
Outer region | remote	1		1	
Very remote	1		1	
Antenatal care				
Late antenatal care	1 1		1 1	

Prognostic factor	Unadjusted	Adj. distal conf. Age + SEP/educ. Not comorb/lifestyle	Adj. distal conf. + Comorb/lifestyle	Adj. distal conf/ comorb/lifestyle + Interventions
No antenatal care	2		1	1
Late/no antenatal care	1			
Inadequate, vs. adequate	1 2			3
USS in first trimester, vs. none	1		1	
OBSTETRIC HISTORY				
Parity				
Nulliparous vs. parous (any)	1 1 4 4 1	1	2 1	4
Nulliparous vs. previous vaginal birth	1		1	
Grand multiparous vs. not	1			
Nulliparous	1 1 7		2	1
Primiparous (para 1, ref)				
Multiparous (any)	2			
Multiparous (para 2-4)	1 2		1	
Grand multiparous (parity >/5)	1 2		1	
Previous CS vs. no previous CS	2 7		1 2 1	1 3
Previous CS vs. prev term vaginal birth or	1 2		1	1
Previous preterm birth vs. term vaginal	1		1	
Previous preterm CS vs. term vaginal	1		1	
Previous ectopic pregnancy | miscarriage	1			

Prognostic factor	Unadjusted	Adj. distal conf. Age + SEP/educ. Not comorb/lifestyle	Adj. distal conf. + Comorb/lifestyle	Adj. distal conf/ comorb/lifestyle + Interventions
LIFESTYLE				
Smoking				
Smoked prior to pregnancy	1			2
Smoking/tobacco use in pregnancy	1 1 3 2 2 1		1 3	2
Substance misuse				
Substance misuse (any)	1 3		1 1	4
Alcohol-related	1		1	1 1
Opioid-related	1 1		1	1
Stimulant-related	1		1	1
Cannabis-related	1			1
Body mass index				
<18.5	2 3 1 1 2	1 1	1 1 1	1
18.5-24.9 (ref)				
25-29.9	3 4 1	1 1	1 2	1
>/30	1 1 1	1		
30-34.9	2 3	1	1 2	1
35-39.9	2 3	1	1 2	1
>/40	2 3	1	2 2	1
Any higher BMI using non-standard	2 7	1	1 1 1	1 2
Gestational weight gain				
Low, vs. normal (any)	1 3	1	1 1	

Prognostic factor	Unadjusted									Adj. distal conf. Age + SEP/educ. Not comorb/lifestyle									Adj. distal conf. + Comorb/lifestyle									Adj. distal conf/ comorb/lifestyle + Interventions								
High, vs. normal (any)								3	1								2								1	1														
PRE-EXISTING COMORBIDITY																																							
Any pre-existing comorbidity							2	7								2	1						1	1	1	1					1		1	4						
Any multimorbidity (>/2 comorbidities)							2		1							1	2							1								1	1						
Stable | unstable chronic conditions							1																	1															
Disability																																							
Physical only | sensory only | multiple							1									1							1															
Intellectual/developmental only							2									1	1							1	1														
Any disability | physical | hearing | vision							1																											1					
Endocrine																																							
DM (vs. no DM or no DM/GDM)							1	11	1															1	3	1								4					
Thyroid disorders								1																															
Thyrotoxicosis																																			1				
Respiratory																																							
Respiratory (any)								2																	1										1					
Asthma								4																	1										2					
Renal																																							
Renal (any)								2																	1										2					
Chronic kidney disease								3																	1										2					

Prognostic factor	Unadjusted	Adj. distal conf. Age + SEP/educ. Not comorb/lifestyle	Adj. distal conf. + Comorb/lifestyle	Adj. distal conf/ comorb/lifestyle + Interventions
Gastrointestinal				
Gallbladder disease	1			
Gastrointestinal (any)	1			1 1
Liver disease	3		1	1
Cardiovascular				
Cardiac (any)	3		2	3
Cardiac, rheumatic	1			1
Cardiac, congenital | valvular | ischaemic	1		1	
Cardiac, conduction | valvular	1			1
Cardiac, chronic congestive failure	1			
Cardiovascular condition (any)	1			1
HTN vs. no-HTN or no-hypertensive	1 14 1		5 2	6
HTN/CVD	1		1	
Pulmonary HTN	2		1	2
Neurological				
Epilepsy with AED or without AED	2	1		
Epilepsy	1 1	1		1
Neurological or CNS condition	2			
Musculoskeletal				
Musculoskeletal condition	1			2
Neuromuscular condition			1	1

Prognostic factor	Unadjusted									Adj. distal conf. Age + SEP/educ. Not comorb/lifestyle									Adj. distal conf. + Comorb/lifestyle									Adj. distal conf/ comorb/lifestyle + Interventions								
Haematological																																						
Haematological condition (any)								2																	1														4
Sickle cell disease							1	1																1														
Anaemia								4	1																1	1													3
Hb <125, vs. 125-129									1																	1												
MCV (1-SD (5 fL) lower)																										1												
Hereditary haemolytic anaemia								1																														
Autoimmune																																						
Any AI, SLE, or connective tissue group								2																	1								1						1
Other comorbidities																																						
HIV/AIDS								3																	2														1
Cancer								1																															1
Maternal mental health																																						
Mental health diagnosis (any)							1	2																1														
Mental health diagnoses ('non-serious')																																	1					
Mental health diagnosis ('serious')								1																									1					2
Depression								1																									1					
Depression, self-reported								1																														
Bipolar disorder								1																														1
Conception																																						
Subfertility (any) vs. fertile								1																														1

Prognostic factor	Unadjusted	Adj. distal conf. Age + SEP/educ. Not comorb/lifestyle	Adj. distal conf. + Comorb/lifestyle	Adj. distal conf/ comorb/lifestyle + Interventions
Subfertility (any) without ART, vs. fertile	1			
Subfertility testing only, vs. fertile	1			1
Subfertility diagnosis only vs. fertile	1			1
ART (any) vs. fertile	2 5		1 1	3
Twin/multiple pregnancy	4 15 1		1 2 1	8
Antenatal morbidity				
Excess vomiting	1			
GDM	5 2 1			1 2
PIH vs. none/no hypertensive disease	2 2 5			4
Pre-eclampsia vs. none/no hypertensive	1 8		1	4
Any hypertensive disease, vs. none			1	
PIH or pre-eclampsia, vs. none	2		2	2
Admission anaemia (<10g/dl)	1			
Admission thrombocytopoenia (<100/uL)	1			
Antepartum haemorrhage	1			
Postpartum haemorrhage	2			2
Obstetric infection	1			1
Chorioamnionitis	1 1			2
				1
Prolonged rupture of membranes	1			1
Abnormal placentation/placenta	1 3			4

Prognostic factor	Unadjusted	Adj. distal conf. Age + SEP/educ. Not comorb/lifestyle	Adj. distal conf. + Comorb/lifestyle	Adj. distal conf/ comorb/lifestyle + Interventions
Non-cephalic presentation	2			1
Polyhydramnios	1			1
Antenatal inpatient admission (any)	1			
Peripartum interventions				
Induction, vs. spontaneous,	2 4			1 1
Augmentation, vs. spontaneous,	1			1
Bishop score <6	1		1	1
Oxytocin	1			1
Prostaglandin	1			1
Foley bulb	1			1
Epidural anaesthesia	1 1			
Length of labour				
>/6 hours vs. <6 hours	1			1
Prolonged second stage vs. not	1			1
Mode of birth				
Vaginal (unassisted/assisted, ref)				
Vaginal (assisted)	1 4	1		3
Caesarean birth	2 12 1	1	1	1 1 6
Planned or non-emergent CS	1 1			
Unplanned or emergent CS or	2 1			
Caesarean birth prior to labour	1			

Prognostic factor	Unadjusted	Adj. distal conf. Age + SEP/educ. Not comorb/lifestyle	Adj. distal conf. + Comorb/lifestyle	Adj. distal conf/ comorb/lifestyle + Interventions
Primary caesarean	1 1			1
Repeat caesarean	1 1			1
Vaginal birth following spontaneous				
Vaginal birth following IOL	1			1
Non-emergent caesarean birth	1			1
Emergency caesarean birth	1			1
Gestational age				
Preterm birth, vs. term	2 6		1	5
Preterm labour	1			
Lower gestational age (continuous)	1		1	
Spontaneous preterm birth, vs. tem	1			
Iatrogenic preterm birth, vs. term	1			
>/41+0, vs. term	1			
37+0-37+6 | >/41+0, vs. 39+0-39+6	1			1
37-38+5 cf 39-40+5	1			
>/41 cf 39-40+5	1			
>/42+0, vs. 39+0-39+6	1 1			1
Birthweight				
<2500g, vs. 2500-2999g/3500-3999g	1 1			1
>/4000g, vs. 2500-2999g/3500-3999g	1 2			2
Fetal macrosomia	1			1

Prognostic factor	Unadjusted	Adj. distal conf. Age + SEP/educ. Not comorb/lifestyle	Adj. distal conf. + Comorb/lifestyle	Adj. distal conf/ comorb/lifestyle + Interventions
Stillbirth/intrauterine death/perinatal	2 | 3		2	2
Admission type				
Elective birth admission	1			1
Weekend birth admission	2			
Hour of birth (levels with similar risk				
11:01-23:00, vs. 07:01-11:00	1			1
23:01-07:00, vs. 07:01-11:00	1			1
Day of birth (levels with similar risk				
Tue-Thur | Sunday, vs. Monday	1			1
Fri-Saturday, vs. Monday	1			1

Adj. adjusted, SEP socioeconomic position/related variables, educ. education, comorb. comorbidity. HSE high school education, SAHHI small-area household income, USS ultrasound, DM diabetes mellitus, GDM gestational diabetes, HTN hypertension, CVD cardiovascular disease, AI autoimmune, SLE systemic lupus erythematosus, AED antiepileptic drug, ART assisted reproductive technology, CS caesarean section (birth).
If multiple prognostic factors demonstrated the same pattern of association as one another, these are reported on the same row, denoted by '|'

Appendix Table B3.4 Harvest Plot of Prognostic Factors for SMM-RNT

1	Protective factor in 1 study at high RoB	1	No association in 1 study at high RoB	1	Risk factor in 1 study at high RoB
1	Protective factor in 1 study at mod RoB	1	No association in 1 study at mod RoB	1	Risk factor in 1 study at mod RoB
1	Protective factor in 1 study at low RoB	1	No association in 1 study at low RoB	1	Risk factor in 1 study at low RoB

Prognostic factor	**Unadjusted**			**Adj. distal conf. Age + SEP/educ/parity; Not comorb/lifestyle**			**Adj. distal conf. + Comorb/lifestyle**			**Adj. distal conf/ comorb/lifestyle + Interventions/ pregnancy outcome**		
	-	=	+	-	=	+	-	=	+	-	=	+
DEMOGRAPHIC												
Race/ethnicity												
Aboriginal/Aboriginal or Torres Strait			1 1					3	1			
African			1						1			
African American		1	1					1				
Asian/PI or Asian	2	2 1	2 7 4		1 1				2 4		2	3
Bangladeshi			1						1			
Indian		1 1						1 1				
Pakistani			1						1			
Black			6 17 5			2 3			6 3		2	1 6
Black African | Black Carribean			1						1			
Dutch Antillean | Moroccan | Turkish		1										

Prognostic factor	Unadjusted	Adj. distal conf. Age + SEP/educ/parity; Not comorb/lifestyle	Adj. distal conf. + Comorb/lifestyle	Adj. distal conf/ comorb/lifestyle + Interventions/ pregnancy outcome
'Far East'	1			
Hispanic/Latina	2 3 3 3 4 9 1	1 1 1	2 4 3	5 1 1
Maori or Polynesian	1		1	
Multi-race	2		1	
Native (American or Alaskan)	1 1 1 5	1 1	1 2 1	1
Sub-Saharan African | Middle Eastern	1			
Surinamese	1			
Minority group (any)	1		1	
White/Caucasian (ref. unless specified)				
Immigration status				
Immigrant, vs. non-migrant	1 1		1	1
Non-Western immigrant, vs. non-migrant	1			
Asylum seeker, vs. non-migrant	1			
Immigrant, long term | insecure residency	1			
Immigration status and place of				
Low-income country	1		1	
Middle-income | high-income country	1		1	
Native (Swedish, ref)				
Caribbean	1		1	
Caribbean and Latin America		1		
North Africa	1			

Prognostic factor	Unadjusted	Adj. distal conf. Age + SEP/educ/parity; Not comorb/lifestyle	Adj. distal conf. + Comorb/lifestyle	Adj. distal conf/ comorb/lifestyle + Interventions/ pregnancy outcome
Africa	1		1	1
Asia	1			
East Asia/Pacific	1	1	1	
Europe	2	1	1	1
Hispanic America			1	
Middle East/Asia	1 1		1	1
Middle East/North Africa		1	1	
North America	1		1	1
South America	2		1	1
South Asia	1	1	1	
Sub-Saharan Africa	2	1	1	
Oceania	1		1	1
Western Nations/Europe	1 1		1	
Maternal age				
Advanced age	1 5 5 2	1	1 5 4	1 2 1
U-shaped association	3 10	1	3 1	1 2
Advanced age (dichotomous)	1 4 2		1	1 3
Age (continuous, linear)				
SOCIOECONOMIC				
Marital status				
Unmarried, vs. married	2 1 1			
Single unsupported vs. married	1			

Prognostic factor	Unadjusted	Adj. distal conf. Age + SEP/educ/parity; Not comorb/lifestyle	Adj. distal conf. + Comorb/lifestyle	Adj. distal conf/ comorb/lifestyle + Interventions/ pregnancy outcome
Sole registration, vs. joint	1		1	1
Divorced vs. married	1			
Single supported vs. married	1			
Lives alone	1			
Maternal education				
<HSE, vs.HSE				
<HSE vs. any post-HSE level	1 2		1 1	
HSE vs. any post-HSE level	1 2			
HSE or below, vs. any post-HSE level	1 2		1 1	
Some college, vs. college	1 1		1 1	
Healthcare funding				
Public insurance, vs. private	1 1 6 12 2	1	1 4 1	1 1 4
Uninsured/self-pay (not 'other') vs. private	3 1 2 4		1	1
Household income				
Lowest SAHHI quantile vs. highest	2 4	1	1 2 1	1 2
Lowest SAHHI quantile vs. higher	2		1	
Most deprived quantile vs. least deprived	1 2 1		1 1 2	1
Rurality of residence				
Rural vs. urban	2 1 1	1	1 1	

Prognostic factor	Unadjusted	Adj. distal conf. Age + SEP/educ/parity; Not comorb/lifestyle	Adj. distal conf. + Comorb/lifestyle	Adj. distal conf/ comorb/lifestyle + Interventions/ pregnancy outcome
Non-metropolitan vs. metropolitan	1			
Large metropolitan	1 2 1 2		1	1
Small-medium/small metropolitan (ref)				
Micropolitan	1 1 2 1		1	1
Rural (noncore)	1 1 3 1 1		1	1
Major cities of Australia (ref)				
Inner regional Australia	1 1		2	
Outer region	1 1		1 1	
Remote	1 1		1 1	
Very remote	1 1		2	
Accessible small towns, vs. large urban	1		1	1
Other urban areas | remote small towns |	1		1	1
Remote rural, vs. large urban	1		1	1
Occupational classification				
Self-employed, vs. professional	1			
Manual/service, vs. professional	2 1		1	
Public service/administrative/sales, vs.	1			
Intermediate | unemployed, vs.	3		1	
Manual | unemployed, vs. non-manual	1			
Non-managerial/professional cf	1		1	

Prognostic factor	Unadjusted									Adj. distal conf. Age + SEP/educ/parity; Not comorb/lifestyle										Adj. distal conf. + Comorb/lifestyle										Adj. distal conf/ comorb/lifestyle + Interventions/ pregnancy outcome									
Antenatal care																																										
Late antenatal care (>1st trimester)				1	1		1	1																1	1			1														
No antenatal care								1																																1	1	
Late/no ANC or late/no/inadequate							1	1																																		
Inadequate, vs. adequate				1				2																1				1													1	
Intermediate inadequate vs. adequate				1	1			1																1				1													1	
<50% recommended visits							1																				1														
50-79% | >/110% of recommended				1																				1																	
Trimester of USS				1																				1																	
OBSTETRIC HISTORY																																										
Parity																																										
Nulliparous, vs. parous (any)			1	1	5	1	2	7																	2			1							1					3	
Grand multiparity >/5, vs. not								1																																		
Nulliparous							1	3																				1	1											1		
Primiparous (parity 1, ref)																																										
Multiparous (parity 2)					1																																				
Multiparous (parity 2-4)				1																						1														
Multiparous (parity >/3)					1																																				
Grand multiparous (parity >/5)				1																						1														
Previous live birth vs. not																								1																	

Prognostic factor	Unadjusted	Adj. distal conf. Age + SEP/educ/parity; Not comorb/lifestyle	Adj. distal conf. + Comorb/lifestyle	Adj. distal conf/ comorb/lifestyle + Interventions/ pregnancy outcome
Parity >/3 vs. not	2 1			
Parity >/4 vs. not	1 1			
Parity >/6 vs. not	1			
Nulliparous, vs. previous vaginal birth	1		1	1
Any previous CS vs. none	2 5 3		1 1 1	1
One previous CS vs. none	1		1	1
>/2 previous CS vs. none	1		1	1
SMM associated with previous CS	1			
Any previous CS vs, previous vaginal birth	1		1	1
Previous CS + vaginal vs. previous vaginal				1
Previous preterm CS	1		1	
Previous PTB	1 1		1	
Previous SGA or LGA or PTB			1	
Previous pregnancy condition	1		1	
Previous PIH	1			
Previous hypertensive disorder (any)	1 1		1	1
Previous pre-eclampsia				1
Previous peripartum haemorrhage/PPH	2			2

Prognostic factor	Unadjusted									Adj. distal conf. Age + SEP/educ/parity; Not comorb/lifestyle									Adj. distal conf. + Comorb/lifestyle									Adj. distal conf/ comorb/lifestyle + Interventions/ pregnancy outcome								
Previous baby >4000g					1																																	
Previous miscarriage								1																1														
Previous pregnancy loss					1																	1															
Previous perinatal death								1																														
LIFESTYLE																																					
Smoking																																					
Smoking prior to pregnancy		1																																			
Smoking in pregnancy		3		1	6	1	1		1											1		2				1			1			1					1
Current smoker vs. non-smoker					1																	1							1								
Ex-smoker vs. non-smoker								1																1														
Substance misuse																																					
Substance misuse (any)								3																2	2					1			1				
Alcohol-related								1												1																	
Opioid-related							2		1							1									1												
Stimulant-related							1		2																1												
Cannabis-related									1														1														
Body mass index																																					
<18.5				2	6	2							2								1	1	1							1							
18.5-24.9 (ref)																																					
25-29.9				1	3	2	1	2					1			1						1	1	1						1							

Prognostic factor	Unadjusted	Adj. distal conf. Age + SEP/educ/parity; Not comorb/lifestyle	Adj. distal conf. + Comorb/lifestyle	Adj. distal conf/ comorb/lifestyle + Interventions/ pregnancy outcome
>/30	2 4	1		
30-34	1			
35-39	1			
30-39.9	2 1 2	1	1 1 1	1
>/40	1 1 1 2 1	1	1 1 2	1
Any higher BMI using non-standard	3 1 5 3		3 2 1 3	2 1
Gestational weight gain				
Low, vs. normal	2 1	1	1	
High, vs. normal	2		1	
1-19 lbs above GWG, vs. normal	1	1		
>/20 lbs above GWG, vs. normal	1	1		
Vitamin mmentation	1			
Folic acid supplementation	1			
PRE-EXISTING COMORBIDITY				
Any pre-existing comorbidity	3 6	1	1 3 2	2 2
Any multimorbidity (>/2 comorbidities)	2 1	1 1	1 1	2
Initial care by obstetrician	1			
Disability				
Any disability | physical | hearing | vision	1			1

Prognostic factor	Unadjusted	Adj. distal conf. Age + SEP/educ/parity; Not comorb/lifestyle	Adj. distal conf. + Comorb/lifestyle	Adj. distal conf/ comorb/lifestyle + Interventions/ pregnancy outcome
Intellectual/developmental disability	3	1	2	1
Endocrine				
DM, vs. no DM/no diabetic disease	1 8 2		5 3	1 2 3
Thyrotoxicosis				1
Respiratory				
Respiratory (any)	1		1	
Asthma	5		2 2	1 3
Renal				
Renal (any)	2		2	1
Chronic kidney disease	4		1 1	3
Gastrointestinal				
Gastrointestinal (any)				1
Liver disease	2		2	
Cardiovascular				
Cardiac (any)	1		1	1
Cardiac, congenital or valvular/congenital	1 1		1 1	1
Cardiac lesions or valvular disease			1	
Cardiac, valvular	2		1	1
Cardiac, conduction	1			1

Prognostic factor	Unadjusted	Adj. distal conf. Age + SEP/educ/parity; Not comorb/lifestyle	Adj. distal conf. + Comorb/lifestyle	Adj. distal conf/ comorb/lifestyle + Interventions/ pregnancy outcome
Cardiac, ischaemic	1		1 1	
Cardiovascular (any)	1		1	
Dyslipidaemia	1			
HTN	1 10		5 3	1 1 4
Elevated BP | stage 1 HTN <20/40, vs.	1		1	
Stage 2 HTN <20/40, vs. normal BP	1		1	
Pulmonary HTN	2		1 1	2
Neurological				
Antiepileptic at booking				1
Epilepsy (with AED | without AED)/ within	2	2	1	
Musculoskeletal				
Neuromuscular condition			1	1
Haematological				
Haematological (any)			1	
SCD	1 1	1	1 1	
Anaemia (pre-existing or in pregnancy)	2		1	1
Iron supplementation at booking				1
Hypercoagulable state/antenatal	1 1		1	1
Coagulation/clotting/bleeding disorder				1
Autoimmune				

Prognostic factor	Unadjusted	Adj. distal conf. Age + SEP/educ/parity; Not comorb/lifestyle	Adj. distal conf. + Comorb/lifestyle	Adj. distal conf/ comorb/lifestyle + Interventions/ pregnancy outcome
Any AI, SLE, or connective tissue group	3		2 1	2
Other comorbidities				
HIV/AIDS	2		1 1 1	1
Bariatric surgery				1
Cancer	2		1	1
Fibroids	1			
Maternal mental health				
Mental health diagnosis (any)	1			
Major mental health disorder				1
Depression | bipolar disorder	1			1
Antidepressant at booking				1
Conception				
ART/IVF	5		1	
IVF autologous oocytes	1		1	
IVF donor oocytes	1		1	
Non-IVF fertility treatment	1			
Twin/multiple pregnancy	1 5 14		1 5 3	1 1 6
Antenatal morbidity				
Admission haemoglobin <10g/dl	1			

Prognostic factor	Unadjusted									Adj. distal conf. Age + SEP/educ/parity; Not comorb/lifestyle										Adj. distal conf. + Comorb/lifestyle										Adj. distal conf/ comorb/lifestyle + Interventions/ pregnancy outcome									
Admission platelets <100 per uL								1																																	
GDM					2		1	4	1													1			1							1		1	1		1	2			
PIH					1		1	2																		1								1							
Hypertensive disorder of pregnancy (any)								2																	1	1														2	
PIH/PET without severe features																										1													1	
Pre-eclampsia								3	1																	1												1	1	
Chorioamnionitis								2																															1	
Placenta accreta								1	1																														2	
Placenta praevia								2	1																	1													2	
Placental disorder/abnormal								2																	1														1	
Haemorrhage in T1-2								1																																
PPH								1																															1	
Seasonal influenza in pregnancy						1																		1															
Non-cephalic presentation							1	3	1																														1	
Small for gestational age								1																	1										1					
Antenatal | postnatal admission vs.								1																																
Early-pregnancy related admission		1																																						
Antenatal anticoagulation																																							1	
Antenatal inpatient admission (one)								1																															1	
Antenatal inpatient admission (>/2)								1																															1	

Prognostic factor	Unadjusted	Adj. distal conf. Age + SEP/educ/parity; Not comorb/lifestyle	Adj. distal conf. + Comorb/lifestyle	Adj. distal conf/ comorb/lifestyle + Interventions/ pregnancy outcome
Antenatal inpatient admission (any)	1			1
Elective (birth) admission	1			1
Weekend (birth) admission	1			
Peripartum interventions				
Induction of labour	3			1
Induction for dates				1
Induction for medical indication				1
Augmentation (oxytocin)	1			1
Hyperstimulation	1			
Active management of the third stage of	1			
Mode of birth				
Unassisted vaginal birth (ref)				
Assisted vaginal birth	5			2
Any CS	2			1
Elective CS	3			1
Emergency CS	2			
Intrapartum CS	1			
Vaginal birth (ref)				
Caesarean birth (any)	4 5 1		1	3 3
Primary CS | repeat CS	1 1			
Elective CS | emergency CS	1 1			

Prognostic factor	Unadjusted									Adj. distal conf. Age + SEP/educ/parity; Not comorb/lifestyle										Adj. distal conf. + Comorb/lifestyle										Adj. distal conf/ comorb/lifestyle + Interventions/ pregnancy outcome									
VBAC cf non-VBAC vaginal birth								1																																
ELCS, vs. attempted vaginal birth								1	1																															
EMCS (undefined), vs. not								1																																1
Assisted vaginal birth, vs. not								1																																
Pre-labour CS, vs. none								1	1																															
Spontaneous onset, vaginal birth (ref)																																								
Induction and vaginal birth								1																																1
Non-emergent CS								1																																1
Emergency CS								1																																1
Home birth		1																																						
PROM/PPROM									1																															
GBS vs. unknown status			1																																				
GBS vs. negative status						1																																	
Antenatal steroids administered								1																																1
Manual removal of placenta																																								1
Gestational age																																							
Preterm birth, vs. term							2	10	1																														1	5

Prognostic factor	Unadjusted	Adj. distal conf. Age + SEP/educ/parity; Not comorb/lifestyle	Adj. distal conf. + Comorb/lifestyle	Adj. distal conf/ comorb/lifestyle + Interventions/ pregnancy outcome
Lower gestational age (continuous)	1		1	
37-38+5, vs. 39-40+5	1			
Birth 41+0-41+6				1
">41 weeks" cf term "37 <41 weeks"	1			1
>/41 weeks cf 39-40+5	1			
Birth >/42+0	2			1
Birthweight				
SGA, vs. appropriate for gestational age	1			
LGA, vs. appropriate for gestational age	1			
BW <2500g cf 3500-2999g	1			
BW >/4000 cf 3500-2999g	1			
Fetal macrosomia	1			1
Polyhydramnios	1			1
Stillbirth/intrauterine death	2 | 3		2	1 | 1

Adj. adjusted, SEP socioeconomic position/related variables, educ. education, comorb. comorbidity. HSE high school education, SAHHI small-area household income, USS ultrasound, SGA small for gestational age, LGA large for gestational age, PTB preterm birth, PIH pregnancy-induced hypertension, DM diabetes mellitus, GDM gestational diabetes, HTN hypertension, CVD cardiovascular disease, AI autoimmune, SLE systemic lupus erythematosus, AED antiepileptic drug, ART assisted reproductive technology, CS caesarean section (birth).
If multiple prognostic factors demonstrated the same pattern of association as one another, these are reported on the same row, denoted by '|'

Appendix Table B3.5 Summary of Prognostic Factors Reported within Racial/Ethnic Groups or Health Inequalities Reported within Subgroups of Prognostic Factors

Study	Outcome	Prognostic factor/group	Race/Ethnic group	Prevalence	Within strata of prognostic factor	Within strata of race/ethnicity	Relative risk ratio of race/ethnicity strata, vs. White
Cudjoe 2023	SMM-RT	Rural residence	Asian	7.8%	OR 1.30 (0.74, 2.64)	-	-
		Rural residence	Black	13%	OR 2.02 (1.58, 2.57)	-	-
		Rural residence	Hispanic	11%	OR 0.76 (0.48, 1.20)	-	-
		Rural residence	White	42%	-		
		Urban residence	Asian	-	OR 1.25 (1.00, 1.57)	-	-
		Urban residence	Black	-	OR 1.90 (1.65, 2.20)	-	-
		Urban residence	Hispanic	-	OR 1.10 (0.92, 1.31)	-	-
Diop 2022	SMM-RT	Age <18	Black	2.6%	-	uOR 0.96 (0.67, 1.39)	RRR 0.77 (0.48, 1.24)
		Age 18-24	Black	26%	-	uOR 0.79 (0.68, 0.93)	RRR 0.93 (0.70, 1.23)
		Age 25-29 (ref)	Black	26%		-	-
		Age 30-34	Black	26%	-	uOR 1.13 (0.97, 1.31)	RRR 1.03 (0.86, 1.23)
		Age 35-39	Black	16%	-	uOR 1.55 (1.32, 1.81)	RRR 1.13 (0.66, 1.94)
		Age ≥40	Black	4.7%	-	uOR 1.87 (1.51, 2.31)	RRR 0.81 (0.28, 2.30)
		Age <18	White	0.90%	-	uOR 1.24 (0.92, 1.67)	-
		Age 18-24	White	14%	-	uOR 0.85 (0.76, 0.95)	-
		Age 25-29 (ref)	White	23%		-	-
		Age 30-34	White	36%	-	uOR 1.10 (1.01, 1.19)	-
		Age 35-39	White	21%	-	uOR 1.37 (1.26, 1.49)	-

Study	Outcome	Prognostic factor/group	Race/Ethnic group	Prevalence	Within strata of prognostic factor	Within strata of race/ethnicity	Relative risk ratio of race/ethnicity strata, vs. White
		Age ≥40	White	4.5%	-	uOR 2.32 (2.07, 2.60)	-
		≤HSE	Black	57%	-	uOR 0.87 (0.76, 0.99)	RRR 0.96 (0.81, 1.14)
		Some college	Black	22%	-	uOR 1.01 (0.87, 1.18)	RRR 1.01 (0.84, 1.20)
		≥College (ref)	Black	20%		-	-
		≤HSE	White	34%	-	uOR 0.91 (0.85, 0.97)	-
		Some college	White	15%	-	uOR 1.00 (0.92, 1.09)	-
		≥College (ref)	White	51%		-	-
		Public insurance	Black	70%	-	uOR 1.18 (1.04, 1.33)	RRR 1.06 (0.88, 1.29)
		Self-pay	Black	2.3%	-	uOR 1.46 (1.06, 2.03)	RRR 0.87 (0.46, 1.66)
		Private insurance (ref)	Black	28%		-	-
		Public insurance	White	27%	-	uOR 1.11 (1.04, 1.18)	-
		Self-pay	White	1.6%	-	uOR 1.67 (1.39, 2.02)	-
		Private insurance (ref)	White	71%		-	-
		Nulliparous (ref)	Black	41%		-	-
		Parity of 1	Black	30%	-	uOR 0.73 (0.64, 0.84)	RRR 1.00 (0.64, 1.57)
		Parity of ≥2	Black	29%	-	uOR 1.08 (0.96, 1.22)	RRR 1.15 (1.00, 1.32)
		Nulliparous (ref)	White	46%		-	-
		Parity of 1	White	35%	-	uOR 0.73 (0.68, 0.77)	-
		Parity of ≥2	White	19%	-	uOR 0.94 (0.88, 1.02)	-
		Multiple pregnancy	Black	2.1%	-	uOR 2.71 (2.15, 3.41)	RRR 0.69 (0.13, 3.75)
		Multiple pregnancy	White	2.4%	-	uOR 3.92 (3.55, 4.34)	-
		Pre-existing hypertension or previous gestational hypertensive disease	Black	8.8%	-	uOR 2.69 (2.36, 3.07)	RRR 1.29 (0.38, 4.43)
		Pre-existing hypertension or previous gestational hypertensive disease	White	5.8%	-	uOR 2.08 (1.89, 2.28)	-

Study	Outcome	Prognostic factor/group	Race/Ethnic group	Prevalence	Within strata of prognostic factor	Within strata of race/ethnicity	Relative risk ratio of race/ethnicity strata, vs. White
		Pre-existing diabetes or previous gestational diabetes	Black	3.9%	-	uOR 2.14 (1.76, 2.60)	RRR 1.34 (0.55, 3.27)
		Pre-existing diabetes or previous gestational diabetes	White	2.6%	-	uOR 1.60 (1.39, 1.85)	-
		Gestational diabetes	Black	6.8%	-	uOR 1.51 (1.26, 1.81)	RRR 1.09 (0.64, 1.85)
		Gestational diabetes	White	5.3%	-	uOR 1.39 (1.25, 1.56)	-
		Inadequate ANC	Black	17%	-	uOR 1.62 (1.37, 1.92)	RRR 1.07 (0.56, 2.02)
		Intermediate inadequate ANC	Black	7.1%	-	uOR 1.27 (1.00, 1.62)	RRR 1.34 (1.01, 1.77)
		Adequate ANC (ref)	Black	36%	-	-	-
		Adequate plus	Black	36%	-	uOR 2.13 (1.86, 2.43)	RRR 1.08 (0.39, 2.98)
		Inadequate ANC	White	6.7%	-	uOR 1.52 (1.35, 1.71)	-
		Intermediate inadequate ANC	White	6.8%	-	uOR 0.95 (0.82, 1.10)	-
		Adequate ANC (ref)	White	45%	-	-	-
		Adequate plus, vs. adequate	White	40%	-	uOR 1.98 (1.86, 2.11)	-
Ha 2023	SMM-T	Sickle cell disease	Black	0.76%	-	uRR 5.6 (4.8, 6.5)	-
	SMM-RT	Sickle cell disease	Black	0.76%	-	uRR 6.5 (5.0, 8.5)	-
Huang 2023	SMM-T	Housing insecure	Asian or PI or other	0.24%	-	uOR 2.24 (1.01, 4.97)	RRR 0.85 (0.24, 3.00)
		Housing insecure	Black	0.65%	-	uOR 1.57 (1.11, 2.22)	RRR 0.59 (0.20, 1.73)
		Housing insecure	Hispanic	0.23%	-	uOR 1.92 (1.09, 3.37)	RRR 0.72 (0.22, 2.34)
		Housing insecure	White	0.30%	-	uOR 2.65 (1.85, 3.80)	-
Kozhimannil 2020	SMM-T	Rural residence	Indigenous	33%	-	aRR 1.3 (1.0, 1.6)	RRR 1.18 (0.90, 1.55)
		Rural residence	White	19%	-	aRR 1.1 (1.1, 1.2)	-
	SMM-RT	Rural residence	Indigenous	33%	-	aRR 0.7 (0.4, 1.0)	RRR 0.70 (0.44, 1.12)

Study	Outcome	Prognostic factor/group	Race/Ethnic group	Prevalence	Within strata of prognostic factor	Within strata of race/ethnicity	Relative risk ratio of race/ethnicity strata, vs. White
		Rural residence	White	19%	-	aRR 1.0 (0.9, 1.3)	-
Kramer 2023	SMM-T	Age <17, vs. 25-29	Black	-	-	aRR 1.2 (1.0, 1.4)	RRR 0.92 (0.67, 1.26)
		Age 17-19, vs. 25-29	Black	-	-	aRR 1.1 (1.0, 1.2)	RRR 1.1 (0.93, 1.30)
		Age 20-24, vs. 25-29	Black	-	-	aRR 1.0 (0.9, 1.1)	RRR 1.0 (0.87, 1.15)
		Age 30-34, vs. 25-29	Black	-	-	aRR 1.1 (1.0, 1.2)	RRR 1.0 (0.90, 1.11)
		Age 35-39, vs. 25-29	Black	-	-	aRR 1.3 (1.2, 1.4)	RRR 1.0 (0.55, 1.80)
		Age ≥40, vs. 25-29	Black	-	-	aRR 1.6 (1.4, 1.8)	RRR 0.89 (0.41, 1.90)
		Age <17, vs. 25-29	White	-	-	aRR 1.3 (1.0, 1.7)	-
		Age 17-19, vs. 25-29	White	-	-	aRR 1.0 (0.9, 1.2)	-
		Age 20-24, vs. 25-29	White	-	-	aRR 1.0 (0.9, 1.1)	-
		Age 30-34, vs. 25-29	White	-	-	aRR 1.1 (1.0, 1.1)	-
		Age 35-39, vs. 25-29	White	-	-	aRR 1.3 (1.2, 2.4)	-
		Age ≥40, vs. 25-29	White	-	-	aRR 1.8 (1.6, 2.1)	-
		Unmarried, vs. married	Black	-	-	aRR 1.1 (1.0, 1.2)	RRR 1.10 (0.99, 1.22)
		Unmarried, vs. married	White	-	-	aRR 1.0 (1.0, 1.1)	-
		Medicaid, vs. Private	Black	-	-	aRR 1.1 (1.1, 1.2)	RRR 0.92 (0.73, 1.15)
		Medicaid, vs. Private	White	-	-	aRR 1.2 (1.1, 1.3)	-
		Medicare, vs. Private	Black	-	-	aRR 1.7 (1.5, 2.0)	RRR 1.42 (0.80, 2.52)
		Medicare, vs. Private	White	-	-	aRR 1.2 (1.0, 1.4)	-
		Self-pay, vs. private	Black	-	-	aRR 1.4 (1.2, 1.7)	RRR 1.27 (0.81, 2.00)
		Self-pay, vs. private	White	-	-	aRR 1.1 (0.8, 1.4)	-
		<HS, vs. ≥some college	Black	-	-	aRR 1.2 (1.0, 1.5)	RRR 0.92 (0.68, 1.26)
		Some HS, vs. ≥some college	Black	-	-	aRR 1.2 (1.1, 1.3)	RRR 0.86 (0.61, 1.21)

Study	Outcome	Prognostic factor/group	Race/Ethnic group	Prevalence	Within strata of prognostic factor	Within strata of race/ethnicity	Relative risk ratio of race/ethnicity strata, vs. White
		High school graduate, vs. ≥some college	Black	-	-	aRR 1.2 (1.1, 1.2)	RRR 1.09 (0.90, 1.33)
		<HS, vs. ≥some college	White	-	-	aRR 1.3 (1.0, 1.6)	-
		Some HS, vs. ≥some college	White	-	-	aRR 1.4 (1.2, 1.5)	-
		High school graduate, vs. ≥some college	White	-	-	aRR 1.1 (1.1, 1.2)	-
		Tobacco use in pregnancy	Black	-	-	aRR 1.0 (0.9, 1.1)	RRR 1.11 (0.96, 1.29)
		Tobacco use in pregnancy	White	-	-	aRR 0.9 (0.8, 1.0)	-
		Large fringe metropolitan, vs. large central metropolitan	Black	-	-	aRR 0.9 (0.8, 0.9)	RRR 0.82 (0.66, 1.01)
		Medium metropolitan, vs. large central metropolitan	Black	-	-	aRR 0.6 (0.5, 0.6)	RRR 0.75 (0.39, 1.43)
		Small metropolitan, vs. large central metropolitan	Black	-	-	aRR 0.7 (0.7, 0.8)	RRR 0.70 (0.52, 0.95)
		Micropolitan, vs. large central metropolitan	Black	-	-	aRR 0.9 (0.8, 0.9)	RRR 0.69 (0.49, 0.97)
		Rural, vs. large central metropolitan	Black	-	-	aRR 0.9 (0.8, 1.0)	RRR 0.69 (0.53, 0.91)
		Large fringe metropolitan, vs. large central metropolitan	White	-	-	aRR 1.1 (1.0, 1.3)	-
		Medium metropolitan, vs. large central metropolitan	White	-	-	aRR 0.8 (0.7, 0.9)	-
		Small metropolitan, vs. large central metropolitan	White	-	-	aRR 1.0 (0.9, 1.1)	-
		Micropolitan, vs. large central metropolitan	White	-	-	aRR 1.3 (1.2, 1.5)	-
		Rural, vs. large central metropolitan	White	-	-	aRR 1.3 (1.1, 1.5)	-
		Multiple pregnancy	Black	-	-	aRR 3.0 (2.7, 3.3)	RRR 0.86 (0.16, 4.46)

Study	Outcome	Prognostic factor/group	Race/Ethnic group	Prevalence	Within strata of prognostic factor	Within strata of race/ethnicity	Relative risk ratio of race/ethnicity strata, vs. White
		Multiple pregnancy	White	-	-	aRR 3.5 (3.1, 3.8)	-
		Parity 1-3, vs. nulliparous	Black	-	-	aRR 1.0 (1.0, 1.1)	RRR 1.25 (0.93, 1.68)
		Party ≥4, vs. nulliparous	Black	-	-	aRR 1.3 (1.2, 1.4)	RRR 1.30 (0.97, 1.75)
		Parity 1-3, vs. nulliparous	White	-	-	aRR 0.8 (0.7, 0.8)	-
		Party ≥4, vs. nulliparous	White	-	-	aRR 1.0 (0.9, 1.2)	-
		Late or no antenatal care	Black	-	-	aRR 1.1 (1.1, 1.2)	RRR 1.0 (0.82, 1.22)
		Late or no antenatal care	White	-	-	aRR 1.1 (0.9, 1.2)	-
		Pre-existing HTN	Black	-	-	aRR 1.9 (1.8, 2.1)	RRR 1.27 (0.58, 2.79)
		Pre-existing HTN	White	-	-	aRR 1.5 (1.3, 1.8)	-
		PIH	Black	-	-	aRR 2.6 (2.5, 2.8)	RRR 1.08 (0.29, 4.00)
		PIH	White	-	-	aRR 2.4 (2.2, 2.6)	-
		GDM	Black	-	-	aRR 1.0 (0.9, 1.1)	RRR 1.00 (0.84, 1.19)
		GDM	White	-	-	aRR 1.0 (0.9, 1.2)	-
	SMM-RT	Age <17, vs. 25-29	Black	-	-	aRR 0.8 (0.5, 1.1)	RRR 0.67 (0.36, 1.23)
		Age 17-19, vs. 25-29	Black	-	-	aRR 1.0 (0.9, 1.2)	RRR 1.25 (0.89, 1.76)
		Age 20-24, vs. 25-29	Black	-	-	aRR 1.0 (0.9, 1.1)	RRR 1.11 (0.35, 3.52)
		Age 30-34, vs. 25-29	Black	-	-	aRR 1.3 (1.2, 1.5)	RRR 1.18 (0.87, 1.61)
		Age 35-39, vs. 25-29	Black	-	-	aRR 1.7 (1.5, 1.9)	RRR 1.21 (0.64, 2.30)
		Age ≥40, vs. 25-29	Black	-	-	aRR 2.3 (1.9, 2.8)	RRR 1.0 (0.31, 3.26)
		Age <17, vs. 25-29	White	-	-	aRR 1.2 (0.7, 1.8)	-
		Age 17-19, vs. 25-29	White	-	-	aRR 0.8 (0.6, 0.9)	-
		Age 20-24, vs. 25-29	White	-	-	aRR 0.9 (0.8, 1.0)	-
		Age 30-34, vs. 25-29	White	-	-	aRR 1.1 (1.0, 1.2)	-
		Age 35-39, vs. 25-29	White	-	-	aRR 1.4 (1.3, 1.6)	-

Study	Outcome	Prognostic factor/group	Race/Ethnic group	Prevalence	Within strata of prognostic factor	Within strata of race/ethnicity	Relative risk ratio of race/ethnicity strata, vs. White
		Age ≥40, vs. 25-29	White	-	-	aRR 2.3 (1.9, 2.8)	-
		Unmarried, vs. married	Black	-	-	aRR 1.0 (0.9, 1.1)	RRR 1.0 (0.31, 3.26)
		Unmarried, vs. married	White	-	-	aRR 1.0 (1.0, 1.1)	-
		Medicaid, vs. Private	Black	-	-	aRR 1.1 (1.0, 1.2)	RRR 1.0 (0.84, 1.19)
		Medicaid, vs. Private	White	-	-	aRR 1.1 (0.9, 1.2)	-
		Medicare, vs. Private	Black	-	-	aRR 2.4 (1.9, 2.9)	RRR 1.71 (0.70, 4.19)
		Medicare, vs. Private	White	-	-	aRR 1.4 (1.0, 1.7)	-
		Self-pay, vs. private	Black	-	-	aRR 1.5 (1.1, 1.8)	RRR 2.5 (1.41, 4.43)
		Self-pay, vs. private	White	-	-	aRR 0.6 (0.4, 1.0)	-
		<HS, vs. ≥some college	Black	-	-	aRR 1.1 (0.8, 1.6)	RRR 0.92 (0.54, 1.56)
		Some HS, vs. ≥some college	Black	-	-	aRR 1.1 (1.0, 1.3)	RRR 0.92 (0.74, 1.13)
		High school graduate, vs. ≥some college	Black	-	-	aRR 1.2 (1.1, 1.3)	RRR 1.09 (0.87, 1.36)
		<HS, vs. ≥some college	White	-	-	aRR 1.2 (0.8, 1.8)	-
		Some HS, vs. ≥some college	White	-	-	aRR 1.2 (1.0, 1.4)	-
		High school graduate, vs. ≥some college	White	-	-	aRR 1.1 (1.0, 1.3)	-
		Tobacco use in pregnancy	Black	-	-	aRR 0.9 (0.8, 1.0)	RRR 0.9 (0.69, 1.18)
		Tobacco use in pregnancy	White	-	-	aRR 1.4 (1.2, 1.7)	-
		Large fringe metropolitan, vs. large central metropolitan	Black	-	-	aRR 0.9 (0.8, 1.0)	RRR 0.64 (0.44, 0.93)
		Medium metropolitan, vs. large central metropolitan	Black	-	-	aRR 0.9 (0.7, 1.0)	RRR 0.64 (0.44, 0.95)
		Small metropolitan, vs. large central metropolitan	Black	-	-	aRR 0.9 (0.8, 1.1)	RRR 0.69 (0.52, 0.92)

Study	Outcome	Prognostic factor/group	Race/Ethnic group	Prevalence	Within strata of prognostic factor	Within strata of race/ethnicity	Relative risk ratio of race/ethnicity strata, vs. White
		Micropolitan, vs. large central metropolitan	Black	-	-	aRR 1.0 (0.9, 1.2)	RRR 0.56 (0.29, 1.05)
		Rural, vs. large central metropolitan	Black	-	-	aRR 1.1 (0.9, 1.3)	RRR 0.65 (0.36, 1.17)
		Large fringe metropolitan, vs. large central metropolitan	White	-	-	aRR 1.4 (1.2, 1.7)	-
		Medium metropolitan, vs. large central metropolitan	White	-	-	aRR 1.4 (1.1, 1.8)	-
		Small metropolitan, vs. large central metropolitan	White	-	-	aRR 1.3 (1.0, 1.6)	-
		Micropolitan, vs. large central metropolitan	White	-	-	aRR 1.8 (1.5, 2.3)	-
		Rural, vs. large central metropolitan	White	-	-	aRR 1.7 (1.4, 2.2)	-
		Multiple pregnancy	Black	-	-	aRR 2.0 (1.7, 2.4)	RRR 0.77 (0.24, 2.45)
		Multiple pregnancy	White	-	-	aRR 2.6 (2.1, 3.0)	-
		Parity 1-3, vs. nulliparous	Black	-	-	aRR 0.7 (0.7, 0.8)	RRR 0.88 (0.58, 1.32)
		Party ≥4, vs. nulliparous	Black	-	-	aRR 0.9 (0.7, 1.0)	RRR 0.9 (0.69, 1.18)
		Parity 1-3, vs. nulliparous	White	-	-	aRR 0.8 (0.7, 0.8)	-
		Party ≥4, vs. nulliparous	White	-	-	aRR 1.0 (0.8, 1.2)	-
		Late or no antenatal care	Black	-	-	aRR 1.1 (1.0, 1.3)	RRR 1.1 (0.83, 1.45)
		Late or no antenatal care	White	-	-	aRR 1.0 (0.8, 1.3)	-
		Pre-existing HTN	Black	-	-	aRR 2.7 (2.3, 3.1)	RRR 1.5 (0.48, 4.70)
		Pre-existing HTN	White	-	-	aRR 1.8 (1.4, 2.3)	-
		PIH	Black	-	-	aRR 3.7 (3.3, 4.0)	RRR 1.23 (0.23, 6.69)
		PIH	White	-	-	aRR 3.0 (2.7, 3.3)	-
		GDM	Black	-	-	aRR 0.9 (0.8, 1.1)	RRR 0.9 (0.70, 1.16)

Study	Outcome	Prognostic factor/group	Race/Ethnic group	Prevalence	Within strata of prognostic factor	Within strata of race/ethnicity	Relative risk ratio of race/ethnicity strata, vs. White
		GDM	White	-	-	aRR 1.0 (0.8, 1.2)	-
Lazariu 2017	SMM-T	Caesarean section	Black	37%	uOR 2.58 (2.49, 2.67)	-	-
		Caesarean section	Hispanic	33%	uOR 1.64 (1.58, 1.70)	-	-
		Caesarean section	White	33%	-	-	-
		Vaginal birth	Black	-	uOR 1.86 (1.77, 1.95)	-	-
		Vaginal birth	Hispanic	-	uOR 1.77 (1.69, 1.85)	-	-
Luke 2021	SMM-T	Urban	Black	43%	-	uOR 1.27 (1.18, 1.37)	RRR 1.19 (0.93, 1.52)
		Suburban	Black	24%	-	uOR 1.12 (1.04, 1.21)	RRR 1.08 (0.95, 1.22)
		Medium city	Black	18%	-	uOR 0.99 (0.92, 1.08)	RRR 0.93 (0.83, 1.03)
		Small city (ref)	Black	7.4%	-	-	-
		Micropolitan	Black	5.0%	-	uOR 1.21 (1.09, 1.34)	RRR 1.02 (0.78, 1.32)
		Rural	Black	3.1%	-	uOR 1.08 (0.96, 1.22)	RRR 0.89 (0.70, 1.12)
		Urban	Hispanic	48%	-	uOR 1.17 (1.06, 1.28)	RRR 1.09 (0.93, 1.29)
		Suburban	Hispanic	18%	-	uOR 1.10 (1.01, 1.21)	RRR 1.06 (0.95, 1.18)
		Medium city	Hispanic	21%	-	uOR 0.97 (0.88, 1.06)	RRR 0.91 (0.81, 1.02)
		Small city (ref)	Hispanic	6.2%	-	-	-
		Micropolitan	Hispanic	4.4%	-	uOR 1.26 (1.13, 1.41)	RRR 1.06 (0.79, 1.42)
		Rural	Hispanic	1.9%	-	uOR 1.37 (1.20, 1.55)	RRR 1.12 (0.78, 1.63)
		Urban	Native American	18%	-	uOR 0.94 (0.68, 1.29)	RRR 0.88 (0.63, 1.22)
		Suburban	Native American	13%	-	uOR 0.75 (0.54, 1.04)	RRR 0.72 (0.52, 1.00)
		Medium city	Native American	20%	-	uOR 1.10 (0.82, 1.48)	RRR 1.03 (0.76, 1.39)
		Small city (ref)	Native American	12%	-	-	-
		Micropolitan	Native American	20%	-	uOR 1.18 (0.87, 1.60)	RRR 0.99 (0.70, 1.41)
		Rural	Native American	17%	-	uOR 1.48 (1.11, 1.98)	RRR 1.21 (0.78, 1.89)

Study	Outcome	Prognostic factor/group	Race/Ethnic group	Prevalence	Within strata of prognostic factor	Within strata of race/ethnicity	Relative risk ratio of race/ethnicity strata, vs. White
		Urban	White	23%	-	uOR 1.07 (1.01, 1.13)	-
		Suburban	White	26%	-	uOR 1.04 (0.99, 1.09)	-
		Medium city	White	21%	-	uOR 1.07 (1.01, 1.13)	-
		Small city (ref)	White	11%	-	-	-
		Micropolitan	White	11%	-	uOR 1.19 (1.13, 1.26)	-
		Rural	White	7.7%	-	uOR 1.22 (1.15, 1.30)	-
		Medicare cf private	Black	-	-	uOR 1.47 (1.35, 1.60)	RRR 1.26 (0.83, 1.91)
		Medicaid cf private	Black	-	-	uOR 1.15 (1.11, 1.20)	RRR 0.93 (0.72, 1.20)
		Medicare cf private	Hispanic	-	-	uOR 1.31 (1.17, 1.48)	RRR 1.12 (0.81, 1.54)
		Medicaid cf private	Hispanic	-	-	uOR 1.21 (1.16, 1.27)	RRR 0.98 (0.73, 1.30)
		Medicare cf private	Native American	-	-	uOR 1.68 (1.18, 2.39)	RRR 1.44 (0.83, 2.47)
		Medicaid cf private	Native American	-	-	uOR 1.44 (1.23, 1.69)	RRR 1.16 (0.76, 1.78)
		Medicare cf private	White	-	-	uOR 1.17 (1.11, 1.24)	-
		Medicaid cf private	White	-	-	uOR 1.24 (1.21, 1.27)	-
		Lowest income quartile	Black	-	-	uOR 1.13 (1.09, 1.17)	RRR 0.94 (0.75, 1.18)
		Lowest income quartile	Hispanic	-	-	uOR 1.15 (1.10, 1.20)	RRR 0.96 (0.76, 1.21)
		Lowest income quartile	Native American	-	-	uOR 1.25 (1.07, 1.46)	RRR 1.04 (0.78, 1.39)
		Lowest income quartile	White	-	-	uOR 1.20 (1.17, 1.24)	-
		Obesity	Black	-	-	uOR 1.43 (1.37, 1.50)	RRR 0.95 (0.56, 1.63)
		Obesity	Hispanic	-	-	uOR 1.38 (1.31, 1.45)	RRR 0.92 (0.55, 1.54)
		Obesity	Native American	-	-	uOR 1.66 (1.38, 1.99)	RRR 1.11 (0.58, 2.11)
		Obesity	White	-	-	uOR 1.50 (1.44, 1.55)	-
Mujahid 2023	SMM-T	Quartile of lowest neighbourhood deprivation	Hispanic	5.6%	-	-	-

Study	Outcome	Prognostic factor/group	Race/Ethnic group	Prevalence	Within strata of prognostic factor	Within strata of race/ethnicity	Relative risk ratio of race/ethnicity strata, vs. White
		Second quartile neighbourhood deprivation	Hispanic	14%	-	uOR 0.96 (0.91, 1.02)	
		Third quartile neighbourhood deprivation	Hispanic	28%	-	uOR 0.94 (0.89, 1.00)	
		Highest quartile neighbourhood deprivation	Hispanic	52%	-	uOR 0.97 (0.93, 1.03)	RRR 0.90 (0.77, 1.05)
		Quartile of lowest neighbourhood deprivation	Black	7.5%	-	-	-
		Second quartile neighbourhood deprivation	Black	16%	-	uOR 0.96 (0.85, 1.08)	
		Third quartile neighbourhood deprivation	Black	28%	-	uOR 0.96 (0.86, 1.07)	
		Highest quartile neighbourhood deprivation	Black	49%	-	uOR 1.01 (0.90, 1.12)	RRR 0.87 (0.77, 0.98)
		Quartile of lowest neighbourhood deprivation	White	33%	-	-	-
		Second quartile neighbourhood deprivation	White	31%	-	uOR 1.01 (0.97, 1.05)	-
		Third quartile neighbourhood deprivation	White	24%	-	uOR 1.03 (0.99, 1.08)	-
		Highest quartile neighbourhood deprivation	White	12%	-	uOR 1.12 (1.06, 1.18)	-
		Quartile of lowest neighbourhood deprivation	Asian or Pacific Islander	32%	-	-	-
		Second quartile neighbourhood deprivation	Asian or Pacific Islander	28%	-	uOR 1.04 (0.98, 1.10)	
		Third quartile neighbourhood deprivation	Asian or Pacific Islander	24%	-	uOR 1.00 (0.94, 1.06)	

Study	Outcome	Prognostic factor/group	Race/Ethnic group	Prevalence	Within strata of prognostic factor	Within strata of race/ethnicity	Relative risk ratio of race/ethnicity strata, vs. White
		Highest quartile neighbourhood deprivation	Asian or Pacific Islander	16%	-	uOR 1.00 (0.93, 1.07)	0.89 (0.78, 1.02)
Murugappan 2020	SMM-T	Subfertility, testing	Asian	0.22%	uOR 1.54 (0.66, 3.59)	-	-
		Subfertility, testing	Black	0.10%	uOR 0.88 (0.20, 3.79)	-	-
		Subfertility, testing	Hispanic	0.15%	uOR 1.68 (0.75, 3.76)	-	-
		Subfertility, testing	White	0.20%	-	-	-
		Subfertility, diagnosis	Asian	3.2%	uOR 0.68 (0.51, 0.90)	-	-
		Subfertility, diagnosis	Black	1.9%	uOR 1.63 (1.27, 2.11)	-	-
		Subfertility, diagnosis	Hispanic	1.8%	uOR 1.17 (0.91, 1.49)	-	-
		Subfertility, diagnosis	White	2.1%	-	-	-
		Subfertility, treatment	Asian	2.6%	uOR 0.86 (0.65, 1.14)	-	-
		Subfertility, treatment	Black	0.75%	uOR 1.53 (1.04, 2.26)	-	-
		Subfertility, treatment	Hispanic	0.75%	uOR 1.16 (0.81, 1.66)	-	-
		Subfertility, treatment	White	1.3%	-	-	-
Rezaeiahari 2023	SMM-T	Age <20 years	Black	14%	-	uOR 0.92 (0.73, 1.18)	RRR 0.87 (0.63, 1.19)
		Age 20-34 years (ref)	Black	79%	-	-	-
		Age 35-39	Black	5%	-	uOR 0.91 (0.62, 1.33)	RRR 0.63 (0.37, 1.07)
		Age <20 years	Hispanic	13%	-	uOR 0.75 (0.39, 1.45)	RRR 0.71 (0.36, 1.41)
		Age 20-34 years (ref)	Hispanic	75%	-	-	-
		Age 35-39	Hispanic	10%	-	uOR 1.14 (0.62, 2.10)	RRR 0.79 (0.39, 1.61)
		Age <20 years	White	11%	-	uOR 1.06 (0.87, 1.30)	-
		Age 20-34 years (ref)	White	82%			
		Age 35-39	White	6%	-	uOR 1.44 (1.15, 1.80)	-

Study	Outcome	Prognostic factor/group	Race/Ethnic group	Prevalence	Within strata of prognostic factor	Within strata of race/ethnicity	Relative risk ratio of race/ethnicity strata, vs. White
		<HSE	Black	16%	-	uOR 1.36 (1.08, 1.70)	RRR 1.18 (0.83, 1.69)
		Some college (ref)	Black	40%	-	-	-
		<HSE	Hispanic	34%	-	uOR 1.00 (0.59, 1.70)	RRR 0.87 (0.50, 1.52)
		Some college (ref)	Hispanic	26%	-	-	-
		<HSE	White	14%	-	uOR 1.15 (0.96, 1.39)	-
		Some college (ref)	White	50%	-	-	-
		Medicaid	Black	66%	-	uOR 1.05 (0.87, 1.27)	RRR 0.94 (0.74, 1.18)
		Private insurance (ref)	Black	27%			
		Medicaid	Hispanic	69%	-	uOR 1.13 (0.70, 1.82)	RRR 1.01 (0.61, 1.66)
		Private insurance (ref)	Hispanic	23%	-	-	-
		Medicaid	White	50%	-	uOR 1.12 (0.98, 1.28)	-
		Private insurance (ref)	White	43%	-	-	-
		Unmarried	Black	91%	-	uOR 1.15 (0.85, 1.54)	RRR 0.93 (0.65, 1.34)
		Unmarried	Hispanic	66%	-	uOR 1.11 (0.73, 1.68)	RRR 0.90 (0.57, 1.44)
		Unmarried	White	61%	-	uOR 1.23 (1.08, 1.40)	-
		Nulliparity	Black	38%	-	uOR 1.15 (0.92, 1.44)	RRR 0.84 (0.57, 1.23)
		Primiparous (ref)	Black	26%	-	-	-
		Nulliparity	Hispanic	31%	-	uOR 1.59 (0.94, 2.68)	RRR 1.16 (0.63, 2.14)
		Primiparous (ref)	Hispanic	26%	-	-	-
		Nulliparity	White	39%	-	uOR 1.37 (1.17, 1.60)	-
		Primiparous (ref)	White	31%	-	-	-
		Multiple pregnancy	Black	2%	-	uOR 3.57 (2.55, 5.01)	RRR 1.16 (0.21, 6.34)
		Multiple pregnancy	White	2%	-	uOR 3.08 (2.30, 4.13)	-
		Insufficient ANC	Black	4%	-	uOR 1.88 (1.38, 2.57)	RRR 1.66 (0.79, 3.49)

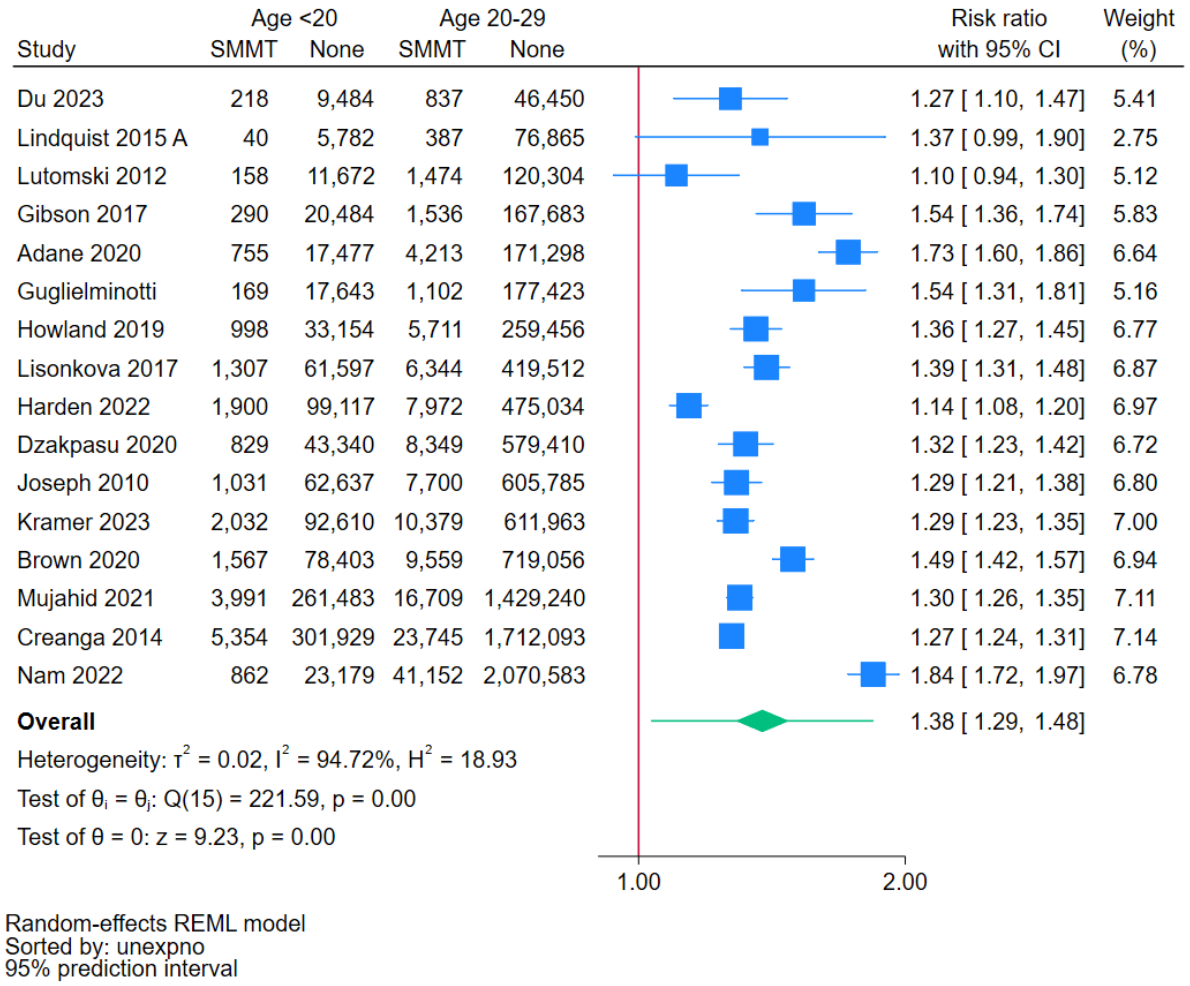
Study	Outcome	Prognostic factor/group	Race/Ethnic group	Prevalence	Within strata of prognostic factor	Within strata of race/ethnicity	Relative risk ratio of race/ethnicity strata, vs. White
		Insufficient ANC	White	2%	-	uOR 1.13 (0.77, 1.66)	-
		Previous CS	Black	13%	-	uOR 2.09 (1.72, 2.54)	RRR 1.27 (0.52, 3.08)
		Previous CS	Hispanic	14%	-	uOR 2.26 (1.45, 3.50)	RRR 1.37 (0.53, 3.55)
		Previous CS	White	11%	-	uOR 1.65 (1.39, 1.95)	-
		Obesity	Black	35%	-	uOR 1.01 (0.85, 1.20)	RRR 0.78 (0.57, 1.06)
		Obesity	Hispanic	31%	-	uOR 1.19 (0.79, 1.79	RRR 0.92 (0.56, 1.49)
		Obesity	White	28%	-	uOR 1.30 (1.14, 1.48)	-
Siddiqui 2021	SMM-T	Indirect 'effect' of ethnic group through obesity	Asian	5.1%	-	0.99 (0.99, 1.00)	-
			Black	29%	-	1.03 (1.02, 1.05)	-
			Latina	22%	-	1.02 (1.01, 1.03)	-
			White	9%	-	-	-
	SMM-RT	Indirect 'effect' of ethnic group through obesity	Asian	Above	-	0.97 (0.97, 0.98)	-
			Black	Above	-	1.15 (1.11, 1.19)	-
			Latina	Above	-	1.10 (1.07, 1.11)	-
Tangel 2019	Death	Medicare	Black	0.9%	aRR 0.88 (0.83, 0.93)	-	-
		Medicare	Hispanic	0.2%	aRR 1.07 (0.99, 1.15)	-	-
		Medicare	White (ref)	0.5%	-	-	-
		Medicaid	Black	62%	aRR 1.14 (1.13, 1.14)	-	-
		Medicaid	Hispanic	66%	aRR 1.23 (1.22, 1.24)	-	-
		Medicaid	White (ref)	32%			
		Private insurance	Black	31%	aRR 1.16 (1.15, 1.17)	-	-

Study	Outcome	Prognostic factor/group	Race/Ethnic group	Prevalence	Within strata of prognostic factor	Within strata of race/ethnicity	Relative risk ratio of race/ethnicity strata, vs. White
		Private insurance	Hispanic	29%	aRR 1.20 (1.19, 1.21)	-	-
		Private insurance	White (ref)	63%	-	-	-
		Self-pay/no charge	Black	3.9%	aRR 1.17 (1.13, 1.21)	-	-
		Self-pay/no charge	Hispanic	3.5%	aRR 1.26 (1.23, 1.30)	-	-
		Self-pay/no charge	White (ref)	1.8%	-	-	-
		Lowest ZIP income quartile	Black	44%	aRR 1.15 (1.14, 1.16)	-	-
		Lowest ZIP income quartile	Hispanic	35%	aRR 1.28 (1.27, 1.29)	-	-
		Lowest ZIP income quartile	White (ref)	20%	-	-	-
		Second ZIP income quartile	Black,	22%	aRR 1.15 (1.14, 1.16)	-	-
		Second ZIP income quartile	Hispanic	28%	aRR 1.18 (1.17, 1.19)	-	-
		Second ZIP income quartile	White (ref)	24%	-	-	-
		Third ZIP income quartile	Black	18%	aRR 1.20 (1.18, 1.21)	-	-
		Third ZIP income quartile	Hispanic	22%	aRR 1.23 (1.22, 1.24)	-	-
		Third ZIP income quartile	White (ref)	26%	-	-	-
		Highest ZIP income quartile	Black	10%	aRR 1.13 (1.12, 1.16)	-	-
		Highest ZIP income quartile	Hispanic	12%	aRR 1.19 (1.18, 1.20)	-	-
		Highest ZIP income quartile	White (ref)	27%	-	-	-
Tangel 2020	SMM-T	Medicare	Black	0.9%	aRR 2.08 (1.78, 2.42)	-	-
		Medicare	White (ref)	0.5%	-	-	-
		Medicaid	Black	62%	aRR 1.40 (1.36, 1.44)	-	-
		Medicaid	White (ref)	32%	-	-	-
		Private insurance	Black	31%	aRR 1.34 (1.30, 1.38)	-	-
		Private insurance	White (ref)	63%	-	-	-
		Self pay/no charge	Black	4%	aRR 1.33 (1.18, 1.48)	-	-

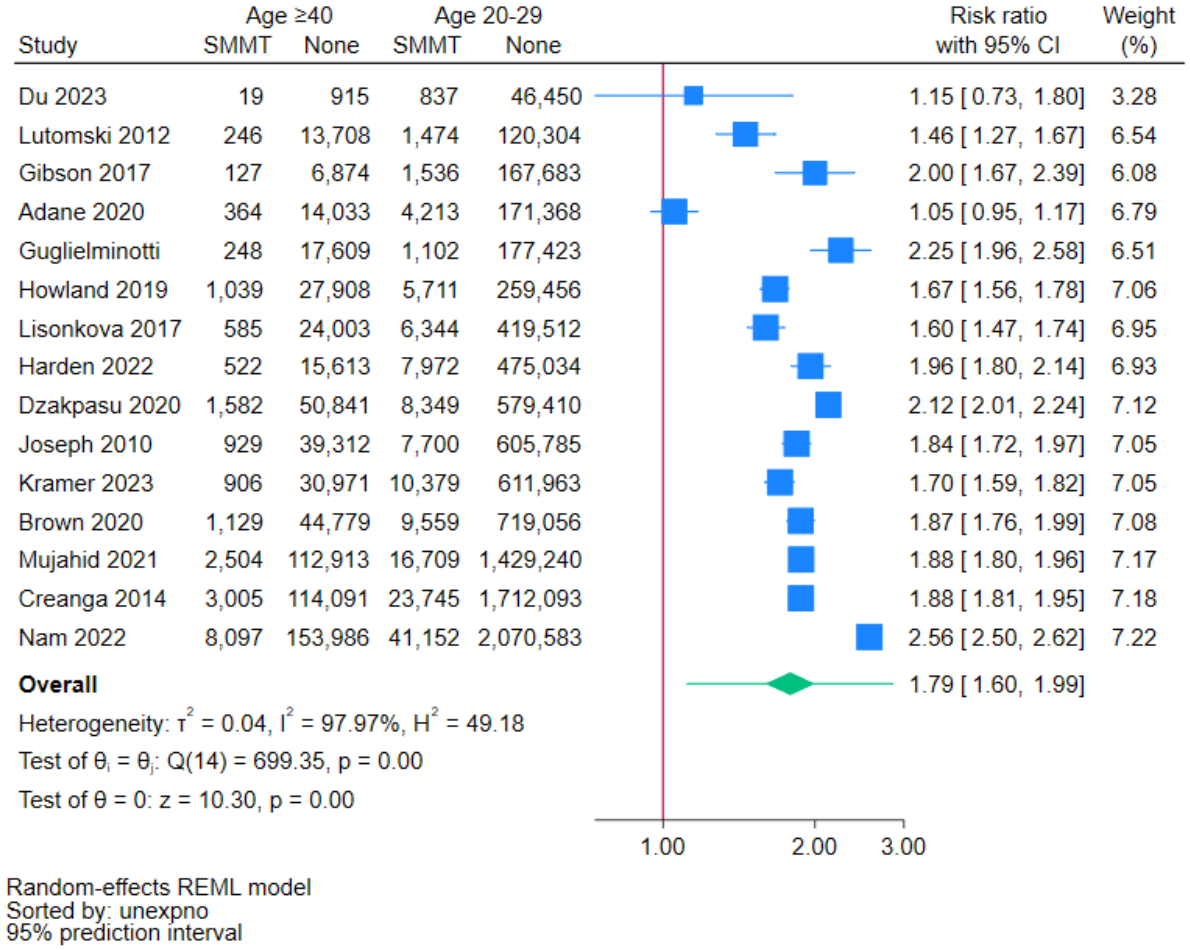
Study	Outcome	Prognostic factor/group	Race/Ethnic group	Prevalence	Within strata of prognostic factor	Within strata of race/ethnicity	Relative risk ratio of race/ethnicity strata, vs. White
		Self pay/no charge	White (ref)	2%	-	-	-
		Lowest ZIP income quartile	Black	44%	aRR 1.38 (1.33, 1.42)	-	-
		Lowest ZIP income quartile	White (ref)	20%	-	-	-
		Second ZIP income quartile	Black	23%	aRR 1.41 (1.36, 1.47)	-	-
		Second ZIP income quartile	White (ref)	24%	-	-	-
		Third ZIP income quartile	Black	18%	aRR 1.39 (1.34, 1.45)	-	-
		Third ZIP income quartile	White (ref)	27%	-	-	-
		Highest ZIP income quartile	Black	10%	aRR 1.40 (1.33, 1.47)	-	-
		Highest ZIP income quartile	White (ref)	27%	-	-	-
		Vaginal, unassisted	Black	59%	aRR 1.23 (1.19, 1.38)	-	-
		Vaginal, unassisted	White (ref)	61%	-	-	-
		Instrumental	Black	3.2%	aRR 0.95 (0.85, 1.06)	-	-
		Instrumental	White (ref)	4.5%	-	-	-
		Caesarean	Black	38%	aRR 1.46 (1.43, 1.50)	-	-
		Caesarean	White (ref)	35%	-	-	-

SMM-RT severe maternal morbidity without 'any transfusion', SMM-T severe maternal morbidity with 'any transfusion'. OR odds ratio, uOR unadjusted odds ratio, aOR adjusted odds ratio, PIH pregnancy-induced hypertension, GDM gestational diabetes, HTN hypertension.

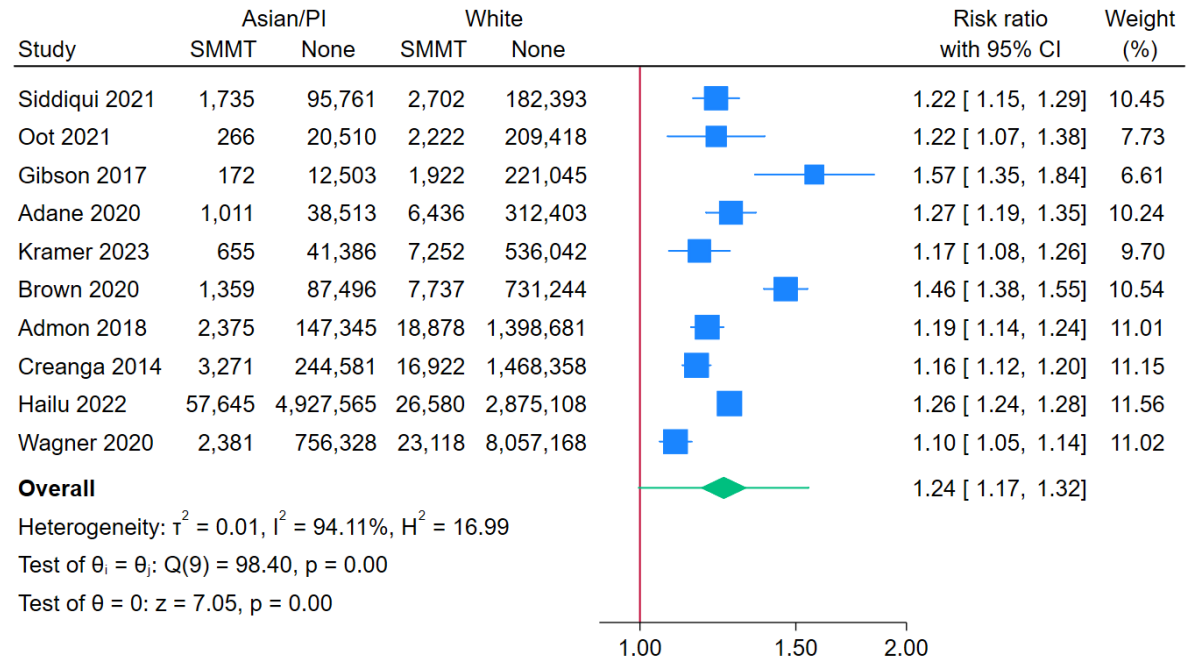
Appendix Figure B3.1 Association between Age <20 Years and SMM-T



Appendix Figure B3.2 Association between Age ≥40 Years and SMM-T

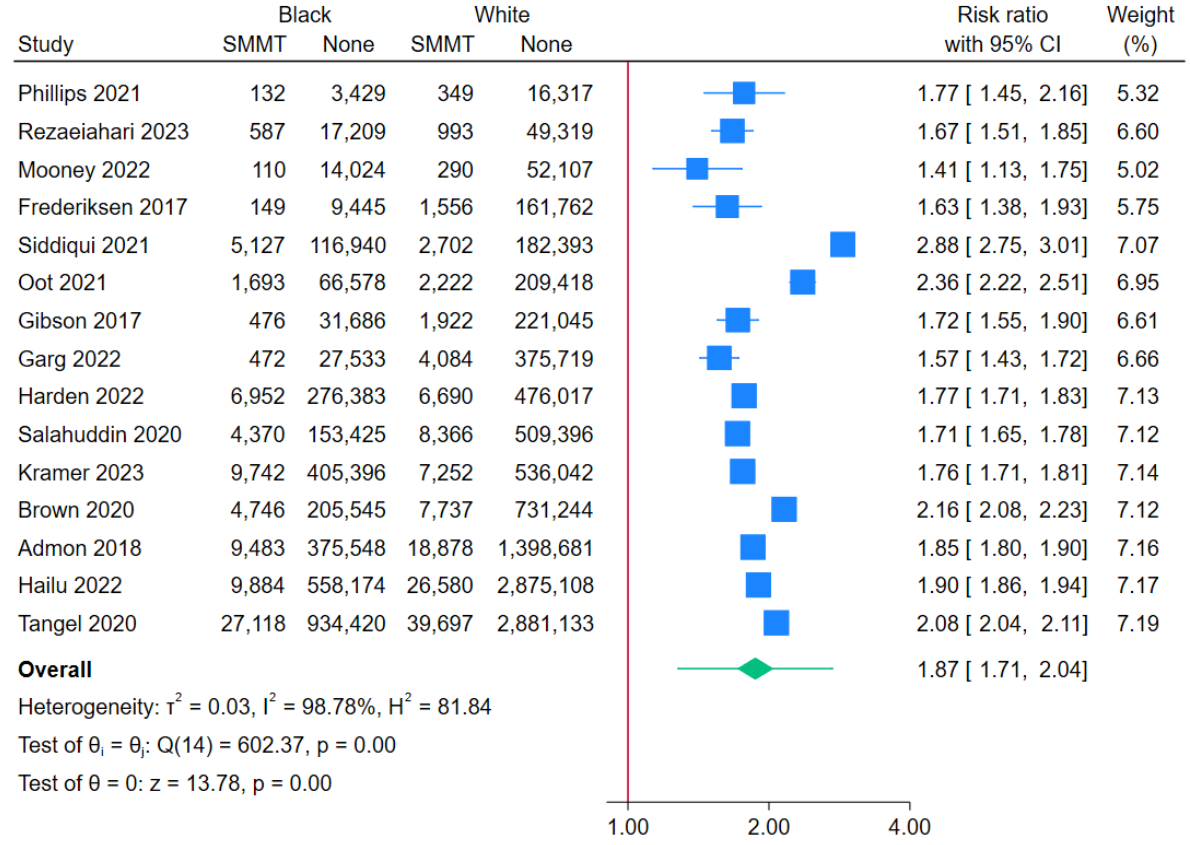


Appendix Figure B3.3 Association between Asian/PI Ethnicity and SMM-T



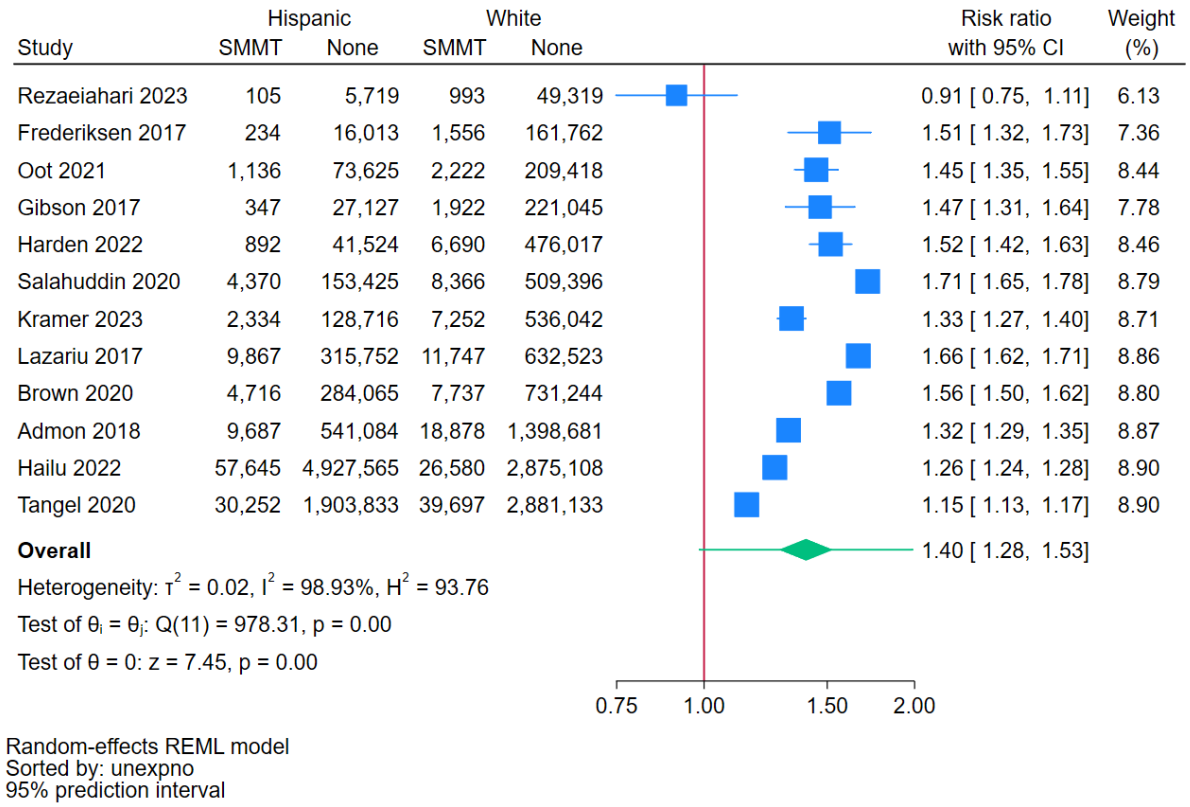
Random-effects REML model
Sorted by: unexpno
95% prediction interval

Appendix Figure B3.4 Association between Black Ethnicity and SMM-T

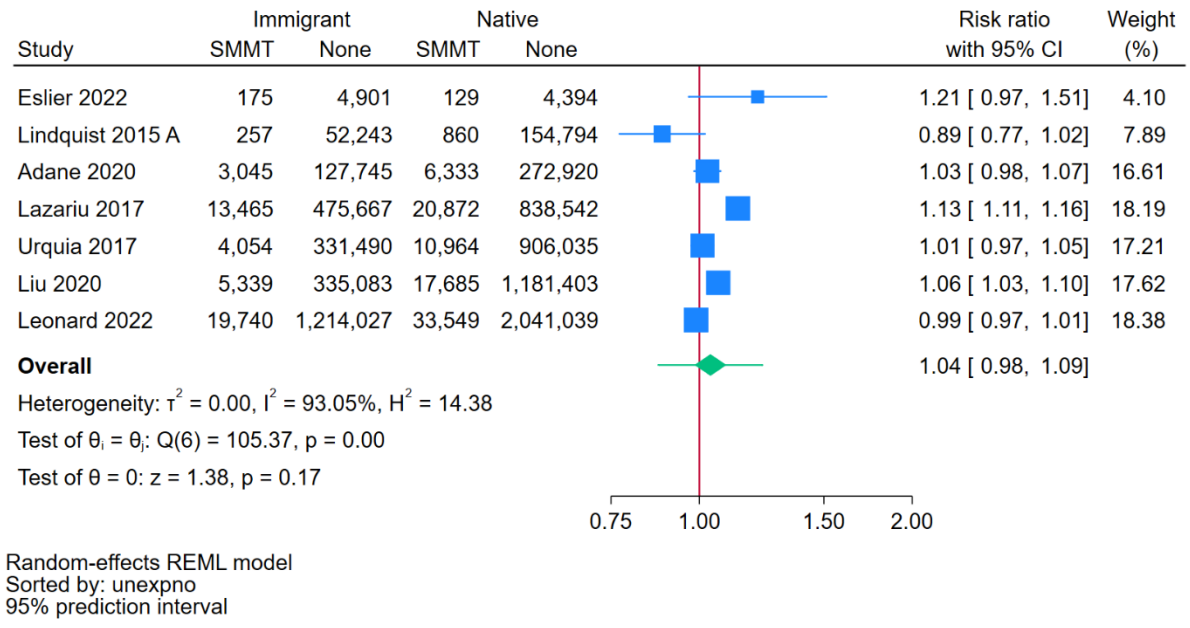


Random-effects REML model
Sorted by: unexpno
95% prediction interval

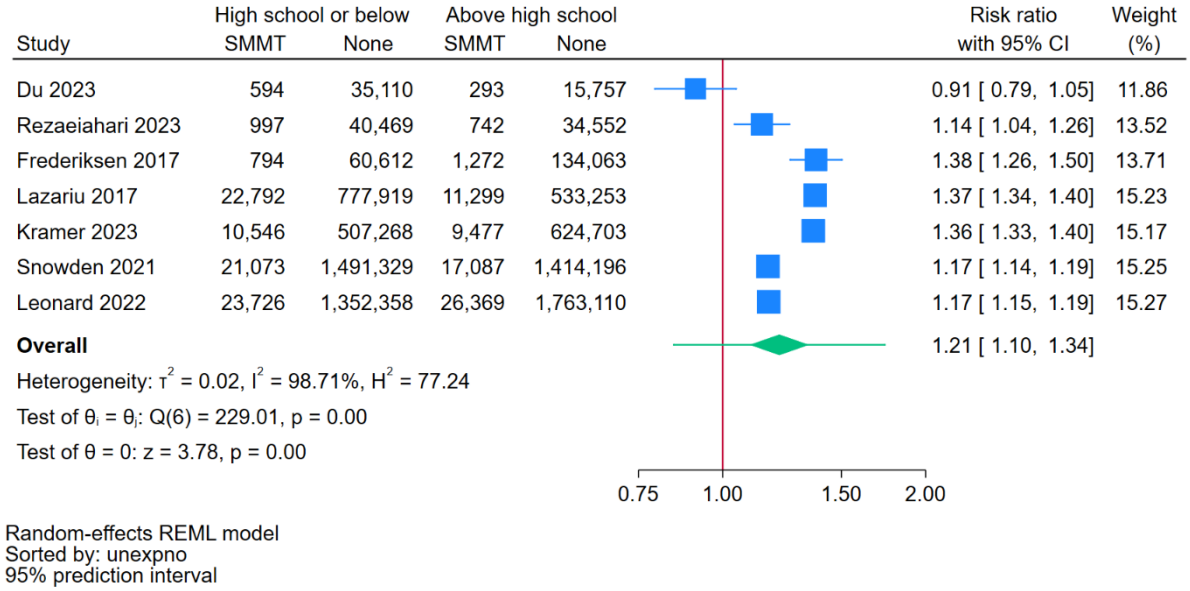
Appendix Figure B3.5 Association between Hispanic Ethnicity and SMM-T



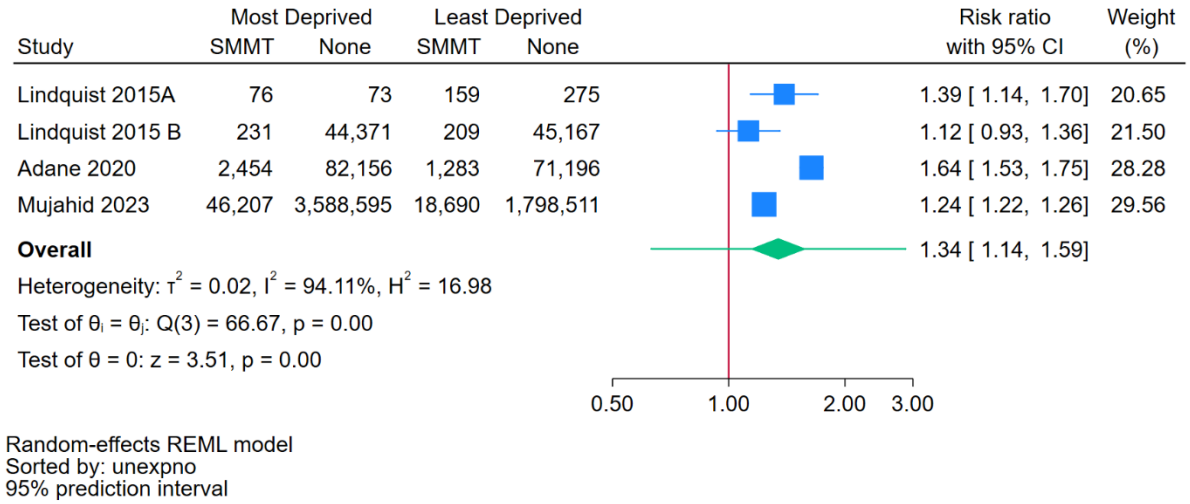
Appendix Figure B3.6 Association between Overall Migrant Status and SMM-T



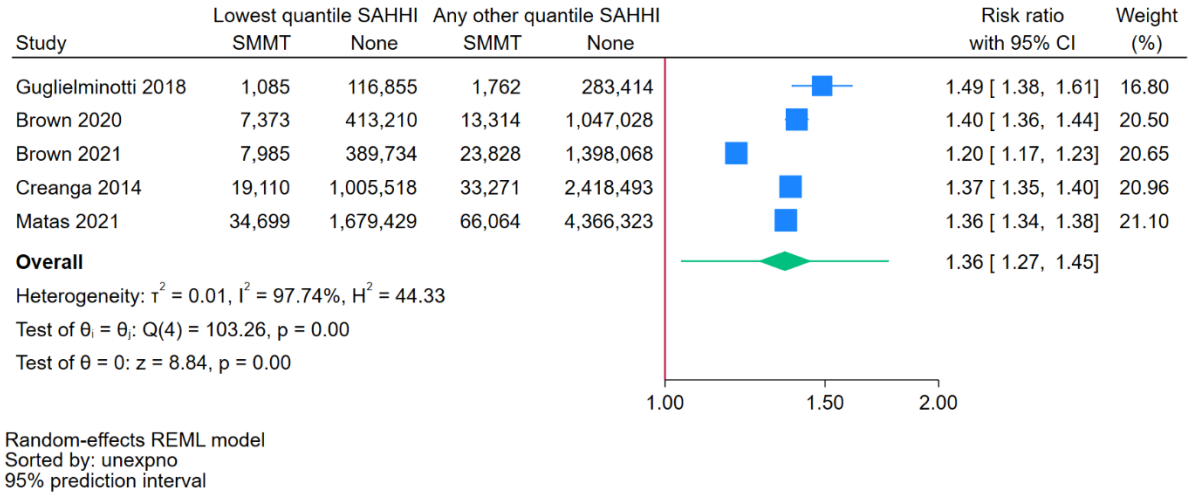
Appendix Figure B3.7 Association between Educational Attainment of High School Level or Above and SMM-T



Appendix Figure B3.8 Association between Neighbourhood Deprivation and SMM-T

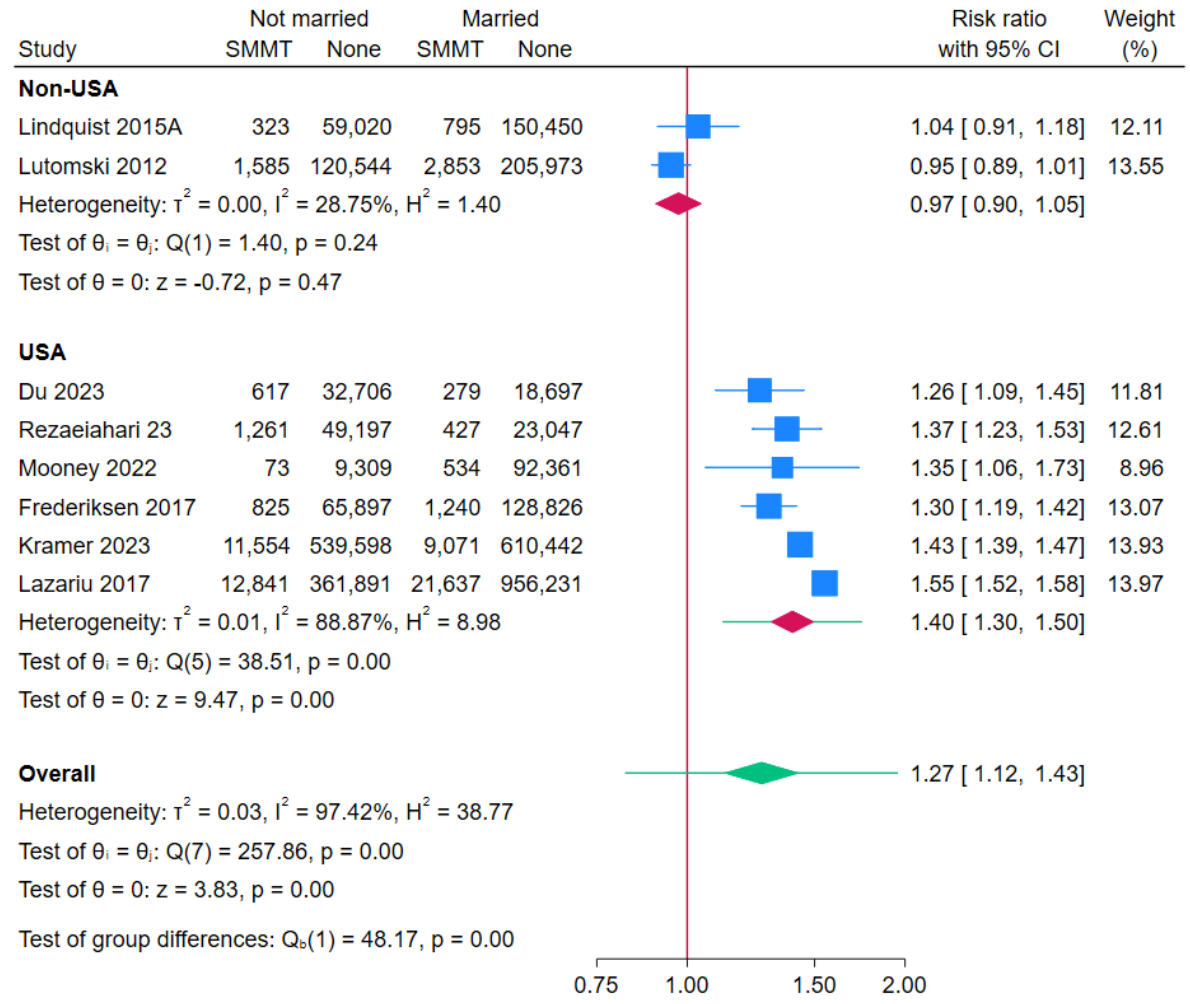


Appendix Figure B3.9 Association between Small Area Household Income and SMM-T



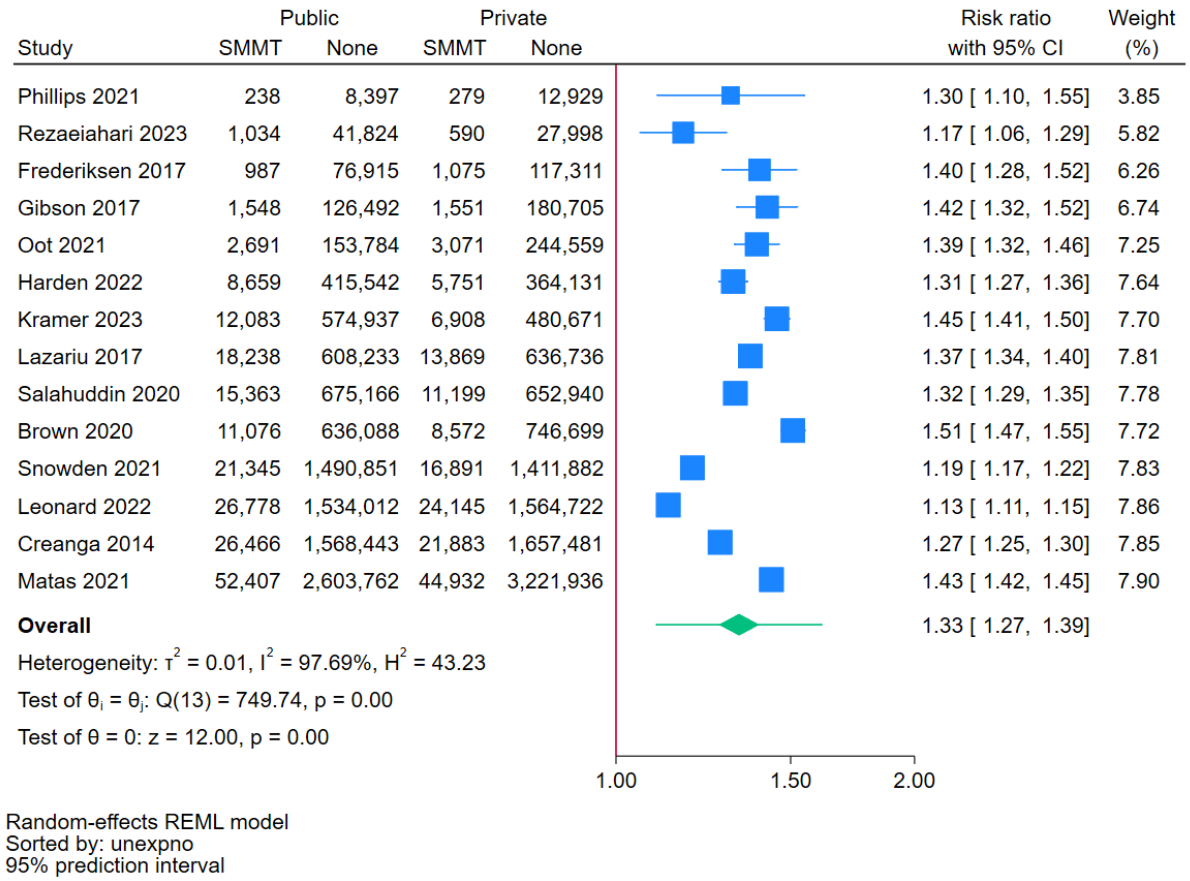
Random-effects REML model
Sorted by: unexpno
95% prediction interval

Appendix Figure B3.10 Association between Marital Status and SMM-T



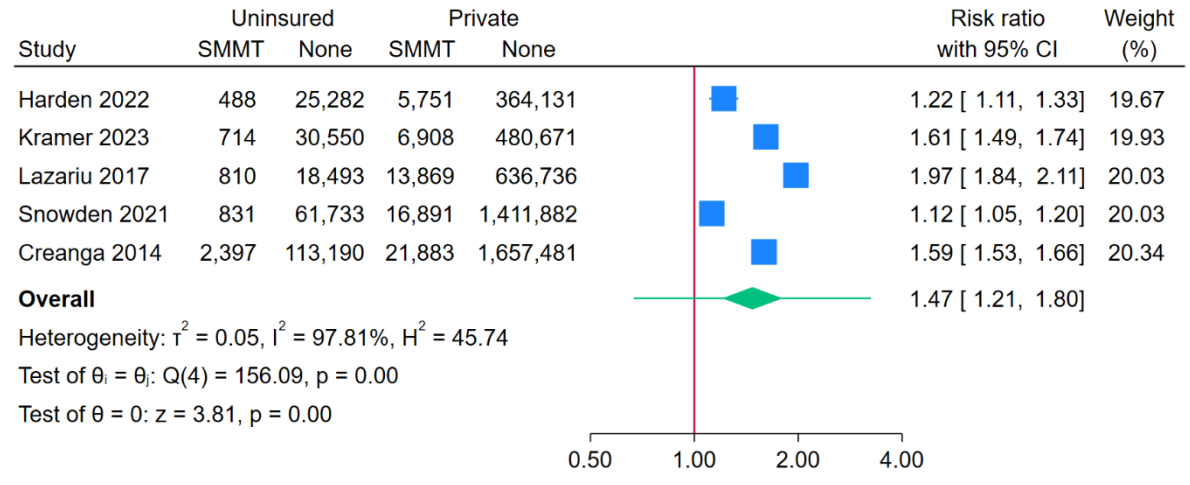
Random-effects REML model
Sorted by: unexpno
95% prediction intervals

Appendix Figure B3.11 Association between Public Health Coverage and SMM-T



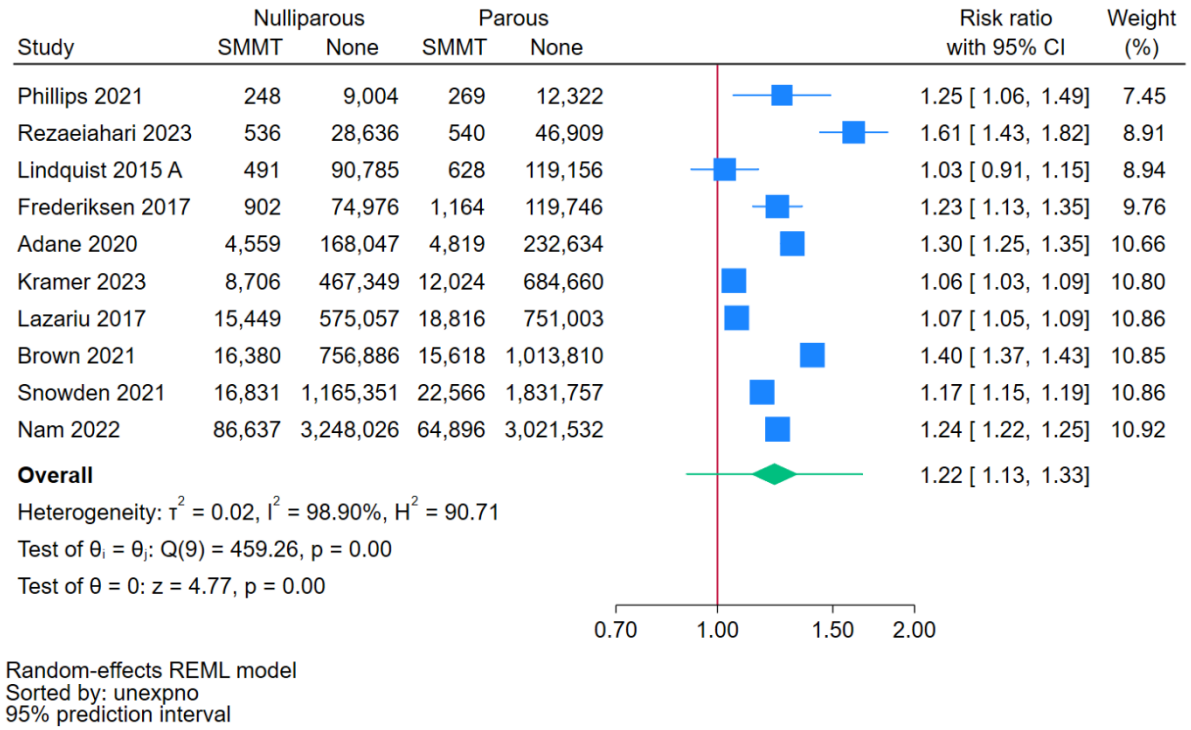
Random-effects REML model
Sorted by: unexpno
95% prediction interval

Appendix Figure B3.12 Association between Uninsured Status and SMM-T

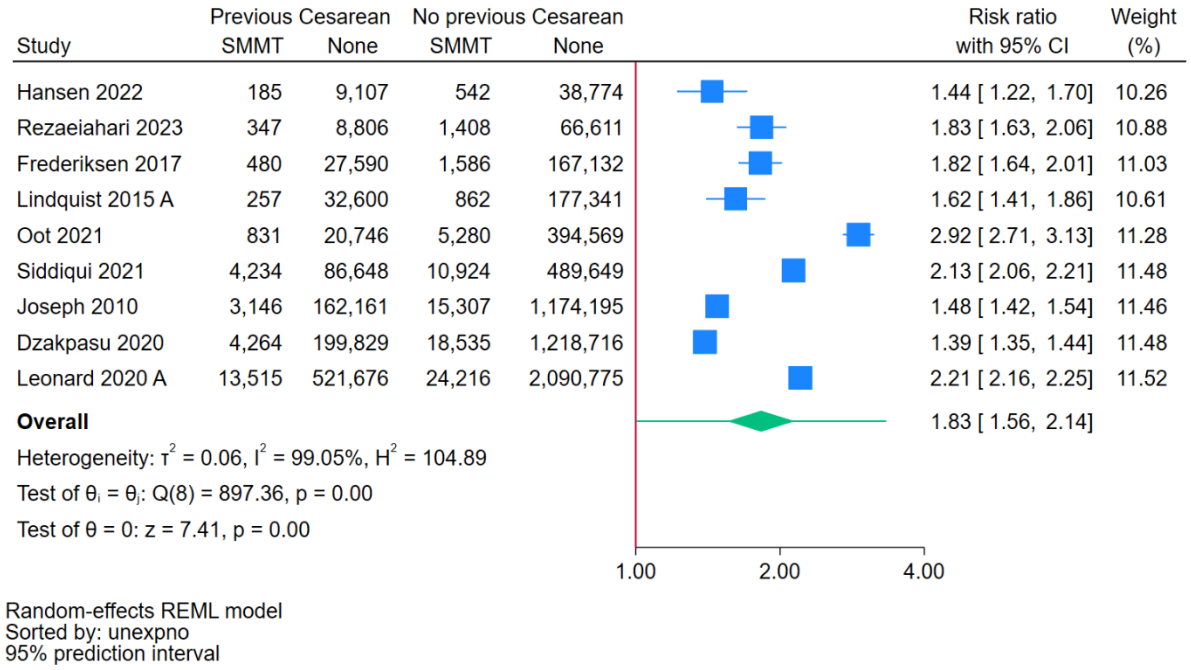


Random-effects REML model
Sorted by: unexpno
95% prediction interval

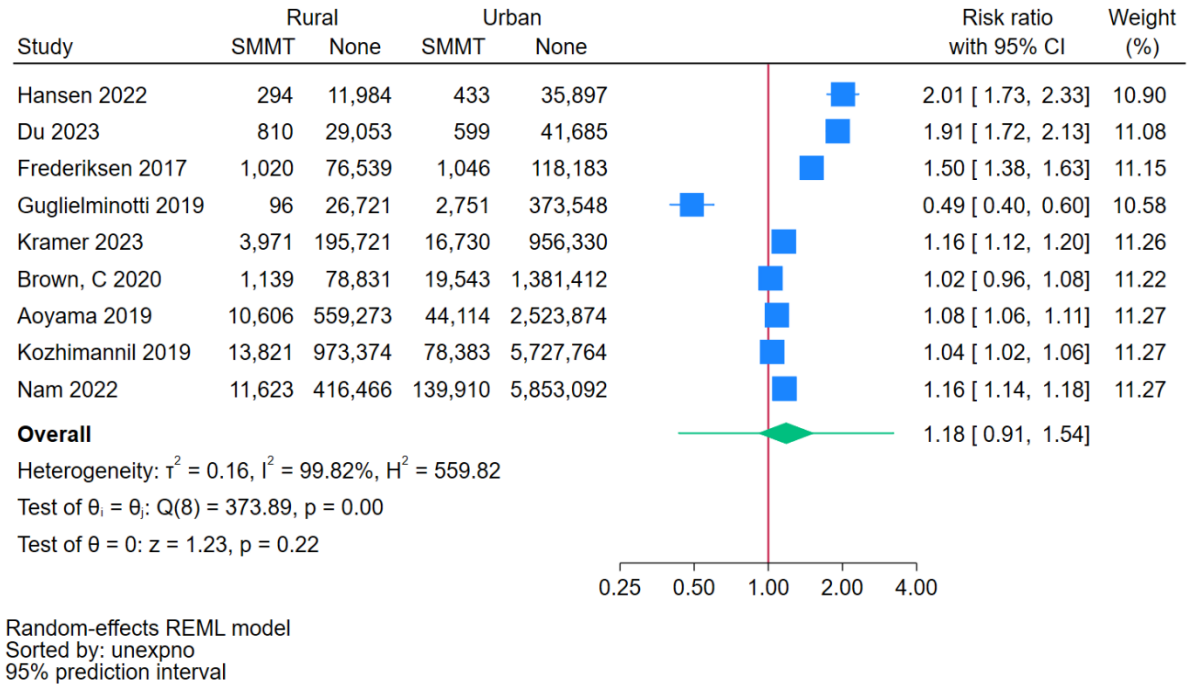
Appendix Figure B3.13 Association between Nulliparity and SMM-T



Appendix Figure B3.14 Association between Previous Caesarean Birth and SMM-T

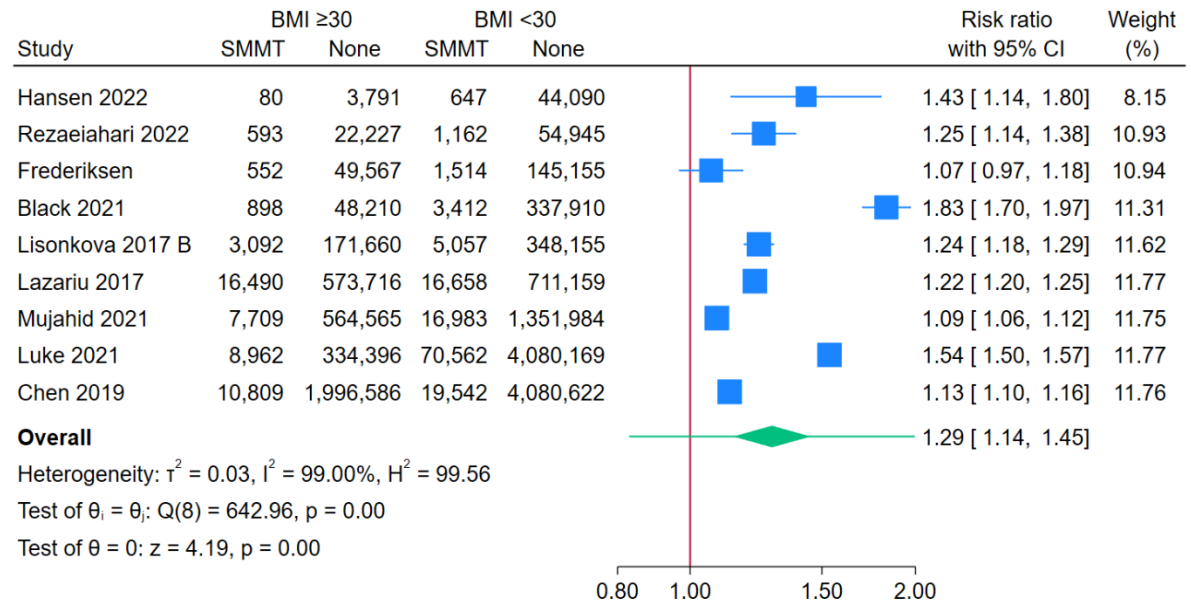


Appendix Figure B3.15 Association between Rural Residence and SMM-T



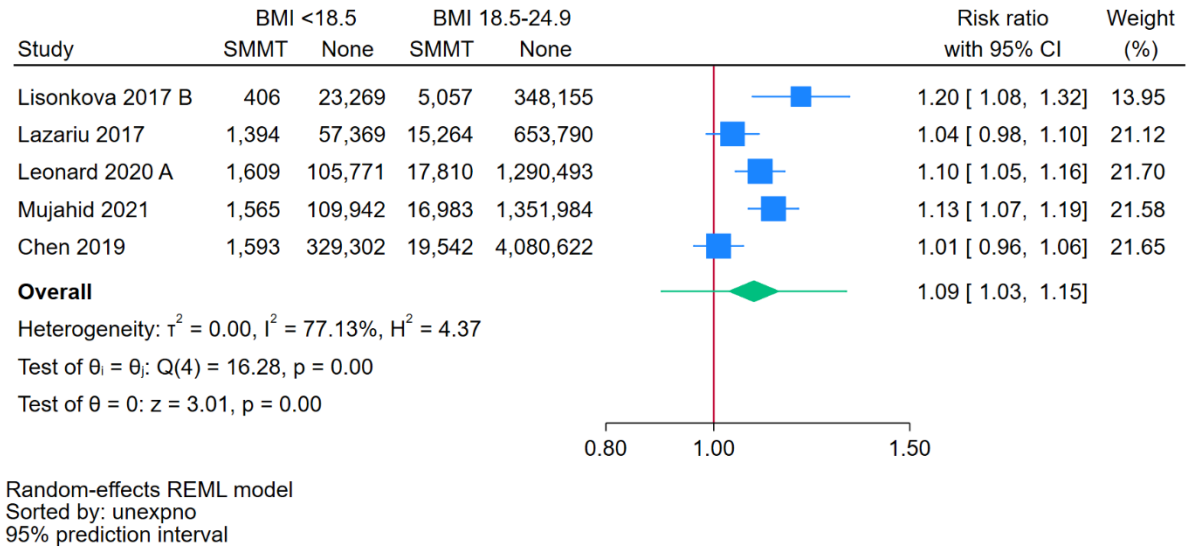
Random-effects REML model
Sorted by: unexpno
95% prediction interval

Appendix Figure B3.16 Association between Obesity and SMM-T



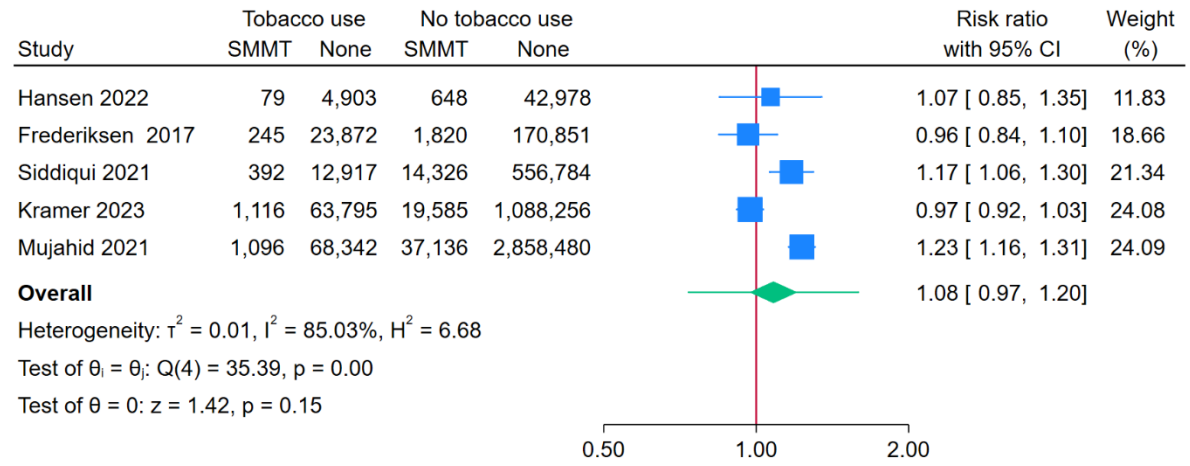
Random-effects REML model
Sorted by: unexpno
95% prediction interval

Appendix Figure B3.17 Association between Underweight and SMM-T



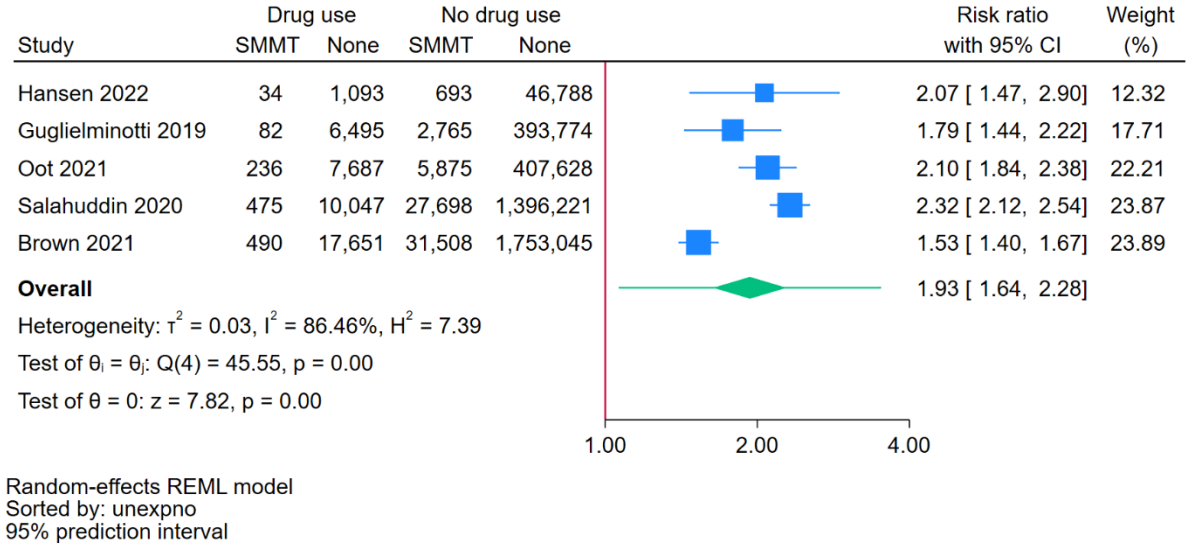
Random-effects REML model
Sorted by: unexpno
95% prediction interval

Appendix Figure B3.18 Association between Tobacco Use and SMM-T

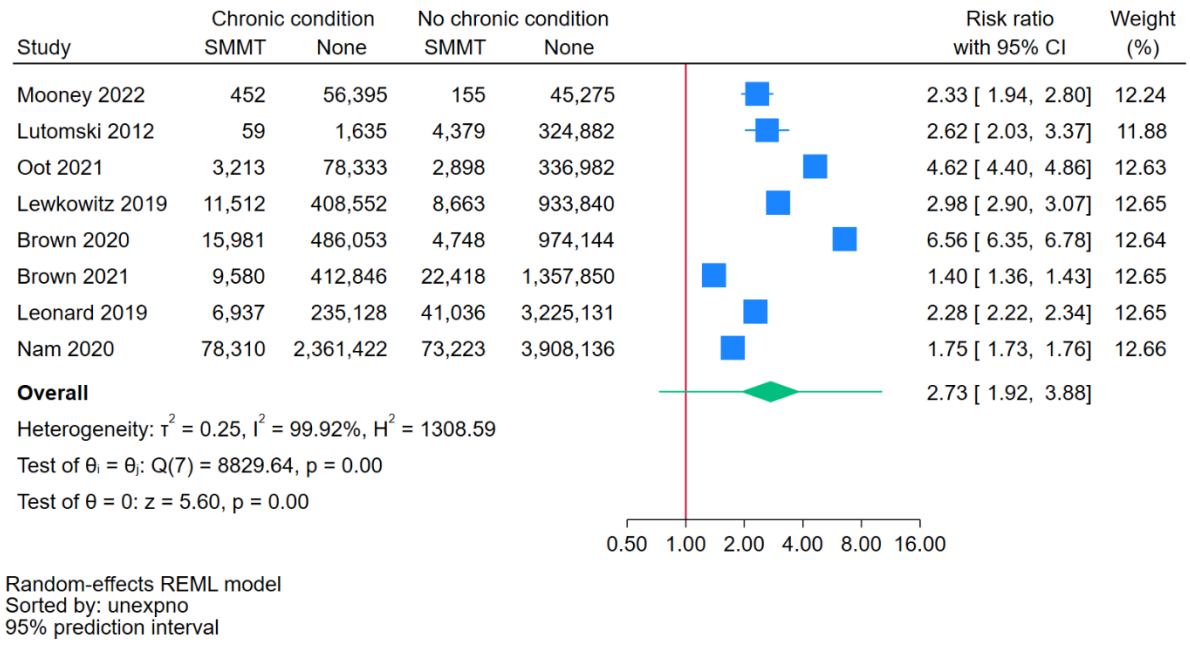


Random-effects REML model
Sorted by: unexpno
95% prediction interval

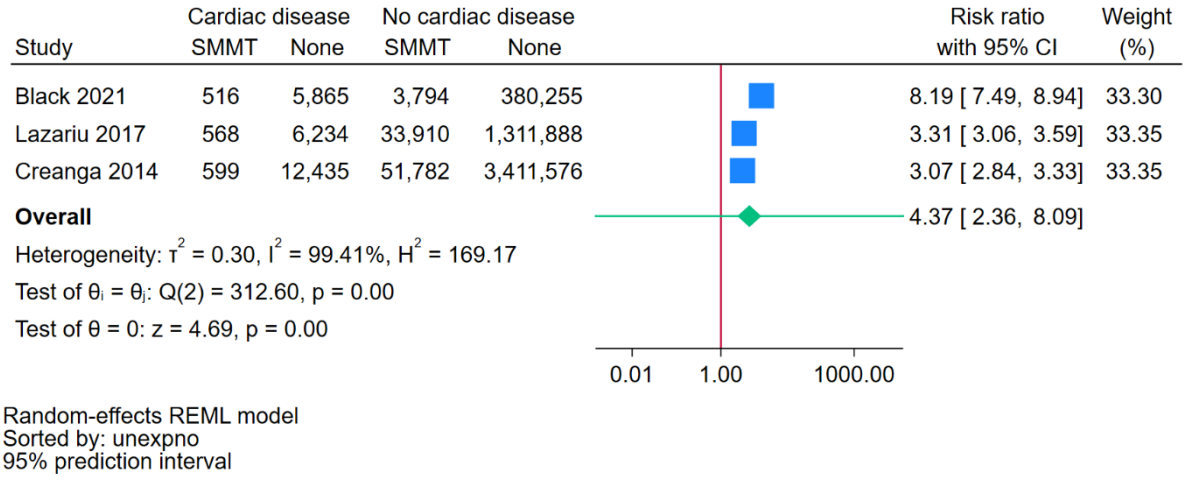
Appendix Figure B3.19 Association between Substance Use and SMM-T



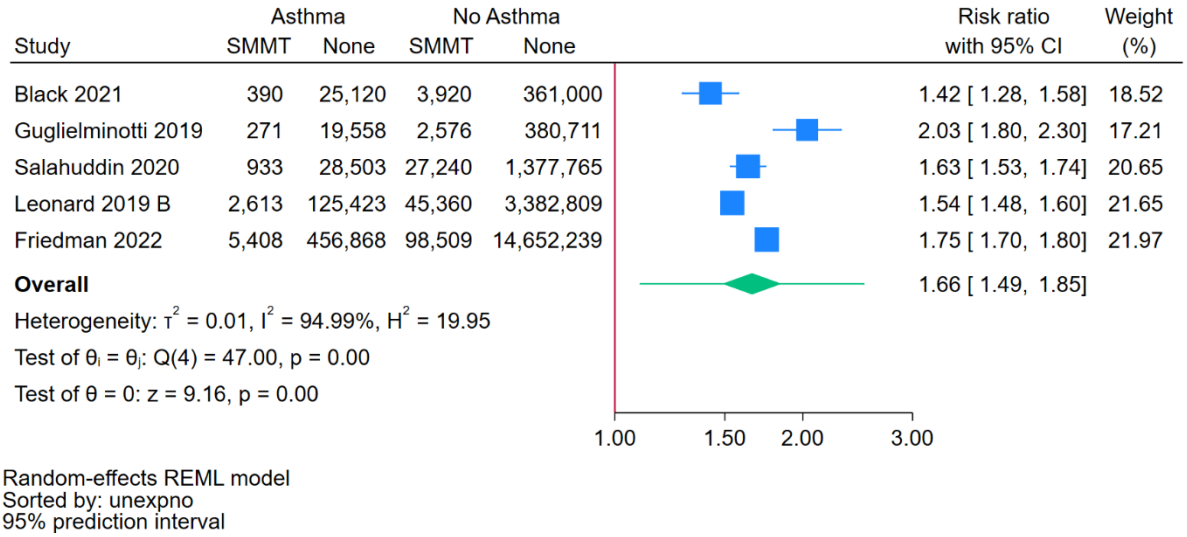
Appendix Figure B3.20 Association between Any Pre-Existing Condition and SMM-T



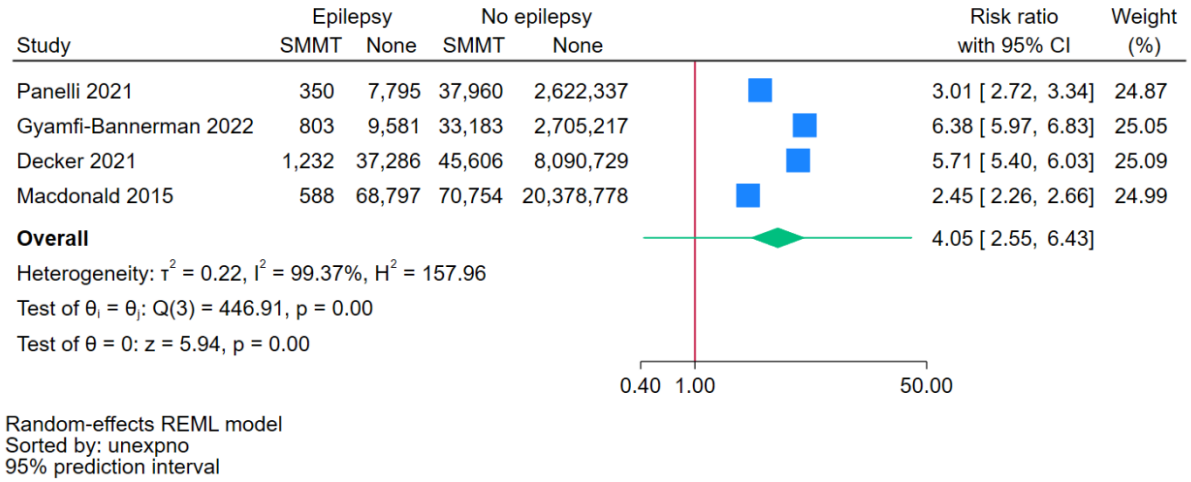
Appendix Figure B3.21 Association between Cardiac Disease and SMM-T



Appendix Figure B3.22 Association between Asthma and SMM-T

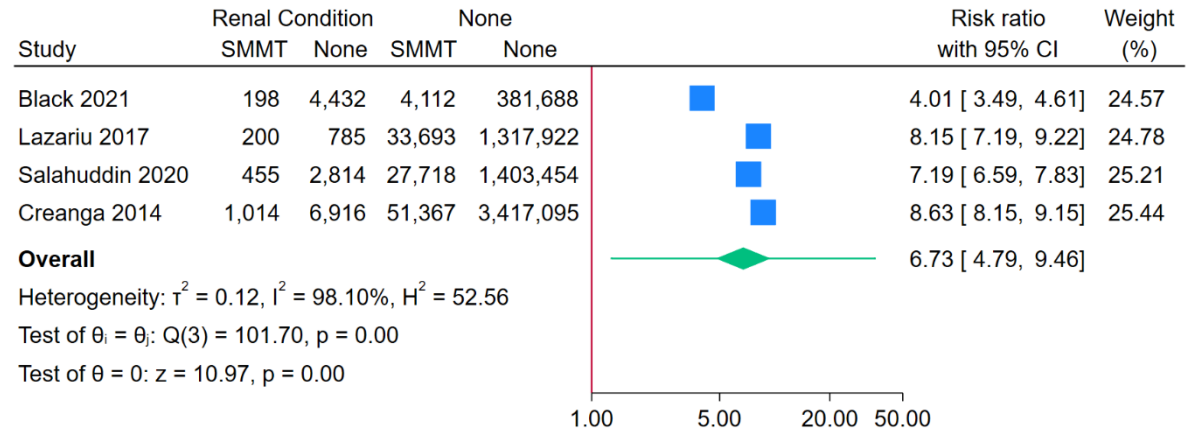


Appendix Figure B3.23 Association between Epilepsy and SMM-T



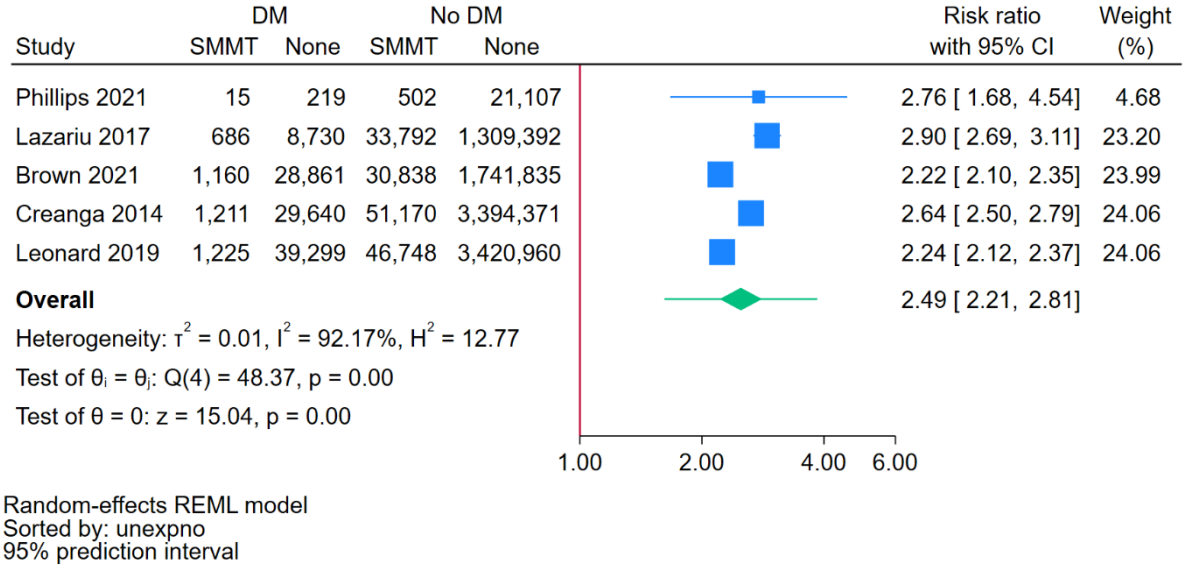
Random-effects REML model
Sorted by: unexpno
95% prediction interval

Appendix Figure B3.24 Association between Renal Disease and SMM-T



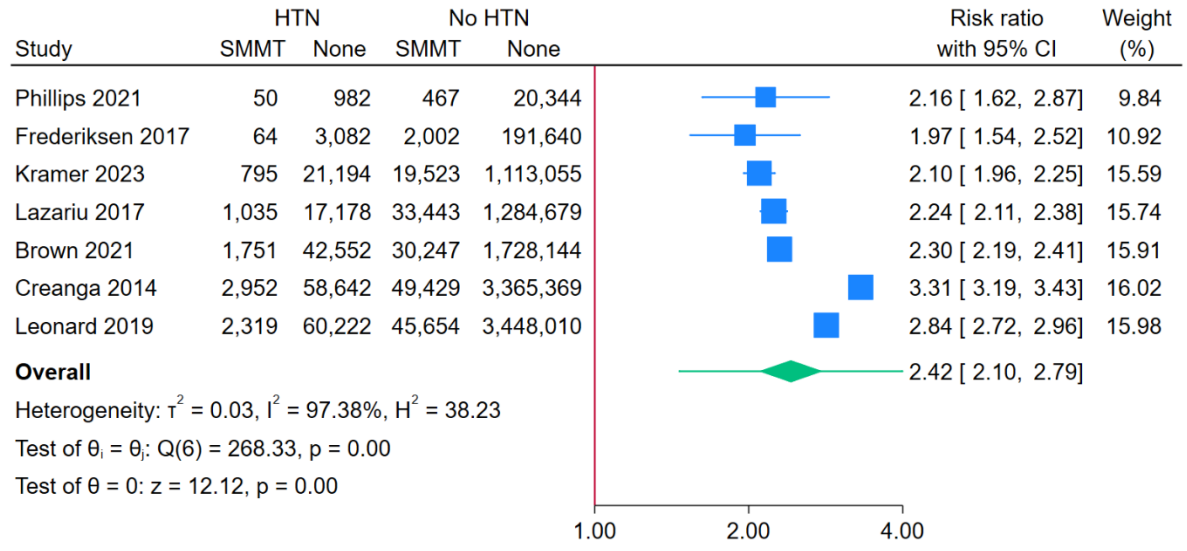
Random-effects REML model
Sorted by: unexpno
95% prediction interval

Appendix Figure B3.25 Association between Diabetes Mellitus and SMM-T



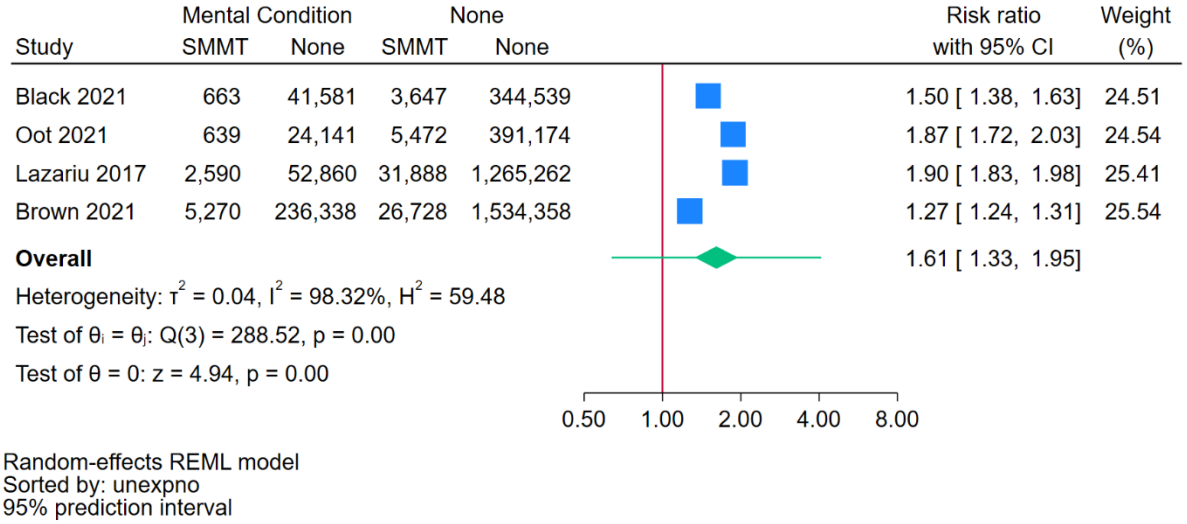
Random-effects REML model
Sorted by: unexpno
95% prediction interval

Appendix Figure B3.26 Association between Chronic Hypertension and SMM-T

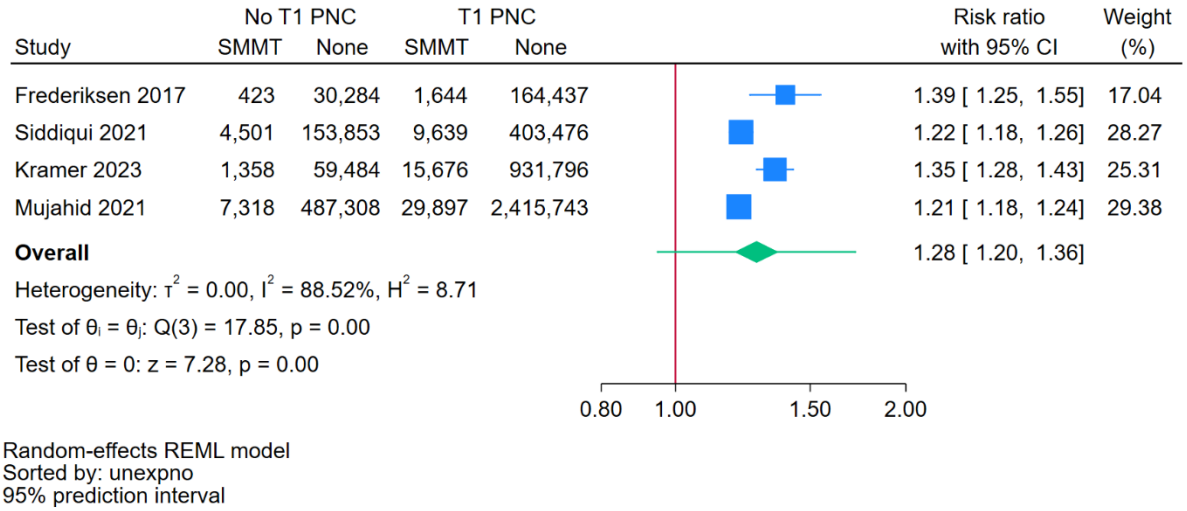


Random-effects REML model
Sorted by: unexpno
95% prediction interval

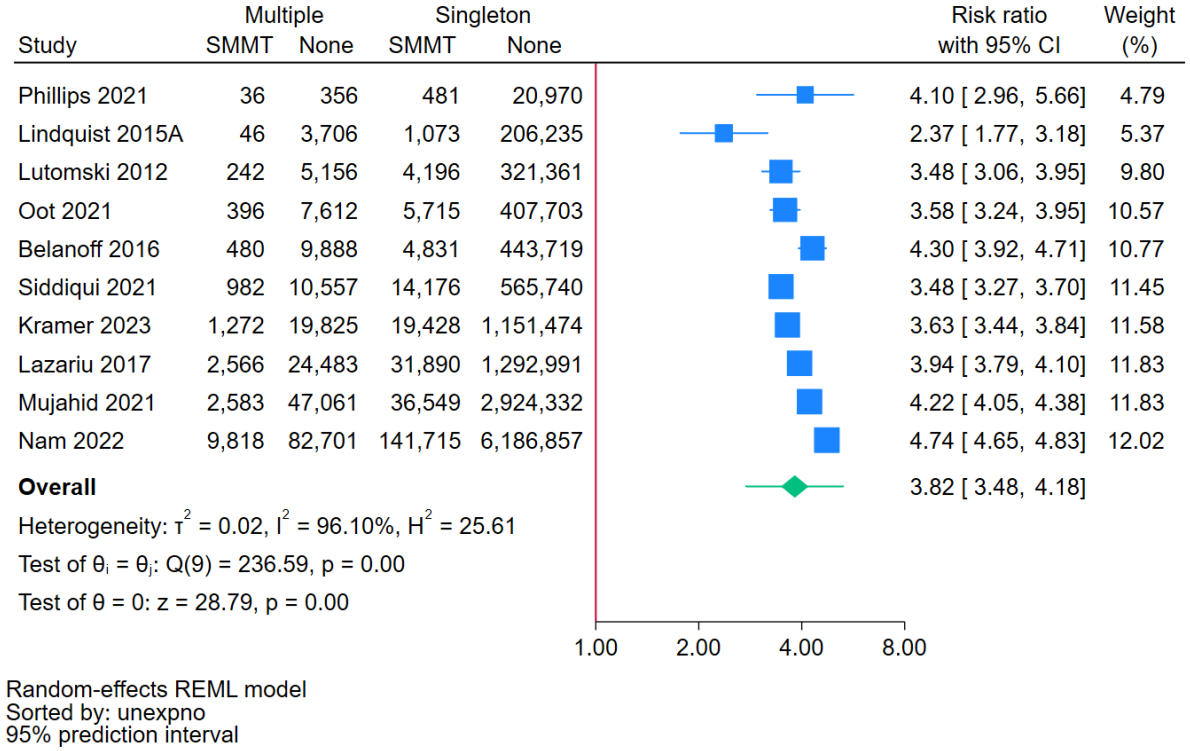
Appendix Figure B3.27 Association between Mental Health Condition and SMM-T



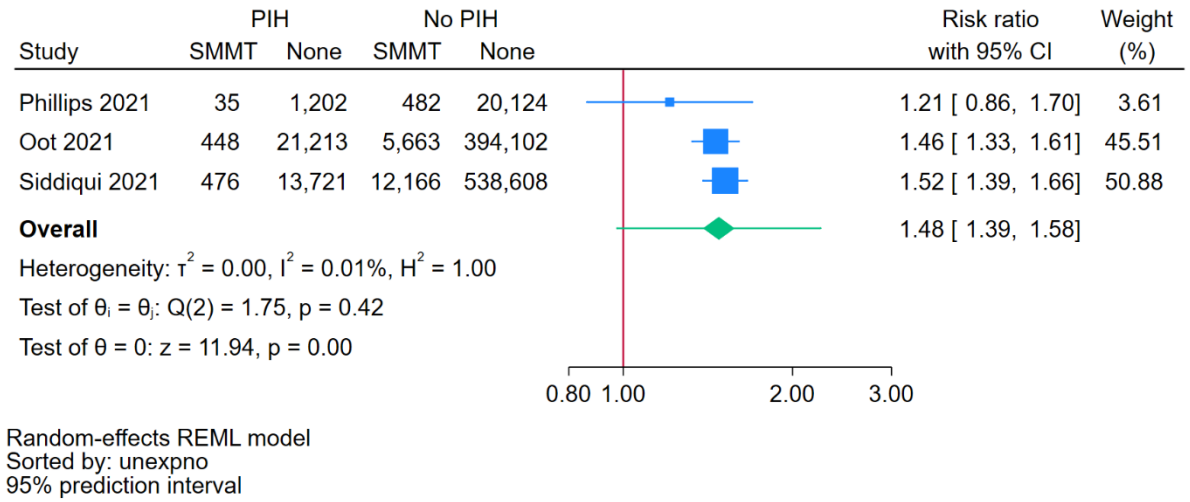
Appendix Figure B3.28 Association between Delayed Initiation of Antenatal Care and SMM-T



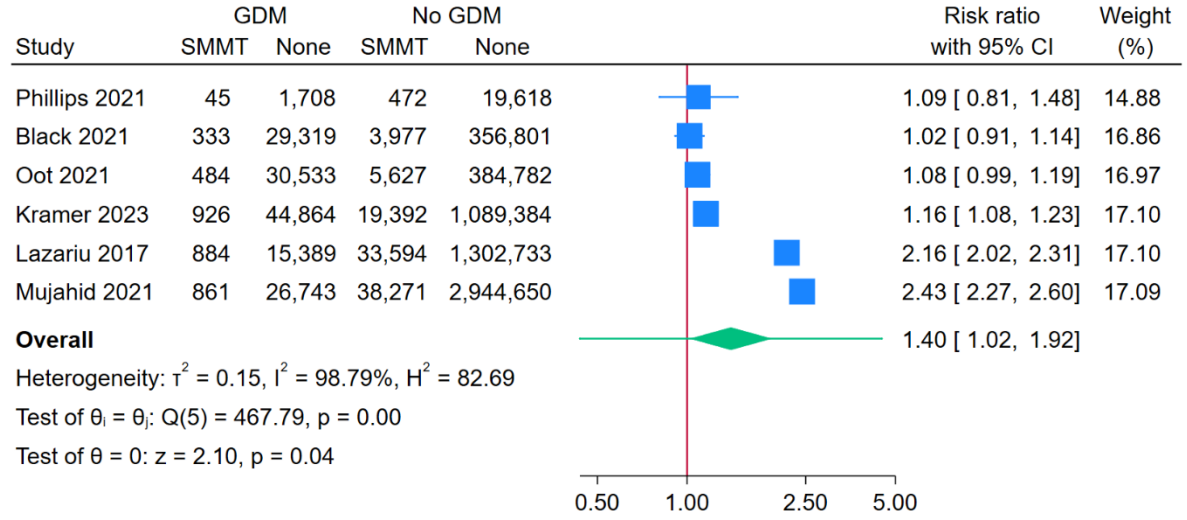
Appendix Figure B3.29 Association between Multiple Pregnancy and SMM-T



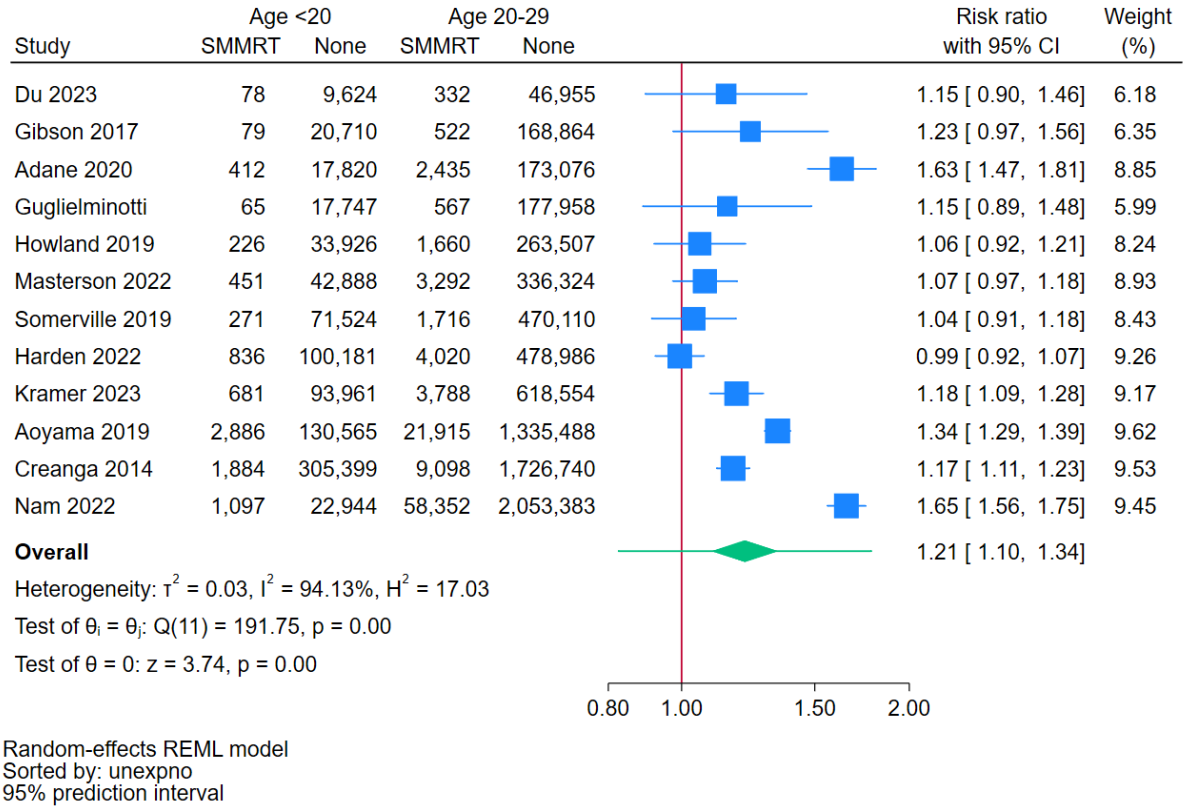
Appendix Figure B3.30 Association between Pregnancy-Induced Hypertension and SMM-T



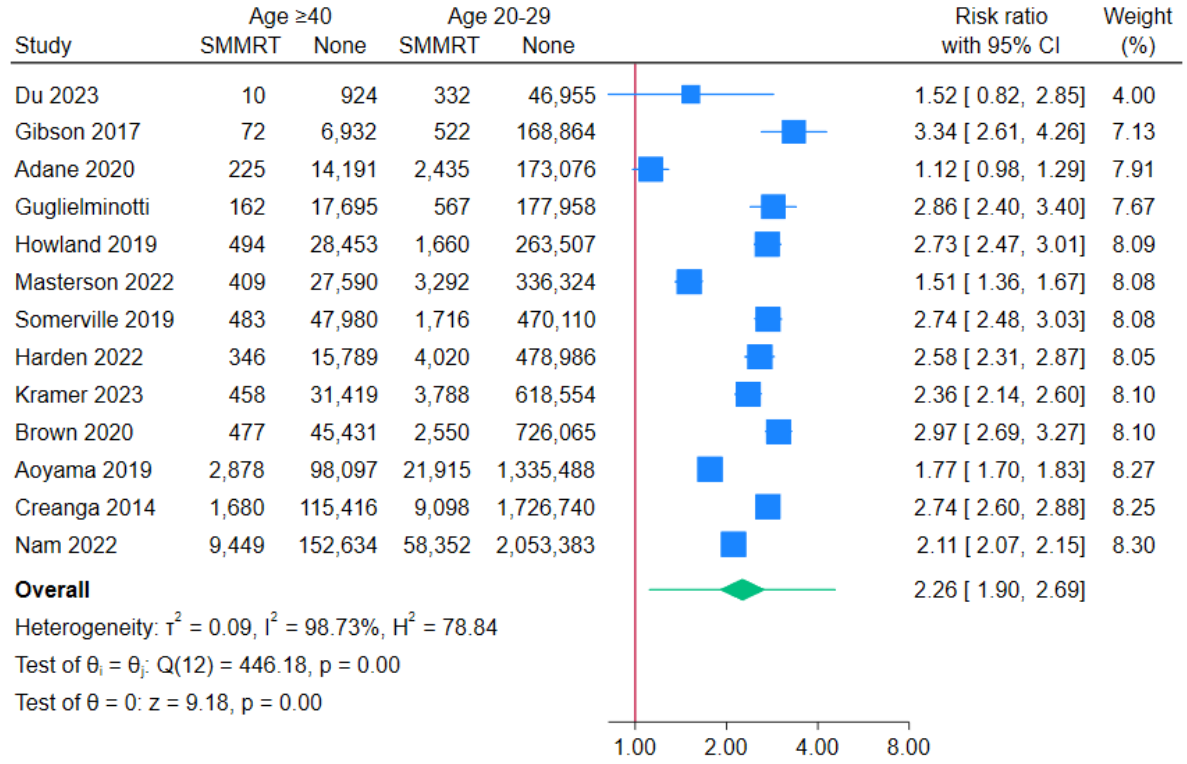
Appendix Figure B3.31 Association between Gestational Diabetes and SMM-T



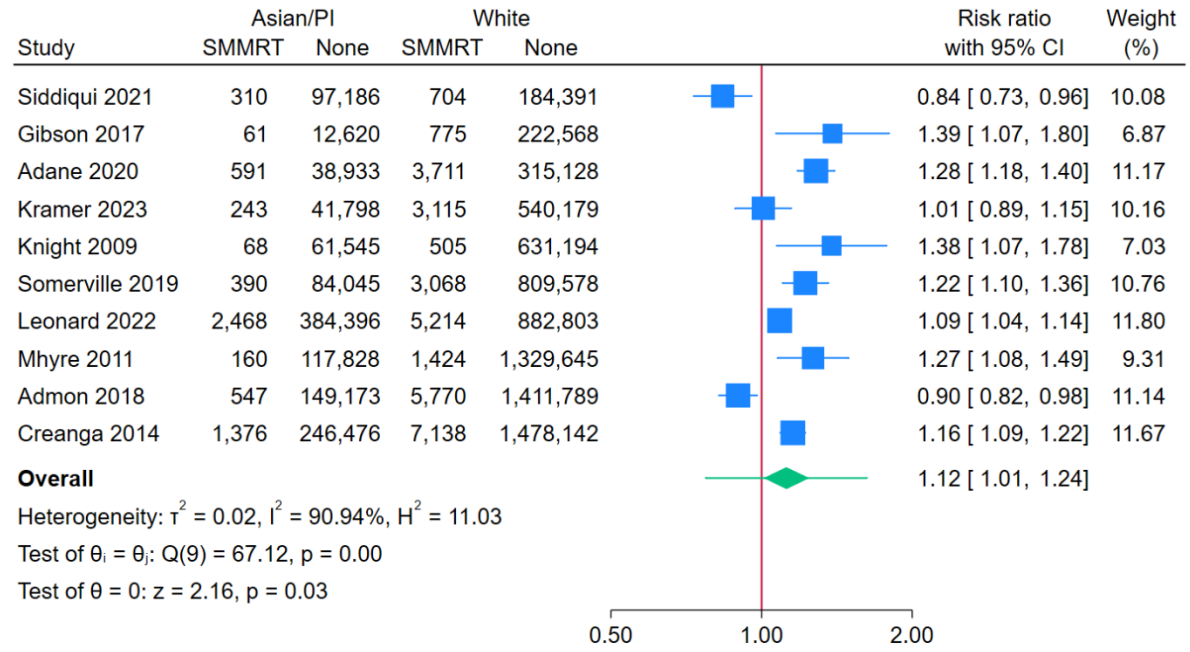
Appendix Figure B3.32 Association between Age under 20 Years and SMM-RT



Appendix Figure B3.33 Association between Age ≥40 Years and SMM-RT

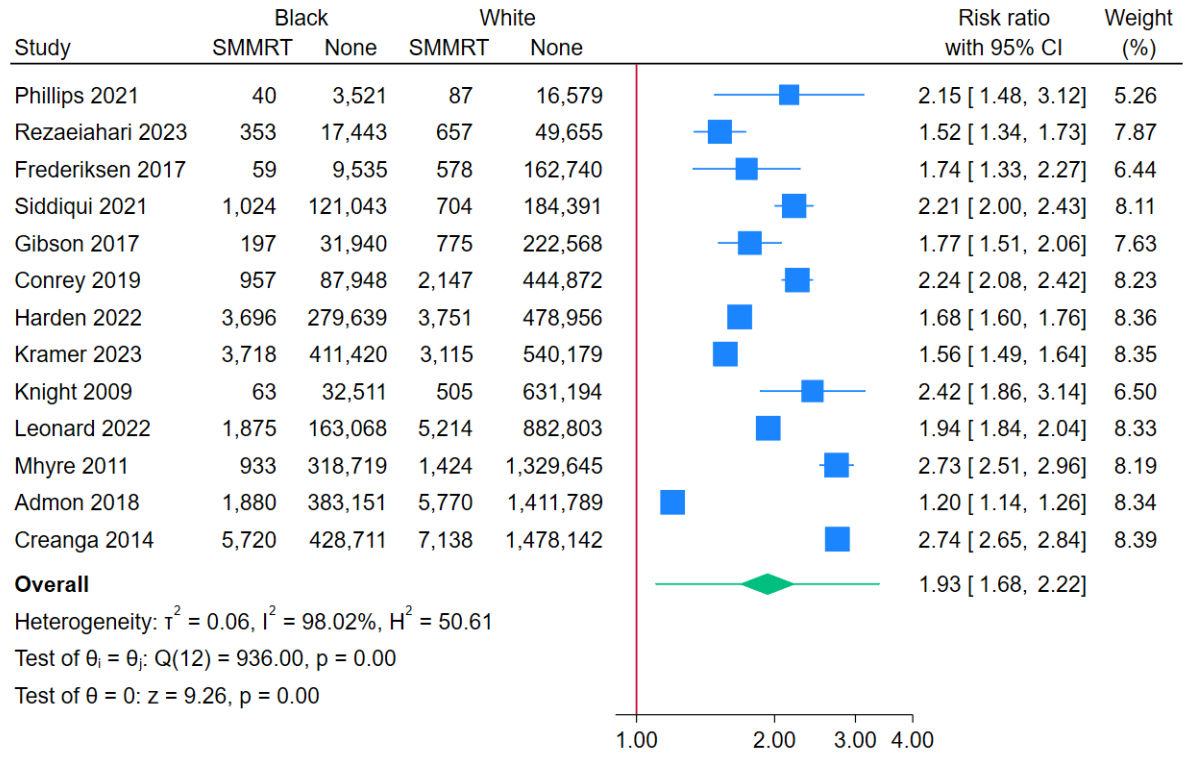


Appendix Figure B3.34 Association between Asian/Pacific Islander Ethnicity and SMM-RT



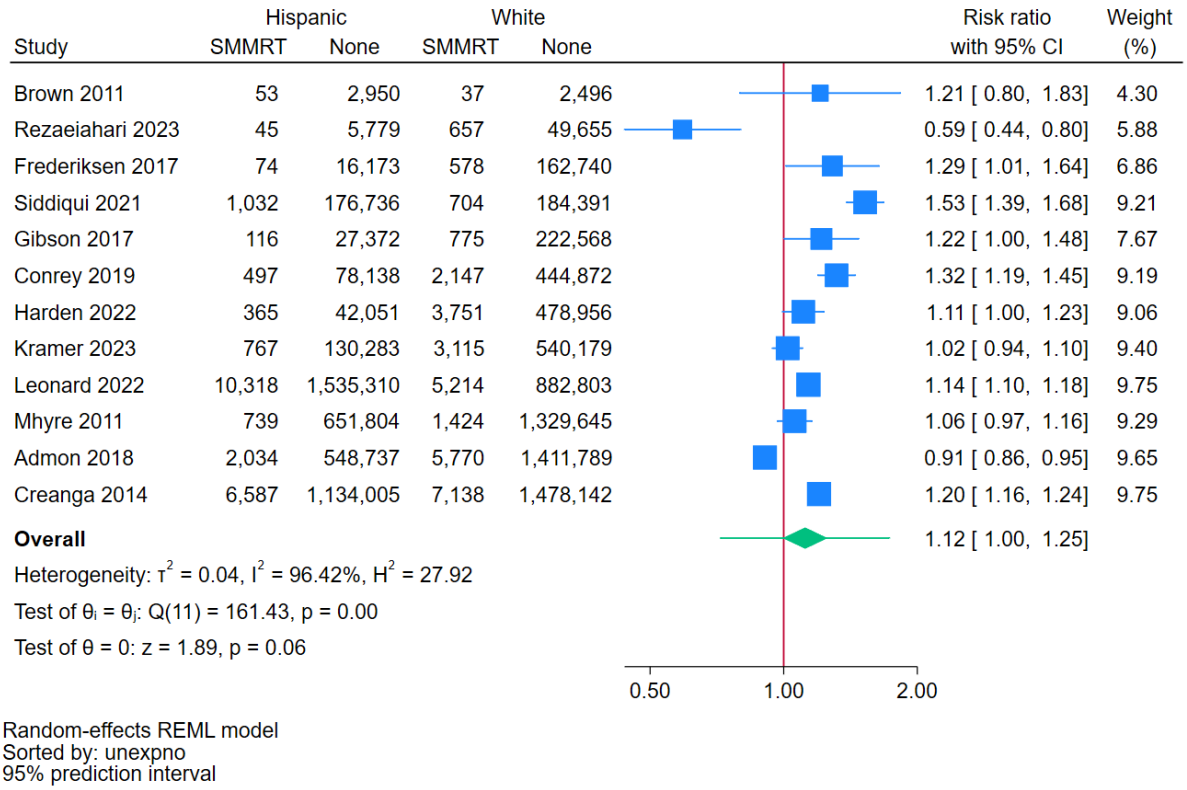
Random-effects REML model
Sorted by: unexpno
95% prediction interval

Appendix Figure B3.35 Association between Black Ethnicity and SMM-RT



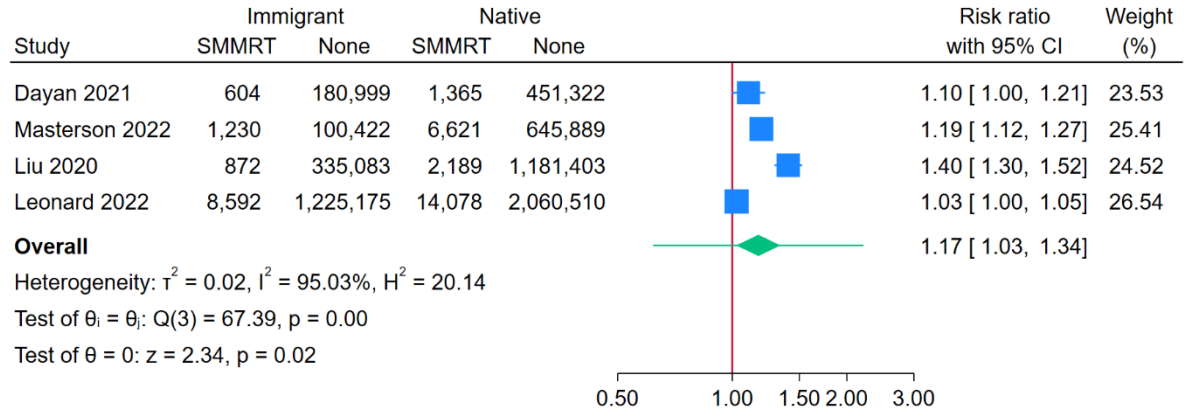
Random-effects REML model
Sorted by: unexpno
95% prediction interval

Appendix Figure B3.36 Association between Hispanic Ethnicity and SMM-RT



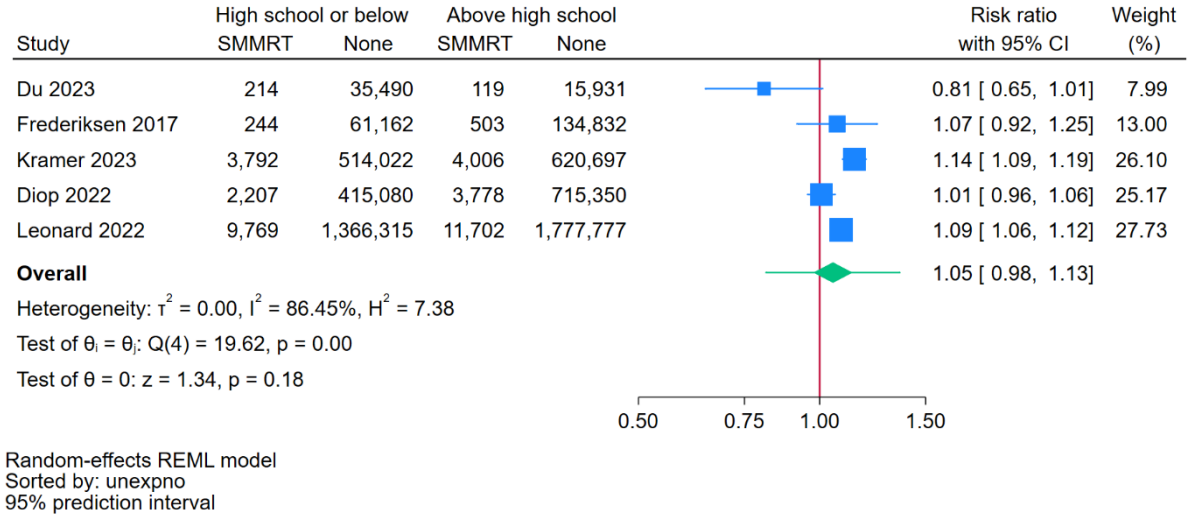
Random-effects REML model
Sorted by: unexpno
95% prediction interval

Appendix Figure B3.37 Association between Overall Migrant Status and SMM-RT

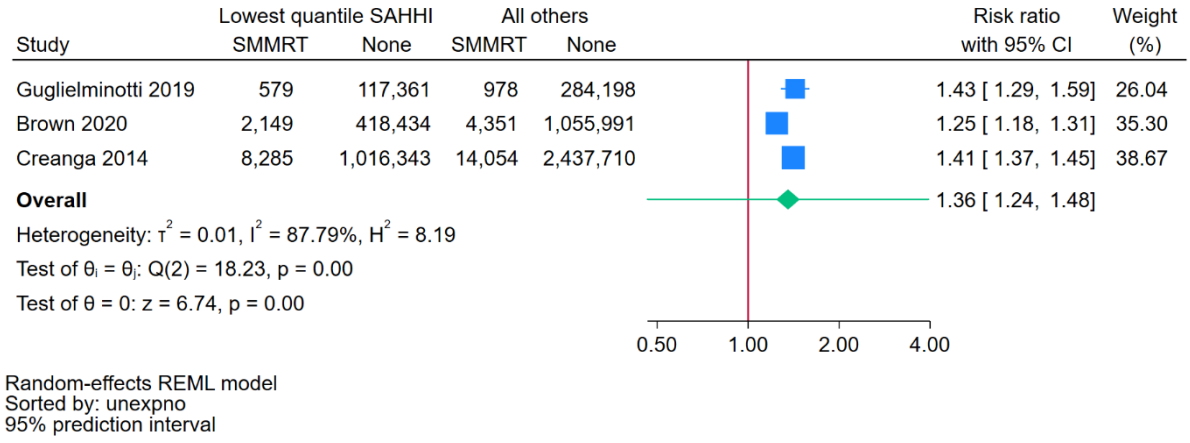


Random-effects REML model
Sorted by: unexpno
95% prediction interval

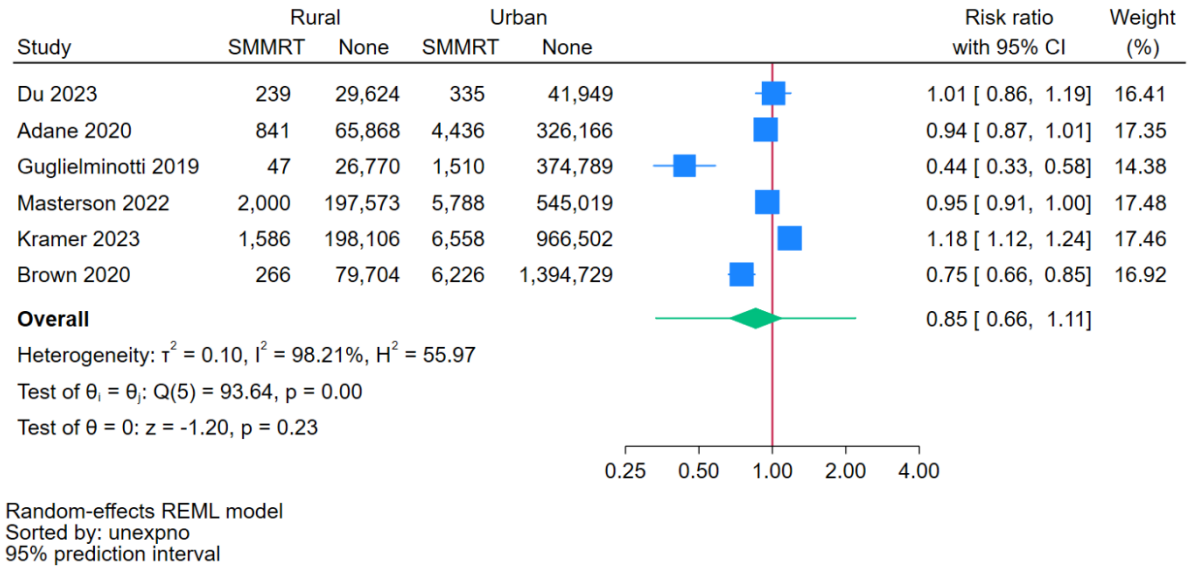
Appendix Figure B3.38 Association between Educational Attainment at or above High School Level and SMM-RT



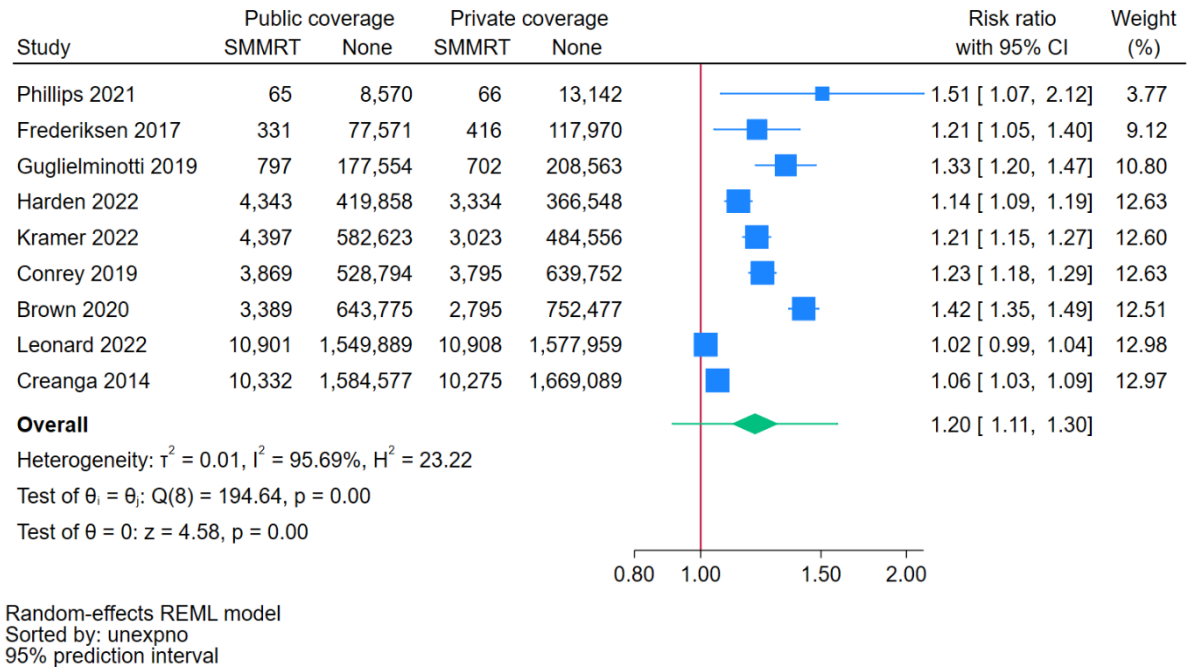
Appendix Figure B3.39 Association between Small Area Household Income and SMM-RT



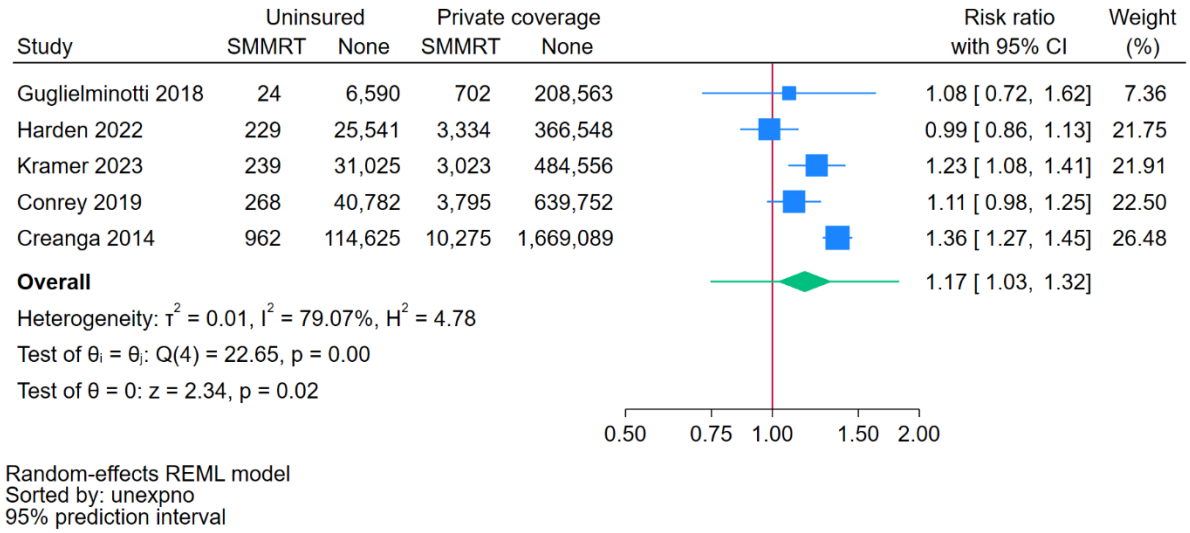
Appendix Figure B3.40 Association between Rural Residence and SMM-RT



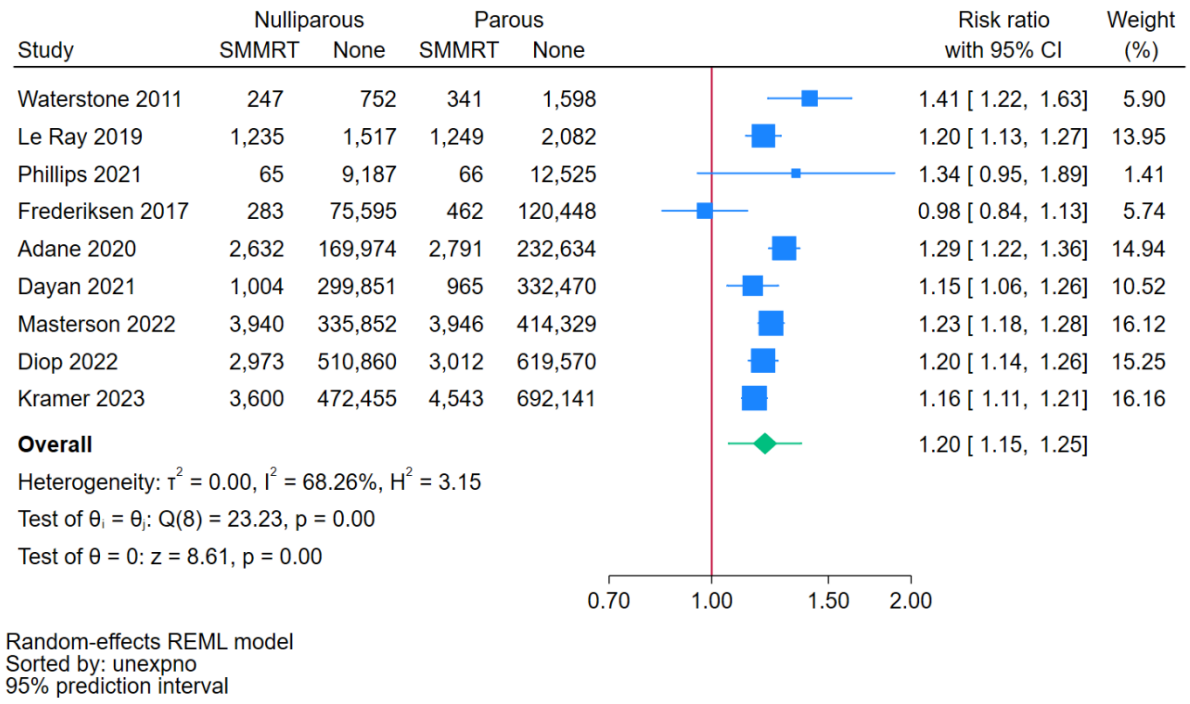
Appendix Figure B3.41 Association between Public Health Coverage and SMM-RT



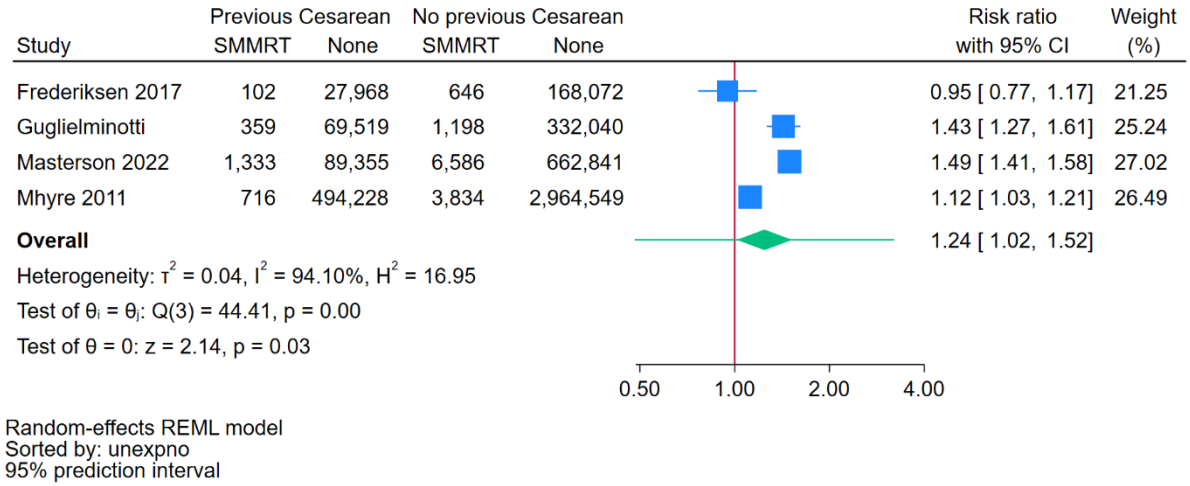
Appendix Figure B3.42 Association between Uninsured Status and SMM-RT



Appendix Figure B3.43 Association between Nulliparity and SMM-RT

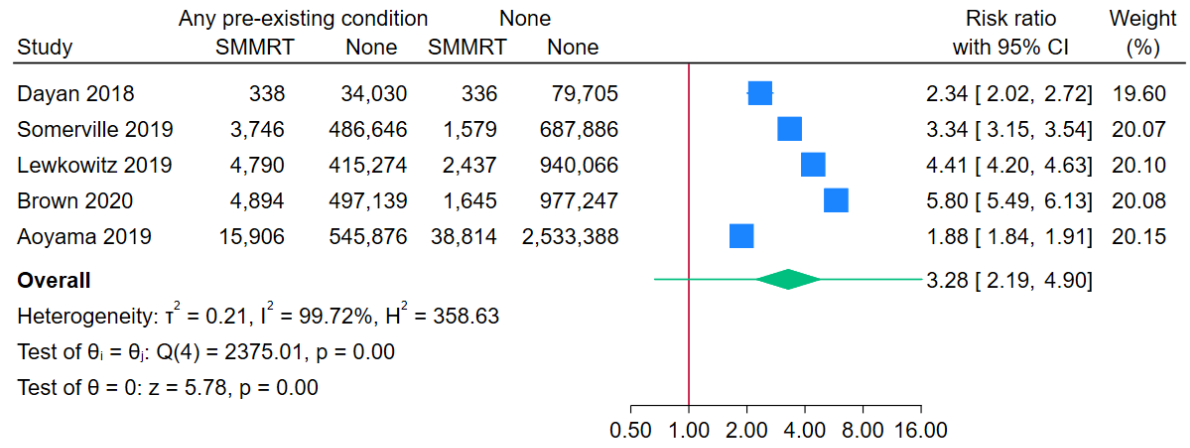


Appendix Figure B3.44 Association between Previous Caesarean Birth and SMM-RT



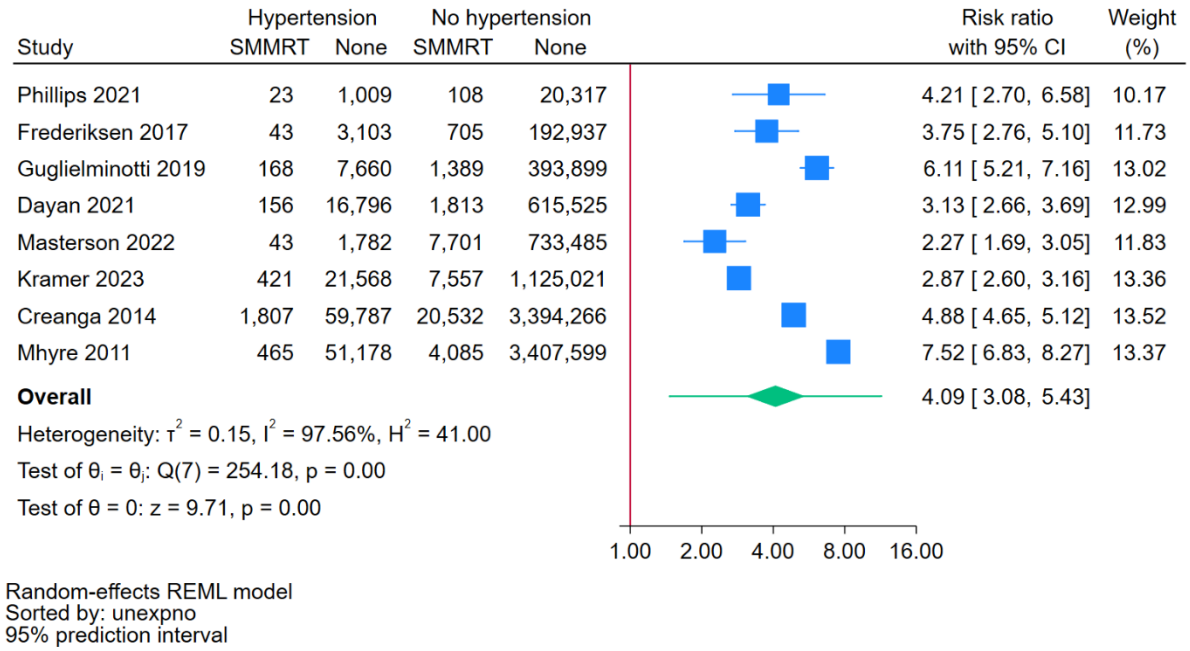
Random-effects REML model
Sorted by: unexpno
95% prediction interval

Appendix Figure B3.45 Association between Any Pre-Existing Condition and SMM-RT

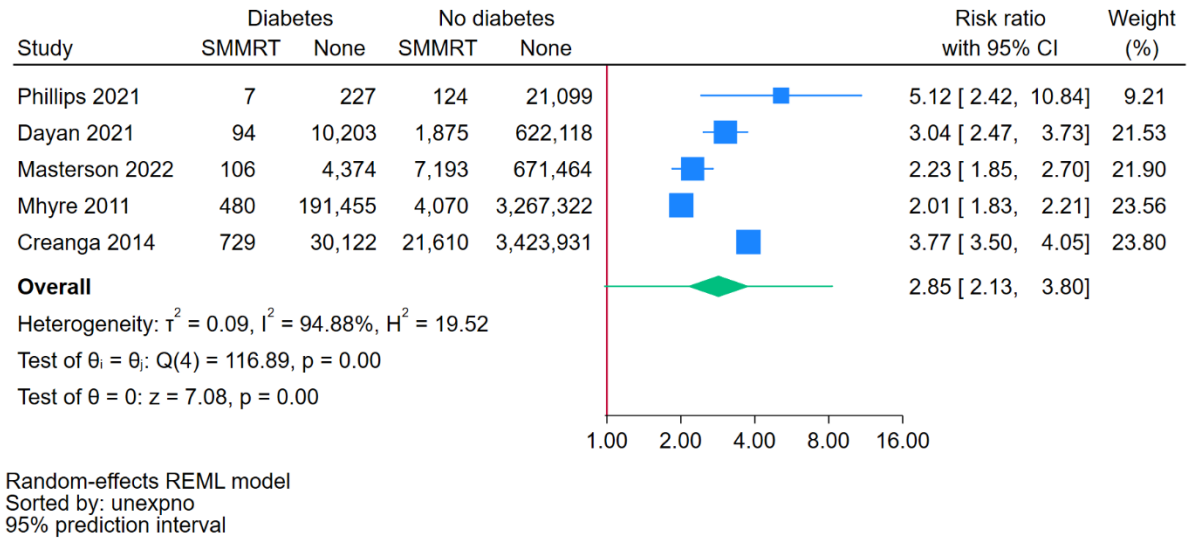


Random-effects REML model
Sorted by: unexpno
95% prediction interval

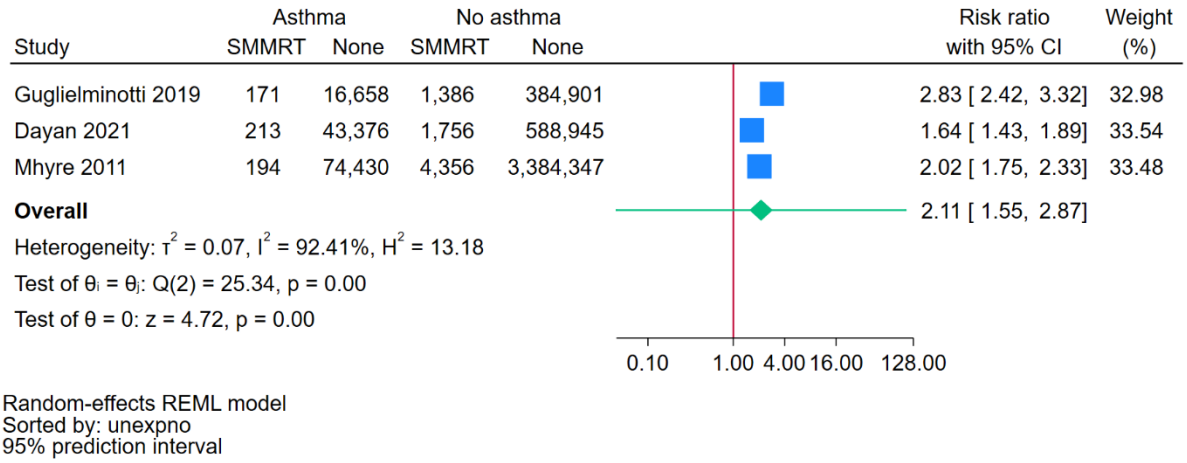
Appendix Figure B3.46 Association between Chronic Hypertension and SMM-RT



Appendix Figure B3.47 Association between Diabetes Mellitus and SMM-RT

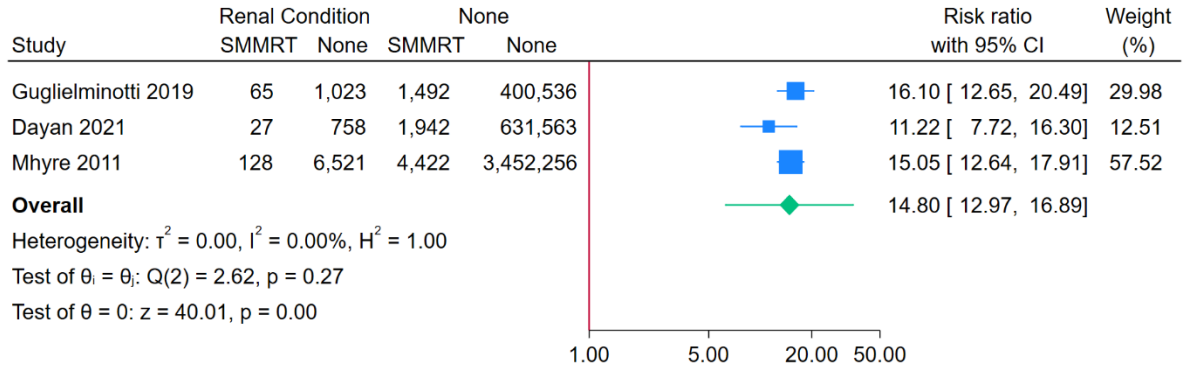


Appendix Figure B3.48 Association between Asthma and SMM-RT



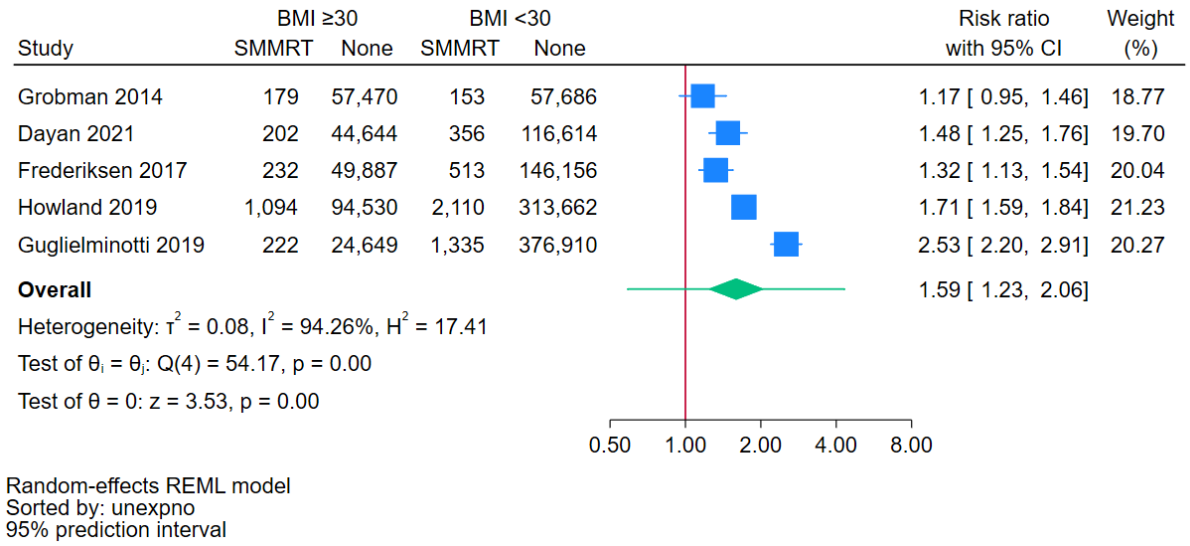
Random-effects REML model
Sorted by: unexpno
95% prediction interval

Appendix Figure B3.49 Association between Renal Conditions and SMM-RT



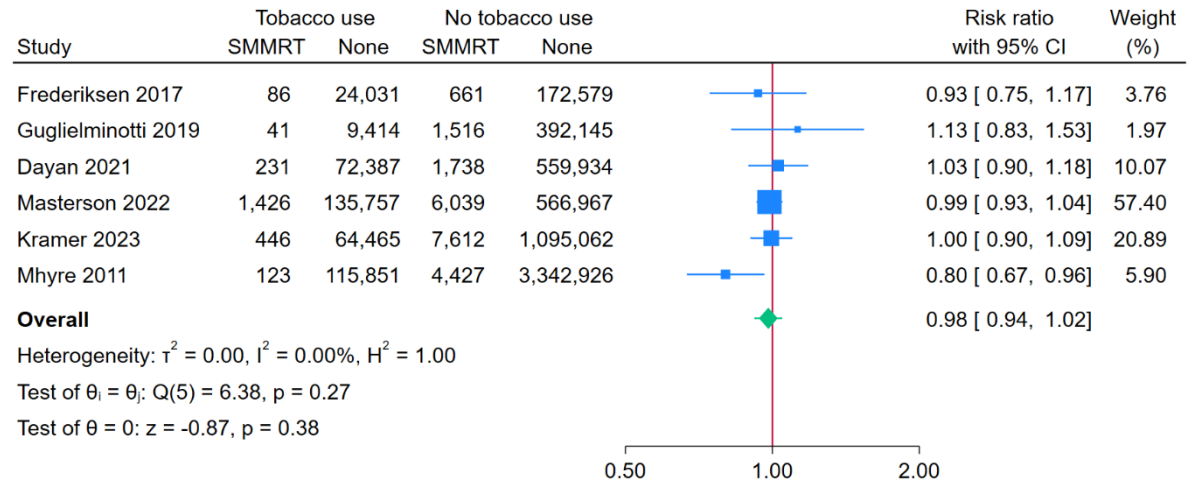
Random-effects REML model
Sorted by: unexpno
95% prediction interval

Appendix Figure B3.50 Association between Obesity and SMM-RT



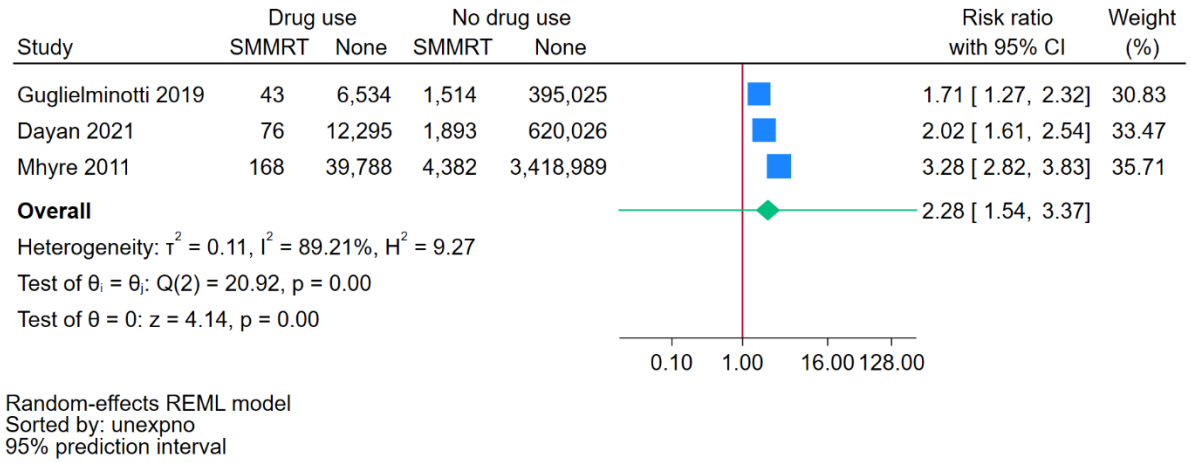
Random-effects REML model
Sorted by: unexpno
95% prediction interval

Appendix Figure B3.51 Association between Tobacco Use and SMM-RT

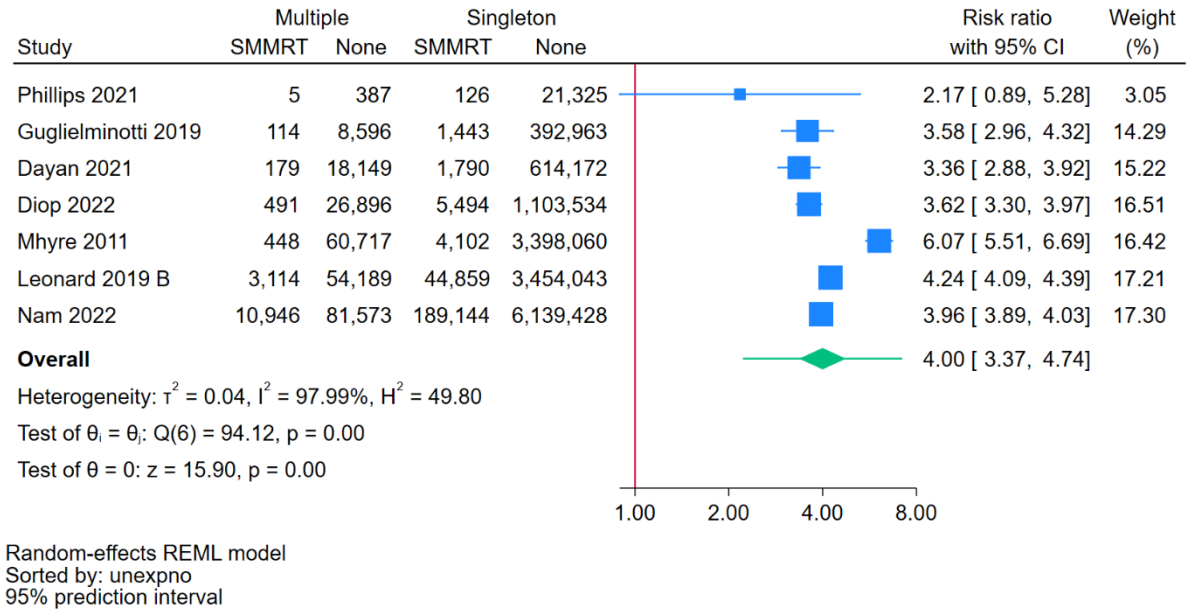


Random-effects REML model
Sorted by: unexpno
95% prediction interval

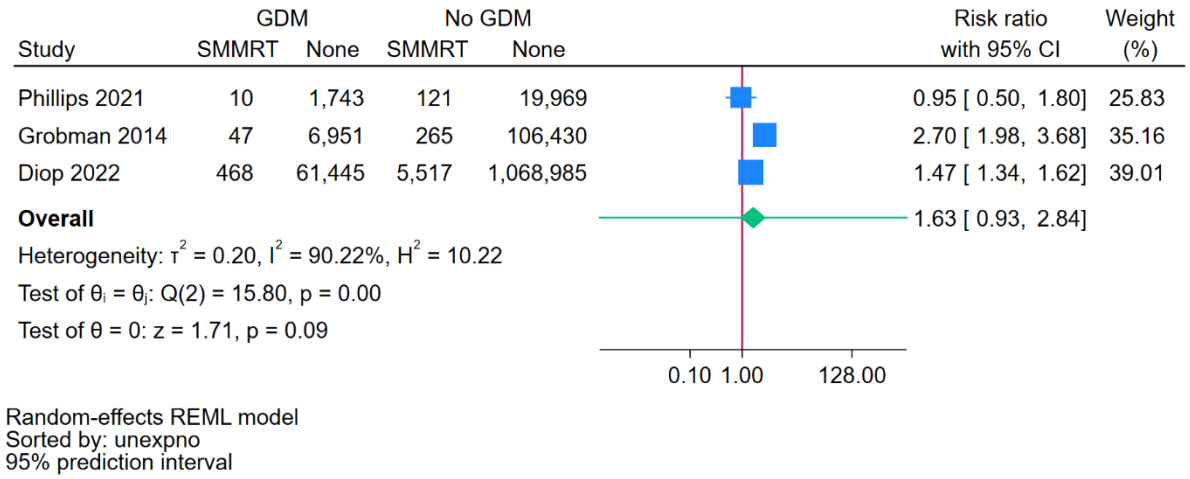
Appendix Figure B3.52 Association between Substance Use and SMM-RT



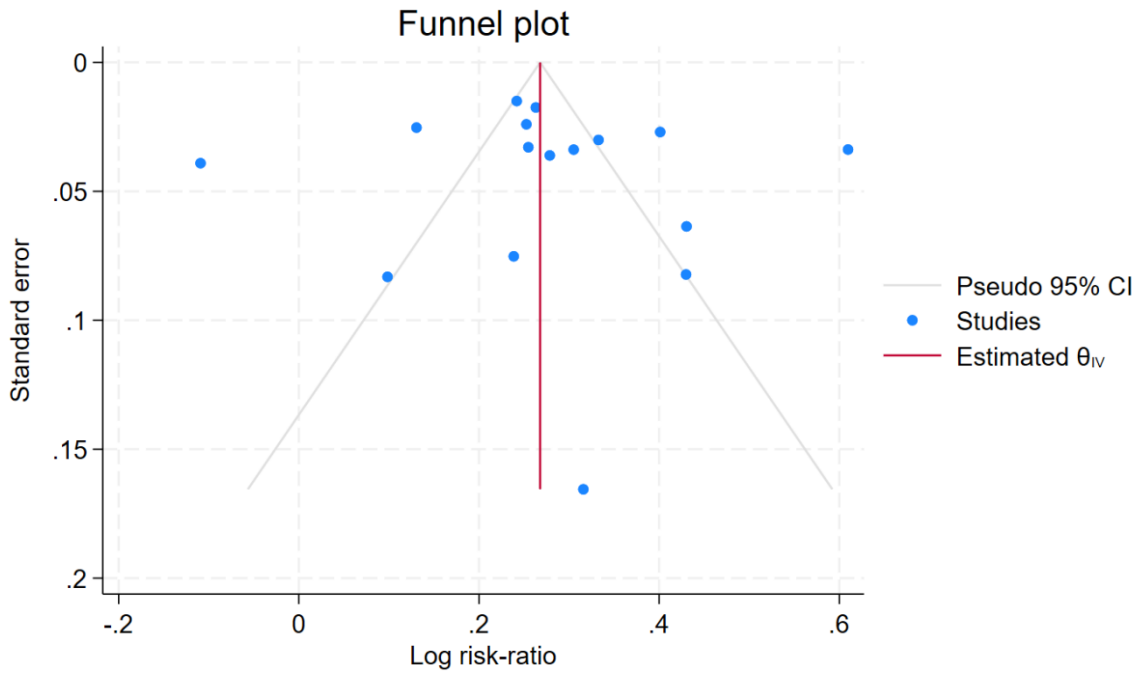
Appendix Figure B3.53 Association between Multiple Pregnancy and SMM-RT



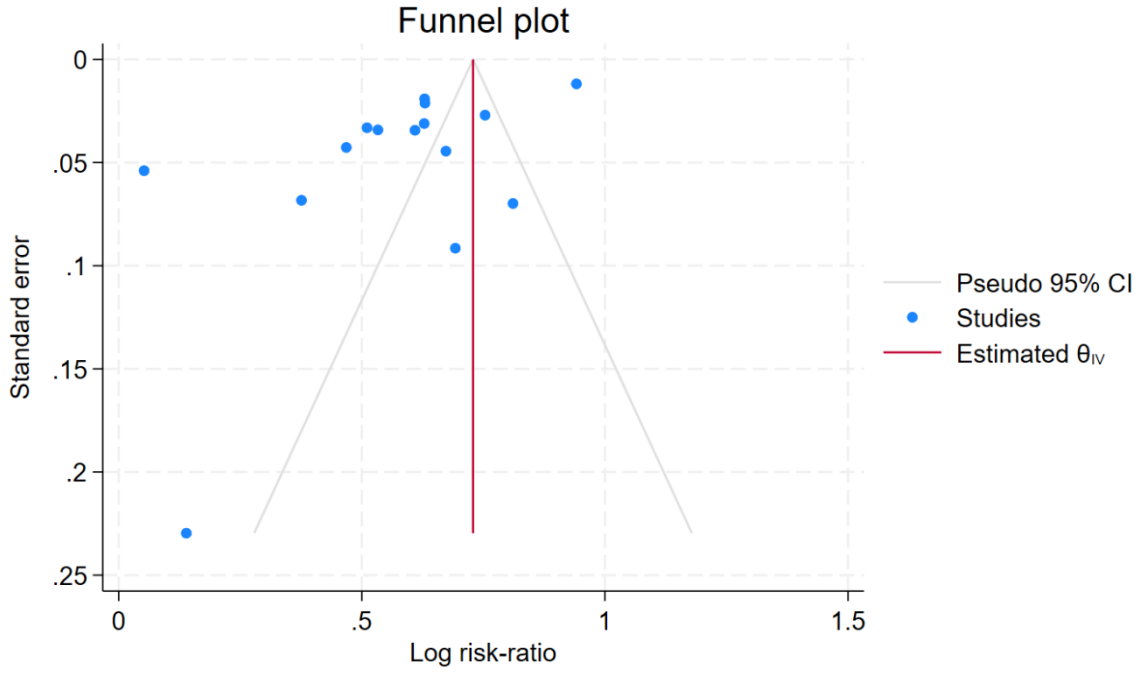
Appendix Figure B3.54 Association between Gestational Diabetes and SMM-RT



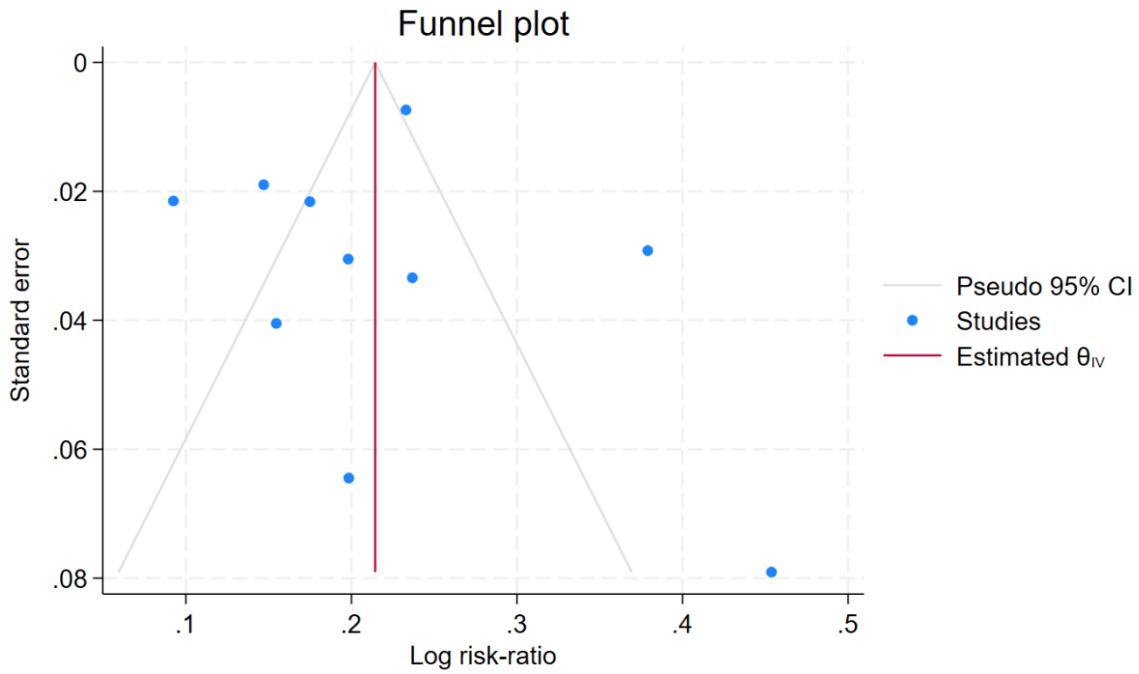
Appendix Figure B3.55 Funnel Plot for the Meta-Analysis of Age <20 Years and SMM-T



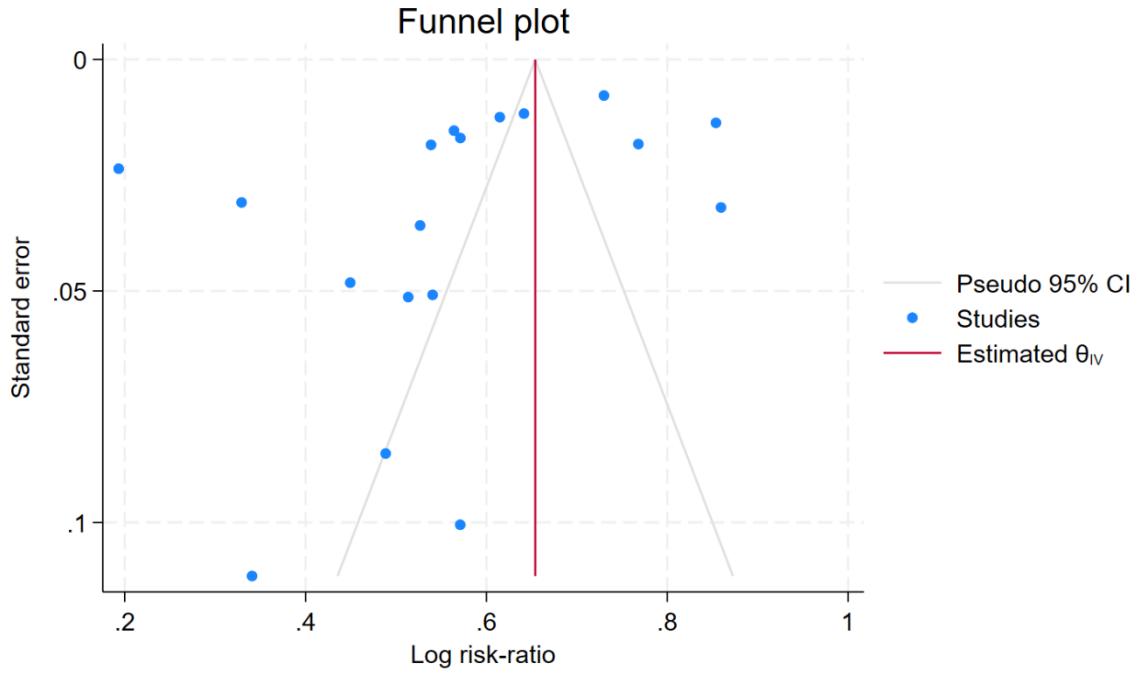
Appendix Figure B3.56 Funnel Plot for the Meta-Analysis of Age ≥40 Years and SMM-T



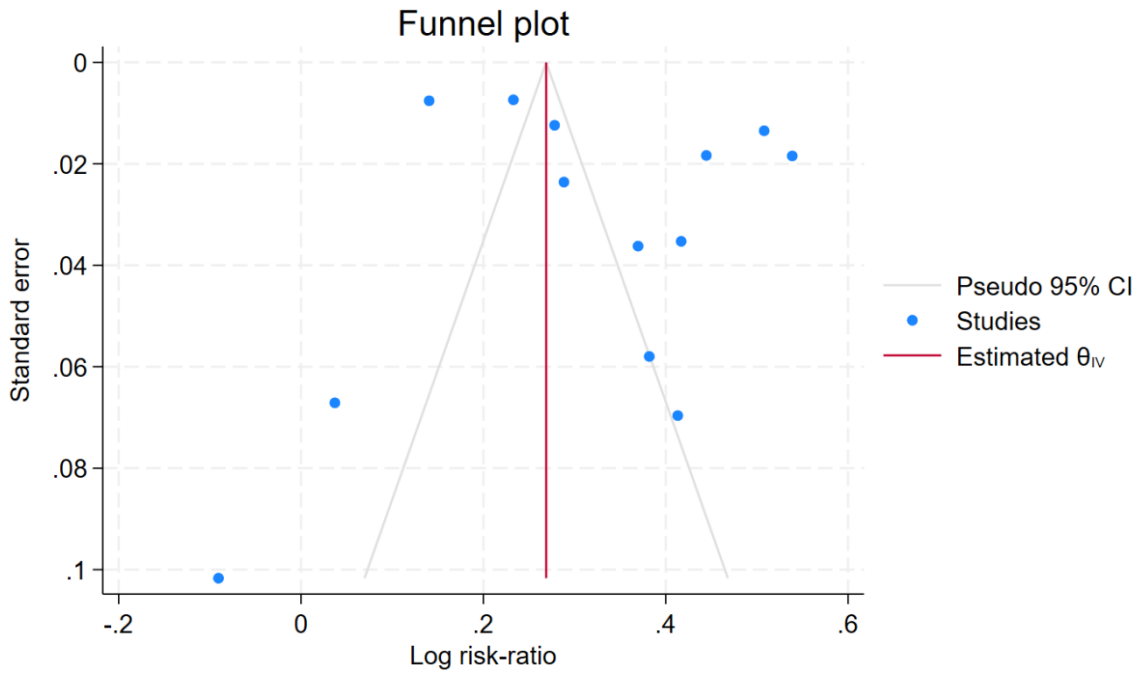
Appendix Figure B3.57 Funnel Plot for the Meta-Analysis of Asian/Pacific Islander Ethnicity and SMM-T



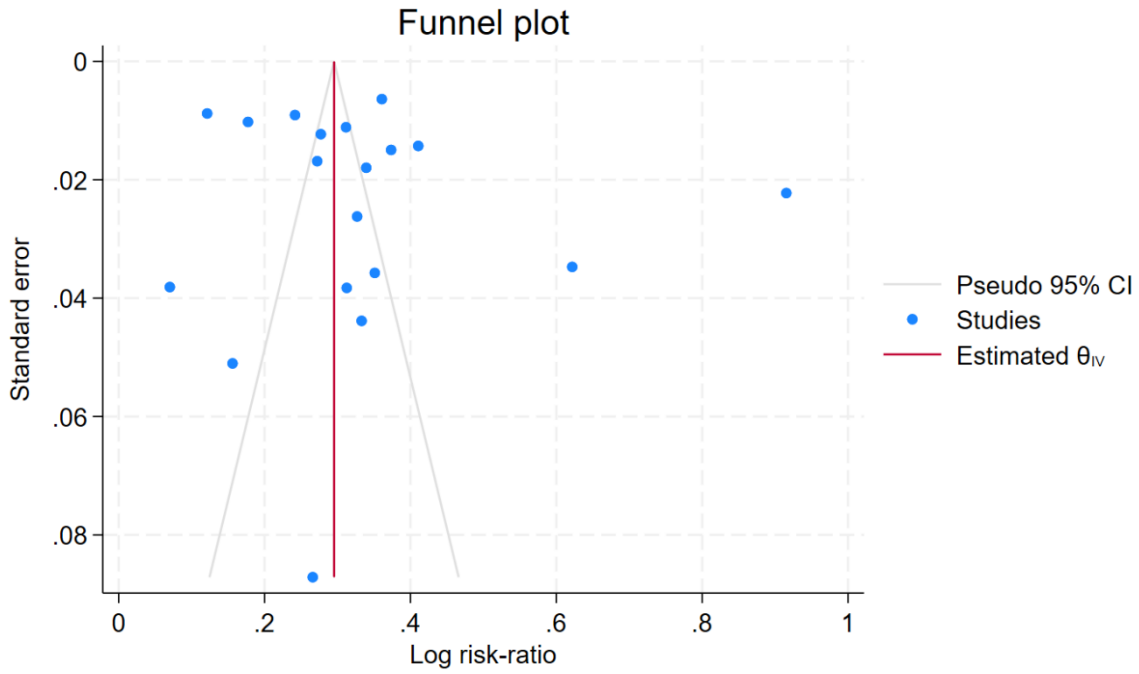
Appendix Figure B3.58 Funnel Plot for the Meta-Analysis of Black Ethnicity and SMM-T



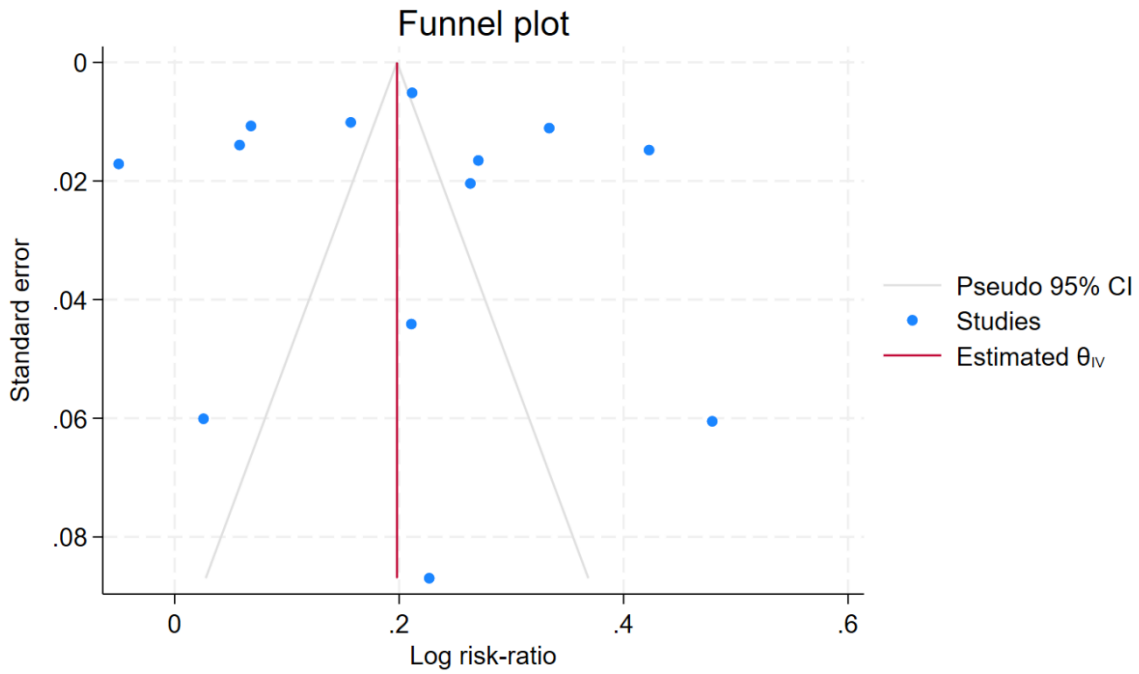
Appendix Figure B3.59 Funnel Plot for the Meta-Analysis of Hispanic Ethnicity and SMM-T



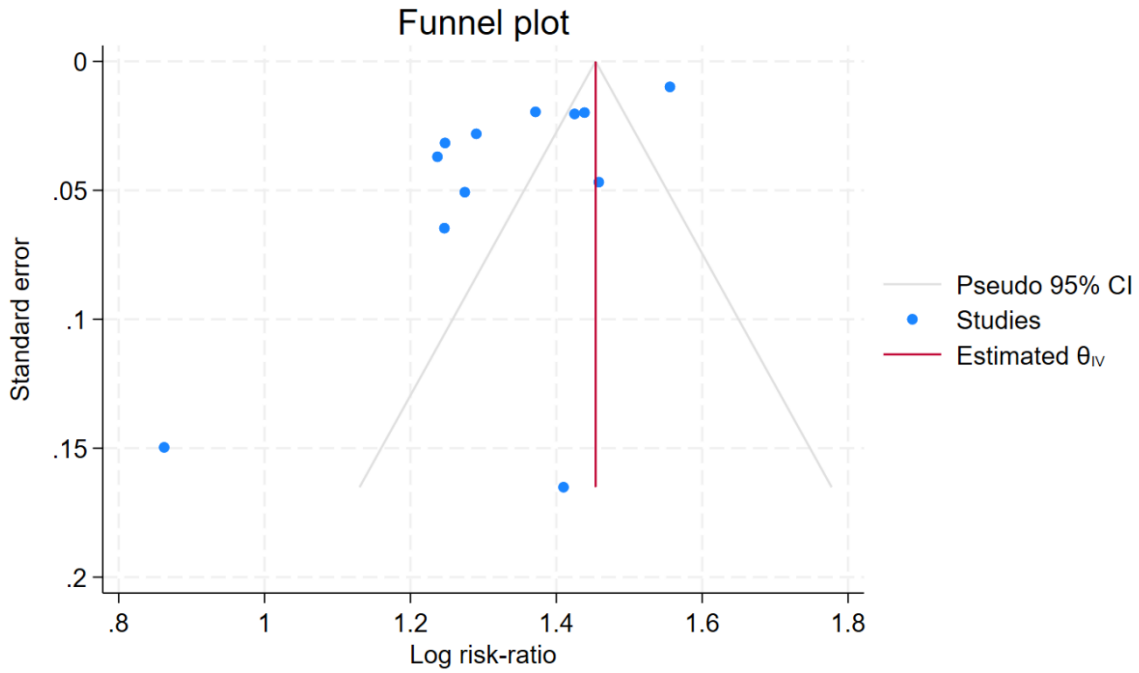
Appendix Figure B3.60 Funnel Plot for the Meta-Analysis of Public Health Coverage and SMM-T



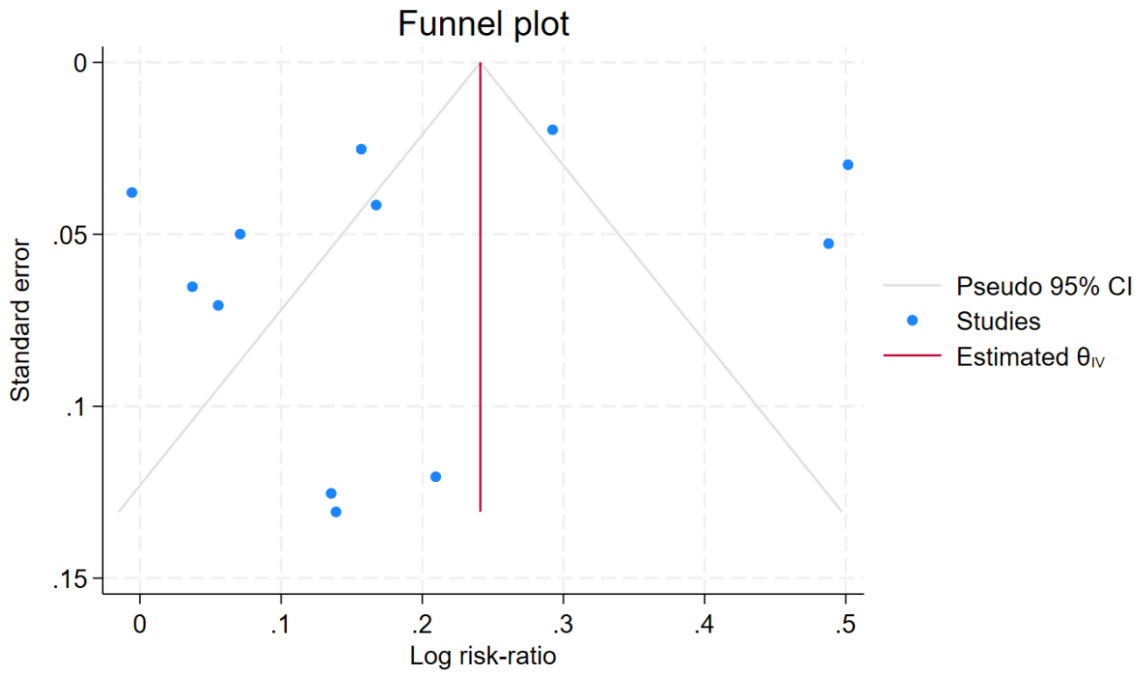
Appendix Figure B3.61 Funnel Plot for the Meta-Analysis of Nulliparity and SMM-T



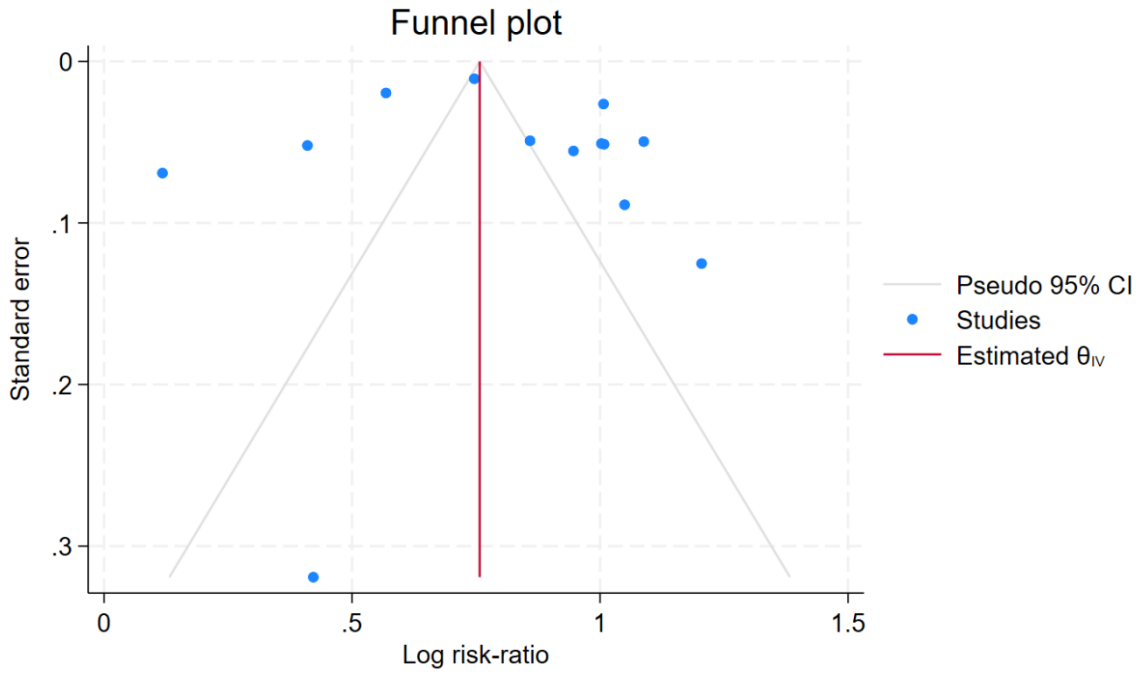
Appendix Figure B3.62 Funnel Plot for the Meta-Analysis of Multiple Pregnancy and SMM-T



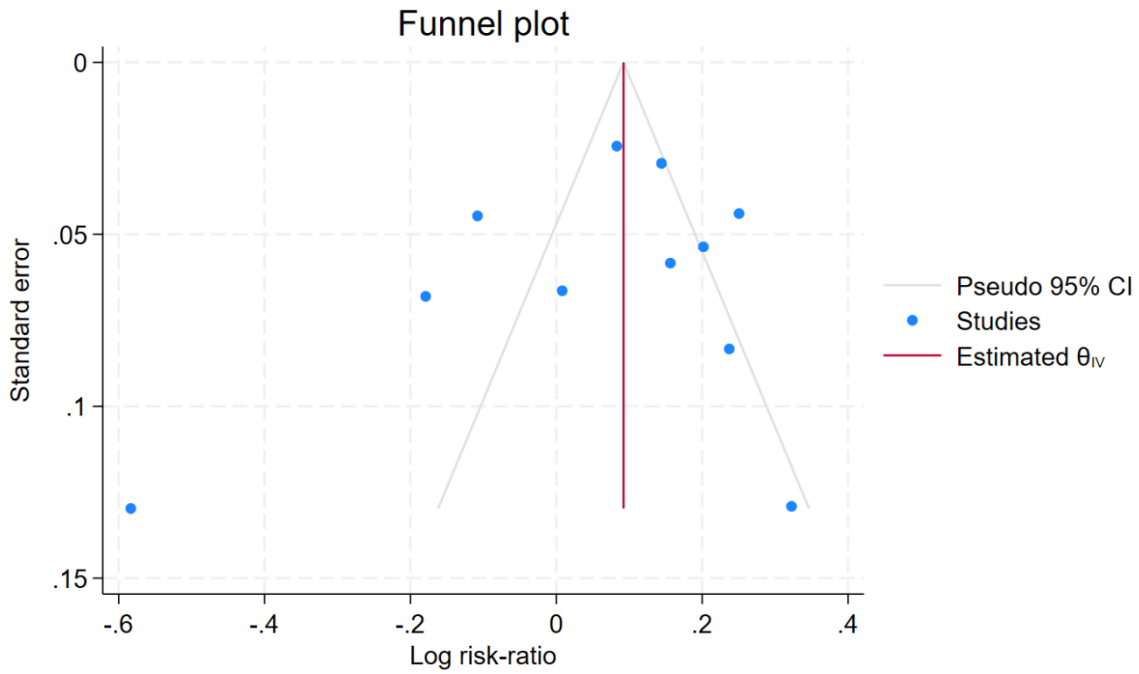
Appendix Figure B3.63 Funnel Plot for the Meta-Analysis of Age <20 Years and SMM-RT



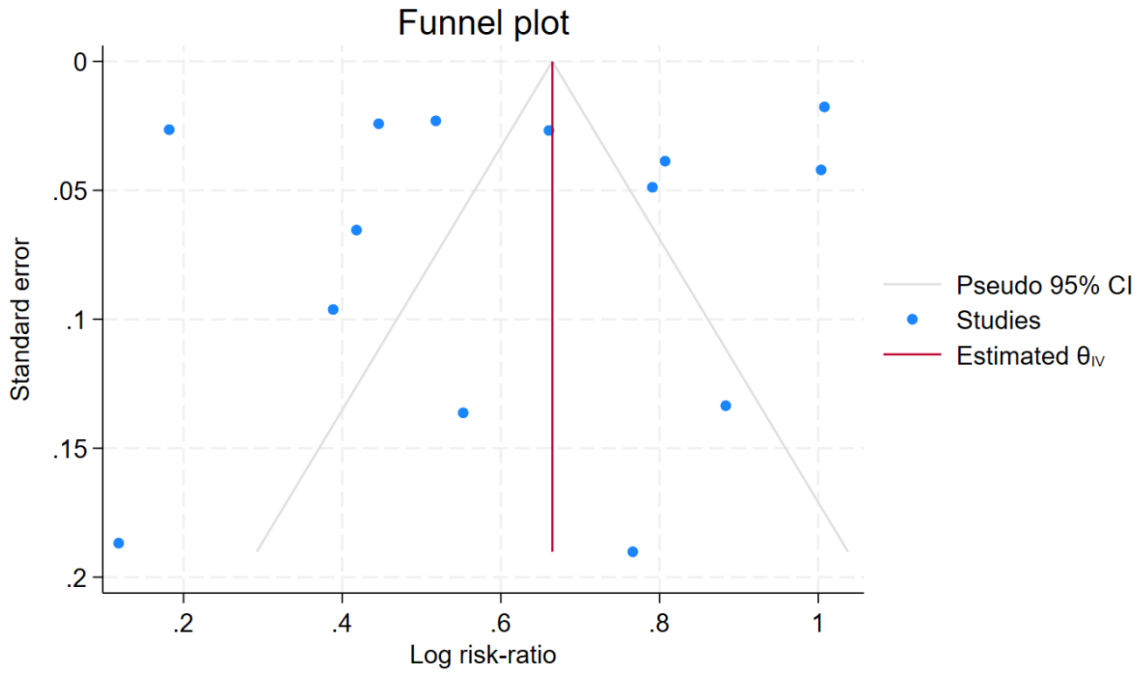
Appendix Figure B3.64 Funnel Plot for the Meta-Analysis of Age ≥40 Years and SMM-RT



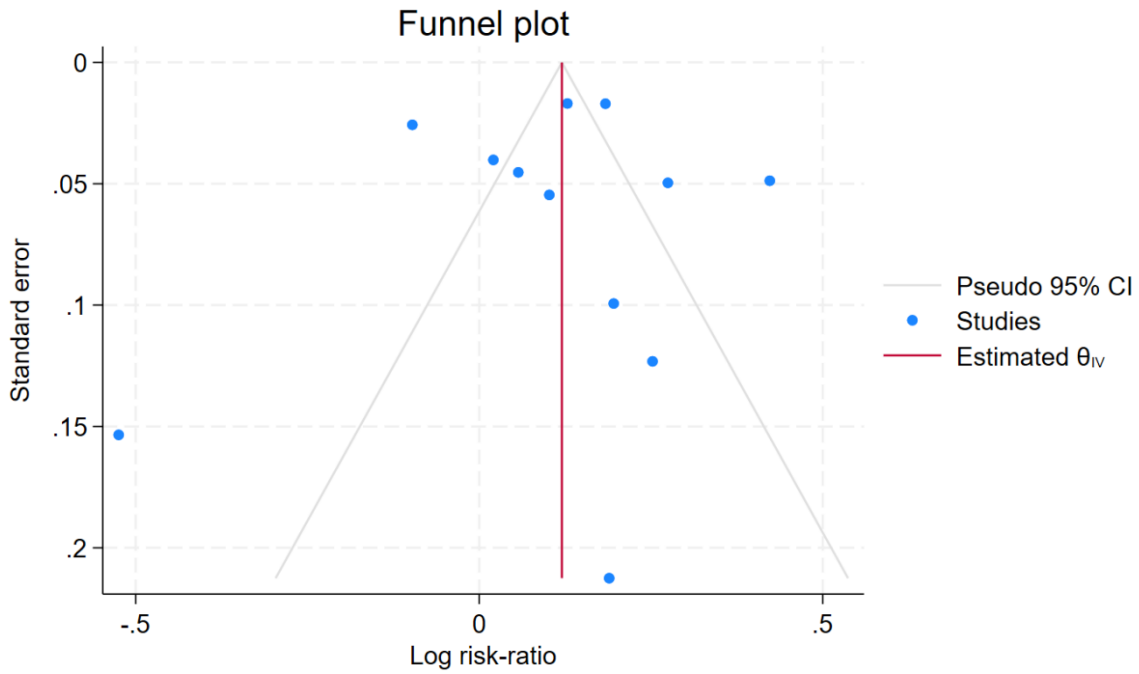
Appendix Figure B3.65 Funnel Plot for the Meta-Analysis of Asian/Pacific Islander Ethnicity and SMM-T



Appendix Figure B3.66 Funnel Plot for the Meta-Analysis of Black Ethnicity and SMM-RT



Appendix Figure B3.67 Funnel Plot for the Meta-Analysis of Hispanic Ethnicity and SMM-RT



Appendix C: Chapter 4

Appendix Table C4.1 Interview Guide

	Question	Additional/complementary prompts
1.	*Could you tell me about your role in the maternity unit?*	*Prompts: level of responsibility, how long in this role, how long in the profession*
	How familiar are you with early warning scores in maternity?	*When did you first come across early warning scores?* *What did you think of the training/ education you had on early warning scores* *How often do you use or respond to EWS in a normal triage/ward/labour ward/community/on call day?* *What would you say is the purpose of early warning scores in maternity?*
2.	How do you use early warning scores in your clinical work?	*When would you use early warning scores in a typical day?* *What makes you decide to check a woman's early warning score?*
3.	Can you tell me about a time when you or your team used an early warning score and that led to successful treatment of a problem?	*What made it work well in that situation? For example, did the EWS recognise a new problem, did it help to communicate the problem, or was it something else that impacted the patient positively?*
4.	Can you tell me about a time when it may have been difficult to use an early warning score for you or someone else in your team?	*Why would you say it was difficult?* *What do you think contributed to that problem?* *Where do the problems lie – eg doing an assessment, actually using the scores, escalating, responding* *If the same situation happened again, what might make it easier to use an EWS effectively?*
5.	What do you feel are the challenges to using early warning scores effectively – for yourself and for other team members?	*Would you say that measuring the scores is manageable in your daily work routine?* *Would you say that the score is easy to calculate and understand?* *Would you say that all team members communicate and interpret the scores in the same way?*
7.	Do you use early warning scores differently in different clinical situations?	*For example, would it make a difference if a woman had (high blood pressure/ very high blood pressure/ a fever/ heavy bleeding/ a high breathing rate/ a high heart rate)?*

8.	Do you feel early warning scores are sometimes used or responded to differently depending on the individual woman?	*For example, do you think early warning scores are used the same in women (with high BMI compared with normal BMI/ of Black ethnicity compared with White ethnicity/who is 40 years old compared with 30 years old)?* *What about if a woman can't communicate very well using English?* *What about sensitive situations, like when a woman has experienced a pregnancy loss?* *Can you recall any examples of when you personally might have used an EWS differently because of the individual patient's characteristics? Could you tell me more about what happened?*
9.	Do you feel that early warning scores are useful when trying to identify and treat illness?	*Can you think of any patients for whom EWSs might be less useful than others?*
10.	How do you think we could improve early warning scores or how they are used in maternity?	*Or, how do you think we could improve 'recognition of the unwell patient'? (alternatively, 'how do you think we could recognise that someone is unwell sooner?')*
11.	Is there anything else about early warning scores that you'd like to say?	

Appendix Item C4.1 Participant Information Sheet for Doctors and Midwives

Clinical Escalation in Maternity

PARTICIPANT INFORMATION SHEET

Central University Research Ethics Committee Approval Reference: R80907/RE001

Introductory paragraph

You are being invited to take part in a research project about how healthcare workers use early warning scores. The scores have different names in different hospitals but involve measuring the vital signs (heart rate, blood pressure, respiratory rate, oxygen saturation, and temperature) to produce a score. Before you decide whether to take part it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether you wish to take part.

Why is this research being conducted?

The purpose of this research study is to understand how healthcare workers use early warning scores in maternity care. Early warning scores involve measurement of the vital signs, the calculation of a score, and the response to the score (or 'escalation'). We want to understand what healthcare workers think of early warning scores and what the warning scores mean to different healthcare workers. We want to understand whether early warning scores are used differently in different clinical situations.

Why have I been invited to take part?

- You have been invited to participate because you may be a healthcare worker who works with early warning scores in maternity care.
- The study will involve approximately 30 different individuals from a range of different healthcare roles (healthcare assistant or midwifery support worker, midwife, doctor).

Do I have to take part?

- It is your decision to take part in this research.

- If you decide to take part, you can change your mind at any time up to 14 days after the interview takes place. If you choose to withdraw during this time, your data will be deleted.
- Your participation will not affect your employment or legal rights and your employer is not involved in this research.

What will happen to me if I take part in the research?

- If you decide to take part or if you have any questions, please complete a short screening questionnaire found here https://tinyurl.com/ewsinterviewscreen; alternatively, if you have any questions, please contact the researcher Ian Henderson (ian.henderson@npeu.ox.ac.uk). Please note that not all eligible participants will be contacted to participate. If you are ineligible or if you are eligible but your healthcare role or ethnic group is already sufficiently represented, you will not be contacted to participate. If this is the case, your data will be deleted.
- The research will involve one interview session of approximately 30-60 minutes. This can either be face-to-face or online or by telephone.
- If you choose to have a face-to-face interview, the researcher will review the consent form with you and will ask you to sign the consent form to confirm you agree to participate. If you choose to have a remote interview, the consent form will be read to you and if you agree then it will be signed on your behalf and sent to you electronically or by post.
- During the interview, you will be asked questions about your thoughts on how early warning scores are checked, how the scores are used, how you communicate the scores, and how you provide care based on the scores. You may be asked about examples from your clinical experience to help understand your perspective.
- If you consent to participate, an audio recording of the interview will be created and turned into a script so that the interview can be analysed. The audio recording will then be deleted once the script has been checked.
- Only one interview will be conducted.
- You will be able to pause or stop the interview at any time.

What are the possible disadvantages and risks in taking part?

Potential disadvantages include the discussion of maternity care that has led to a poor outcome for women or babies. You do not have to discuss any experiences that you do not wish to. The interview questions are related to use of early warning scores and how they are responded to. You do not have to answer any questions that you do not wish to. You can skip a question or pause or end the interview at any point.

Are there any benefits in taking part?

There are no personal benefit to you from taking part in this research. The main benefit is participating in research to try to improve the safety of maternity care for women.

Expenses and payments

There will be no payment for taking part in this research.

What information will be collected and why is the collection of this information relevant for achieving the research objectives?

We will collect information on your role in maternity and your ethnic group so that we ensure that we collect the views of a range of healthcare workers. The interview will include questions about your views on early warning scores, how you use early warning scores, and examples of how you have used early warning scores. This information will be used to understand how early warning scores are used 'in real life', including in different situations and for different patients. We hope to understand the limitations of early warning scores to help develop better early warning scores and tools to identify patients who are unwell.

Your audio recording will be produced using an encrypted audio recorder or remote conferencing software and securely stored on the University of Oxford server in a password-protected file. Interview transcripts will be produced using a third-party processor that is compliant with the University of Oxford data security requirements, who will have access to the information during this time. The audio recordings will be securely transferred to this third party for the transcripts to be produced. Access to the data will then be restricted to members of the research team conducting the analysis. The Medical Research Council may be given access to the data if requested in order to check that the research is being conducted appropriately. The audio recordings will be deleted from the third-party once the script has been produced and checked. If participants disclose any information that could reveal their identity or place of work during the interview, this will be removed from the script.

You will have 14 days from the interview to reconsider and withdraw from the study. After this stage, the recording will be transcribed and analysis will commence so withdrawal will not be possible. Transcripts will be checked against the audio records and then recordings will be deleted.

Physical identifiable data (including consent forms) will be stored in a locked filing cabinet in a locked office on a swipe card access controlled corridor in the National Perinatal Epidemiology Unit at the University of Oxford. Digital identifiable data will be stored in a password protected file on the secure server at the University of Oxford. Identifiable information/contact details and audio recordings or transcripts will always will be stored in separate password protected files in separate areas of the secure server.

After the research has been completed, interview transcripts will be stored in the Oxford Research Archive for Data. This is a research data storage system and means that other researchers may review or analyse the data for further related research into early warning scores. This means that your participation may have benefit beyond the current research study. If researchers wish to access the data, they will still need to apply for permission and any requests will be considered by the

research team. Other research data including consent forms will be stored digitally for 10 years after publication or public release of the work of the research but will not be made available to other researchers. The paper consent forms will be destroyed once digitised, at the end of the study.

Will the research be published? Could I be identified from any publications or other research outputs?

The findings of this research will be published in a research journal and may be presented at a conference. A summary of the research will be provided to you electronically unless you do not wish to receive the results. Some of the research being undertaken will also contribute to the fulfilment of an educational requirement (a doctoral thesis).

We would like your permission to use direct quotations in any research output. Quotations will be accompanied by your healthcare role ("Midwifery Support Worker", "Midwife", "Senior Midwife", "Obstetrician", "Senior Obstetrician", "Anaesthetist", "Senior Anaesthetist").

A copy of my thesis will be deposited both in print and online in the Oxford University Research Archive where it will be publicly available to facilitate its use in future research.

Data Protection

The University of Oxford is the data controller with respect to your personal data, and as such will determine how your personal data is used in the research. The University will process your personal data for the purpose of the research outlined above. Research is a task that is performed in the public interest. Further information about your rights with respect to your personal data is available from the University's Information Compliance website at https://compliance.admin.ox.ac.uk/individual-rights.

Who is funding the research?

This research is sponsored by the University of Oxford. Funding for the research has been obtained from the Medical Research Council (MRC) as part of a clinical research fellowship on early warning scores to identify severe maternal morbidity.

Who has reviewed this research?

This research has received ethics approval from a subcommittee of the University of Oxford Central University Research Ethics Committee (ethics reference: R80907/RE001).

Who do I contact if I have a concern about the research or I wish to complain?

If you have a concern about any aspect of this research, please contact Ian Henderson (ian.henderson@npeu.ox.ac.uk) or Dr Jenny McLeish (jenny.mcleish@npeu.ox.ac.uk) and we will do our best to answer your query. We will acknowledge your concern within 10 working days and give you an indication of how it will be dealt with. If you remain unhappy or wish to make a formal complaint, please contact the University of Oxford Research Governance, Ethics & Assurance (RGEA) team at rgea.complaints@admin.ox.ac.uk or on 01865 616480.

Further Information and Contact Details

If you would like to discuss the research with someone beforehand (or if you have questions afterwards), please contact:

Ian Henderson
National Perinatal Epidemiology Unit
Old Road Campus, Headington, University of Oxford, Oxford, OX3 7LF
University tel: 07395549802
University email: ian.henderson@npeu.ox.ac.uk

Appendix D: Chapter 6

Appendix Table D6.1 Mean vital signs by ethnicity

	Asian	Black	Mixed	Other	White
Heart rate (95% CI)	90.3 (90.1-90.5)	88.4 (88.0-88.7)	88.6 (88.0-89.2)	89.0 (88.5-89.4)	88.2 (88.0-88.3)
Respiratory rate (95% CI)	15.6 (15.6-15.6)	15.6 (15.6-15.6)	15.5 (15.5-15.6)	15.5 (15.5-15.6)	15.4 (15.4-15.4)
Systolic blood pressure (95% CI)	115 (115-115)	117 (116-117)	117 (116-117)	115 (114-115)	118 (118-118)
Diastolic blood pressure (95% CI)	73.4 (73.3-73.5)	73.7 (73.4-74.0)	73.5 (73.1-74.0)	72.6 (72.3-73.0)	74.7 (74.6-74.8)
Temperature (95% CI)	36.7 (36.7-36.8)	36.7 (36.7-36.7)	36.7 (36.7-36.7)	36.7 (36.7-36.8)	36.7 (36.7-36.7)

Appendix Table D6.2 Positive predictive values of the MEWS at clinical protocol thresholds

Score threshold	Overall	Asian	Black	Mixed	Other	White
1 (low risk)	0.16%	0.13%	0.26%	0.08%	0.20%	0.16%
2 (low-medium risk)	0.38%	0.33%	0.76%	0.41%	0.32%	0.31%
5 (medium risk)	0.51%	0.81%	1.17%	-	-	0.09%
8 (high risk)	2.99%	4.65%	-	-	-	-

Score thresholds represent the grouped clinical escalation categories from the national maternal early warning score.

Appendix Table D6.3 Discrimination according to the c-statistic by ethnicity (12-hour time horizon)

	Overall	Asian	Black	Mixed	Other	White
(1) MEWS	0.64 (0.60-0.67)	0.64 (0.59-0.70)	0.71 (0.63-0.79)	0.71 (0.38-1.00)	0.57 (0.44-0.70)	0.61 (0.57-0.66)
(1) + GA	0.64 (0.62-0.68)	0.64 (0.58-0.70)	0.71 (0.63-0.79)	0.72 (0.41-1.00)	0.60 (0.48-0.71)	0.64 (0.60-0.69)
(1) + age	0.67 (0.64-0.71)	0.69 (0.64-0.75)	0.71 (0.63-0.79)	0.74 (0.45-1.00)	0.52 (0.36-0.69)	0.66 (0.62-0.71)
(1) + parity	0.65 (0.62-0.68)	0.66 (0.60-0.72)	0.74 (0.67-0.82)	0.68 (0.31-1.00)	0.54 (0.39-0.69)	0.62 (0.57-0.67)
(1) + CS	0.65 (0.62-0.68)	0.67 (0.61-0.72)	0.72 (0.64-0.80)	0.75 (0.46-1.00)	0.55 (0.42-0.69)	0.63 (0.58-0.67)
(1) + morb	0.65 (0.62-0.68)	0.68 (0.62-0.73)	0.72 (0.64-0.80)	0.70 (0.38-1.00)	0.57 (0.44-0.71)	0.62 (0.58-0.67)
(1) + plurality	0.64 (0.61-0.67)	0.66 (0.60-0.71)	0.72 (0.64-0.80)	0.70 (0.38-1.00)	0.59 (0.44-0.73)	0.61 (0.57-0.66)
(1) + booking	0.65 (0.61-0.68)	0.65 (0.59-0.71)	0.72 (0.63-0.80)	0.78 (0.50-1.00)	0.56 (0.40-0.72)	0.62 (0.58-0.67)
(1) + ethnicity	0.66 (0.62-0.69)	0.64 (0.59-0.70)	0.71 (0.63-0.79)	0.71 (0.38-1.00)	0.57 (0.44-0.70)	0.61 (0.57-0.66)
(2) MEWS + all	0.70 (0.67-0.73)	0.73 (0.68-0.78)	0.73 (0.65-0.80)	0.75 (0.50-1.00)	0.54 (0.36-0.72)	0.69 (0.65-0.73)
(2) + eth	0.72 (0.69-0.75)	0.73 (0.68-0.78)	0.73 (0.66-0.80)	0.75 (0.48-1.00)	0.56 (0.39-0.73)	0.69 (0.65-0.73)
MEWS x GA	0.65 (0.62-0.68)	0.65 (0.59-0.71)	0.71 (0.63-0.80)	0.73 (0.42-1.00)	0.57 (0.43-0.70)	0.65 (0.60-0.69)
MEWS x eth	0.66	0.64	0.71	0.71	0.57	0.61

	(0.63-0.69)	(0.59-0.70)	(0.63-0.79)	(0.38-1.00)	(0.44-0.70)	(0.57-0.66)
MEWS x parity						
(2) + eth + MEWS x GA + MEWS x eth + MEWS x parity	0.70 (0.67-0.73)	0.70 (0.65-0.76)	0.76 (0.69-0.84)	0.73 (0.40-.100)	0.54 (0.39-0.69)	0.66 (0.62-0.71)

MEWS maternal early warning score; GA gestational age; CS denotes previous caesarean section; pre-existing denotes pre-existing conditions; x denotes an interaction term.
Figures rounded to two significant figures.

Appendix Table D6.4 Discrimination according to the c-statistic by ethnicity (24-hour time horizon)

	Overall	**Asian**	**Black**	**Mixed**	**Other**	**White**
(1) MEWS	0.60 (0.58-0.62)	0.61 (0.57-0.65)	0.67 (0.61-0.73)	0.73 (0.50-0.96)	0.56 (0.45-0.66)	0.57 (0.54-0.61)
(1) + GA	0.62 (0.60-0.65)	0.62 (0.58-0.66)	0.67 (0.60-0.73)	0.74 (0.53-0.95)	0.57 (0.47-0.68)	0.61 (0.58-0.65)
(1) + age	0.65 (0.63-0.67	0.67 (0.64-0.71)	0.67 (0.61-0.73)	0.77 (0.58-0.97)	0.50 (0.38-0.62)	0.63 (0.59-0.66)
(1) + parity	0.61 (0.59-0.64)	0.63 (0.59-0.67)	0.70 (0.64-0.75)	0.77 (0.57-0.96)	0.52 (0.40-0.65)	0.58 (0.54-0.61)
(1) + CS	0.62 (0.59-0.64)	0.65 (0.61-0.69)	0.69 (0.63-0.74)	0.75 (0.55-0.95)	0.54 (0.43-0.64)	0.58 (0.54-0.62)
(1) + morb	0.62 (0.59-0.64)	0.64 (0.60-0.68)	0.67 (0.61-0.73)	0.70 (0.47-0.94)	0.56 (0.45-0.67)	0.59 (0.55-0.62)
(1) + plurality	0.61 (0.59-0.63)	0.63 (0.59-0.67)	0.68 (0.62-0.74)	0.72 (0.49-0.95)	0.59 (0.48-0.70)	0.57 (0.54-0.60)
(1) + booking	0.61 (0.59-0.64)	0.63 (0.59-0.67)	0.67 (0.61-0.73)	0.80 (0.59-1.00)	0.58 (0.46-0.70)	0.58 (0.54-0.62)
(1) + ethnicity	0.62 (0.60-0.65)	0.61 (0.57-0.65)	0.67 (0.61-0.73)	0.73 (0.50-0.96)	0.56 (0.45-0.66)	0.57 (0.54-0.61)
(2) MEWS + all	0.68 (0.66-0.71)	0.72 (0.69-0.76)	0.68 (0.63-0.73)	0.76 (0.60-0.93)	0.57 (0.44-0.70)	0.66 (0.63-0.69)
(2) + eth	0.70 (0.68-0.72)	0.72 (0.69-0.76)	0.68 (0.63-0.74)	0.75 (0.57-0.92)	0.59 (0.46-0.71)	0.66 (0.63-0.69)
MEWS x GA	0.62 (0.60-0.65	0.62 (0.58-0.66)	0.67 (0.61-0.73)	0.75 (0.54-0.95)	0.57 (0.46-0.68)	0.62 (0.59-0.65)

MEWS x eth	0.62 (0.60-0.65)	0.61 (0.57-0.65)	0.67 (0.61-0.73)	0.73 (0.50-0.96)	0.56 (0.45-0.66)	0.57 (0.54-0.61)
MEWS x parity	0.62 (0.59-0.64)	0.63 (0.59-0.67)	0.69 (0.64-0.75)	0.78 (0.59-0.96)	0.52 (0.39-0.64)	0.58 (0.55-0.62)
(2) + eth + MEWS x GA + MEWS x eth + MEWS x parity	0.68 (0.66-0.70)	0.71 (0.67-0.75)	0.70 (0.64-0.76)	0.74 (0.53-0.95)	0.59 (0.47-0.71)	0.63 (0.60-0.66)

MEWS maternal early warning score; GA gestational age; CS denotes previous caesarean section; pre-existing denotes pre-existing conditions; x denotes an interaction term.
Figures rounded to two significant figures.

Appendix Table D6.5 Discrimination according to the c-statistic by ethnicity (48-hour time horizon)

	Overall	**Asian**	**Black**	**Mixed**	**Other**	**White**
(1) MEWS						
(1) + GA	0.59 (0.57-0.61)	0.60 (0.57-0.63)	0.62 (0.57-0.68)	0.73 (0.55-0.91)	0.57 (0.48-0.65)	0.59 (0.56-0.61)
(1) + age	0.63 (0.61-0.65)	0.65 (0.62-0.68)	0.64 (0.60-0.69)	0.71 (0.49-0.93)	0.52 (0.42-0.62)	0.61 (0.58-0.64)
(1) + parity	0.57 (0.55-0.59)	0.59 (0.55-0.62)	0.66 (0.61-0.71)	0.66 (0.41-0.90)	0.57 (0.48-0.65)	0.54 (0.51-0.57)
(1) + CS	0.59 (0.57-0.60)	0.62 (0.59-0.65)	0.65 (0.60-0.70)	0.72 (0.52-0.91)	0.52 (0.43-0.61)	0.55 (0.53-0.58)
(1) + morb	0.59 (0.57-0.61)	0.62 (0.59-0.65)	0.65 (0.60-0.69)	0.71 (0.50-0.92)	0.53 (0.44-0.62)	0.56 (0.53-0.58)
(1) + plurality	0.58 (0.57-0.60)	0.61 (0.58-0.64)	0.64 (0.59-0.69)	0.69 (0.49-0.90)	0.58 (0.49-0.67)	0.54 (0.52-0.57)
(1) + booking	0.59 (0.57-0.61)	0.61 (0.57-0.64)	0.63 (0.58-0.68)	0.77 (0.57-0.96)	0.55 (0.46-0.65)	0.56 (0.53-0.59)
(1) + ethnicity	0.60 (0.58-0.61)	0.59 (0.56-0.62)	0.64 (0.59-0.69)	0.71 (0.50-0.91)	0.53 (0.45-0.62)	0.55 (0.52-0.57)
(2) MEWS + all	0.66 (0.65-0.68)	0.71 (0.68-0.74)	0.65 (0.61-0.70)	0.70 (0.52-0.88)	0.59 (0.48-0.69)	0.65 (0.62-0.67)
(2) + eth	0.68 (0.67-0.70)	0.71 (0.69-0.74)	0.66 (0.62-0.71)	0.68 (0.50-0.86)	0.61 (0.51-0.70)	0.65 (0.62-0.67)
MEWS x GA	0.60 (0.58-0.61)	0.61 (0.57-0.64)	0.62 (0.57-0.68)	0.74 (0.56-0.91)	0.56 (0.48-0.65)	0.59 (0.57-0.62)

MEWS x eth	0.60 (0.58-0.62)	0.59 (0.56-0.62)	0.64 (0.59-0.69)	0.71 (0.50-0.91)	0.53 (0.45-0.62)	0.55 (0.52-0.57)
MEWS x parity	0.58 (0.56-0.60)	0.60 (0.57-0.63)	0.67 (0.62-0.72)	0.69 (0.49-0.89)	0.49 (0.39-0.60)	0.54 (0.51-0.57)
(2) + eth + MEWS x GA + MEWS x eth + MEWS x parity	0.65 (0.64-0.67)	0.69 (0.66-0.72)	0.66 (0.60-0.71)	0.72 (0.54-0.90)	0.63 (0.53-0.72)	0.60 (0.57-0.62)

MEWS maternal early warning score; GA gestational age; CS denotes previous caesarean section; pre-existing denotes pre-existing conditions; x denotes an interaction term.
Figures rounded to two significant figures.

Appendix Table D6.6 Percentage change in Brier score compared with MEWS-only model (12-hour time horizon)

	Overall	Asian	Black	Mixed	Other	White
(1) MEWS	***0.0010***	***0.00089***	***0.0016***	***0.00051***	***0.0013***	***0.0011***
(1) + GA	-0.55	0.72	-2.9	-4.6	-3.5	-0.63
(1) + age	-0.78	0.75	-2.9	-4.4	-3.4	-0.56
(1) + IMD	0.095	0.28	-1.9	-1.2	-3.9	0.69
(1) + parity	-0.0057	-0.013	0.0030	-0.037	0.014	-0.0023
(1) + CS	-0.0053	-0.0096	-0.0030	-0.025	-0.014	-0.0012
(1) + morb	0.26	0.0085	-<0.0001	-0.052	-0.021	-0.022
(1) + plurality	-0.25	-0.28	-0.63	-0.88	-0.56	-0.44
(1) + booking	0.33	1.7	-0.61	-0.89	-0.74	-0.50
(1) + ethnicity	0.0019	-0.0025	0.044	0.0076	-0.27	-0.0030
(2) MEWS + all	-0.24	2.9	-5.4	-6.8	-4.5	-0.30
(2) + eth	0.45	2.0	-2.4	-2.1	-1.1	0.20
MEWS x GA	0.21	-0.046	0.016	-0.048	-0.027	-0.075
MEWS x eth	0.0094	<0.0001	0.012	-0.060	0.051	0.011
MEWS x parity	0.014	0.087	-0.20	0.0088	-0.026	-0.017
All	0.46	2.1	-2.5	-2.2	-1.0	0.18
All + location	1.6	1.7	-0.87	-3.3	-1.6	2.0

MEWS maternal early warning score; GA gestational age; CS denotes previous caesarean section; pre-existing denotes pre-existing conditions; x denotes an interaction term.
Figures rounded to two significant figures.
Scaled Brier scores within subgroups do not sum to the overall scaled Brier score.

Appendix Table D6.7 Percentage change in Brier score compared with MEWS-only model (24-hour time horizon)

	Overall	Asian	Black	Mixed	Other	White
(1) MEWS	***0.0018***	***0.0016***	***0.0028***	***0.0021***	***0.0022***	***0.0019***
(1) + GA	0.74	0.68	-1.3	-4.6	-3.5	0.70
(1) + age	0.018	0.019	-<0.0001	0.10	-0.55	0.026
(1) + IMD	0.45	0.38	-0.51	-1.2	-0.40	0.97
(1) + parity	-0.0025	-0.0029	0.0019	-0.014	-0.011	-0.0030
(1) + CS	-0.0033	<0.0001	-<0.0001	-0.023	-0.016	-0.0036
(1) + pre-existing	0.11	-0.0057	-0.017	-0.057	-0.0086	--0.022
(1) + plurality	-0.39	-0.28	-0.62	-0.90	-0.58	-0.44
(1) + booking	-0.0092	0.78	-0.63	-0.84	-0.72	-0.49
(1) + ethnicity	0.010	0.0022	0.062	0.12	-0.0074	-0.0012
(2) MEWS + all	0.39	1.2	-1.1	-2.2	-1.1	0.51
(2) + ethnicity	0.39	1.2	-1.1	-2.0	-1.1	0.51
MEWS x GA	0.74	0.71	-1.3	-4.6	-3.5	0.68
MEWS x eth	0.013	0.0048	0.045	0.086	0.027	0.0067
MEWS x parity	0.011	0.046	0.0028	0.033	0.0068	-0.0085
All	0.39	1.3	-1.1	-2.1	-1.0	0.49
All + location	1.8	1.4	0.81	-3.2	-1.6	1.9

MEWS maternal early warning score; GA gestational age; CS denotes previous caesarean section; pre-existing denotes pre-existing conditions; x denotes an interaction term.
Figures rounded to two significant figures.
Scaled Brier scores within subgroups do not sum to the overall scaled Brier score.

Appendix Table D6.8 Percentage change in Brier score compared with MEWS-only model (48-hour time horizon)

	Overall	Asian	Black	Mixed	Other	White
(1) MEWS	***0.0030***	***0.0026***	***0.0043***	***0.00092***	***0.0033***	***0.0031***
(1) + GA	0.030	-0.034	-0.029	-0.057	-0.022	-0.012
(1) + age	0.034	0.037	0.0095	0.11	-0.066	0.042
(1) + IMD	0.53	0.30	0.80	-1.2	-3.7	0.78
(1) + parity	0.0010	0.0022	0.010	-0.024	0.0067	-0.0013
(1) + CS	-<0.0001	0.0085	-0.0036	-0.029	-0.017	-0.0025
(1) + morb	0.049	<0.0001	-0.0056	-0.031	-0.017	-0.024
(1) + plurality	-0.44	-0.24	-0.58	-0.94	-0.56	-0.45
(1) + booking	-0.070	1.1	-0.64	-0.85	-0.74	-0.49
(1) + ethnicity	0.015	0.0041	0.076	0.37	-0.0010	-<0.0001
(2) MEWS + all	0.53	1.5	0.26	-2.2	-1.0	0.34
(2) + eth	0.53	1.5	0.28	-1.8	-1.0	0.34
MEWS x GA	0.037	0.011	-0.066	--0.046	-0.026	-0.029
MEWS x eth	0.020	0.0071	0.078	0.36	0.0077	0.0072
MEWS x parity	0.0053	0.015	0.029	-0.040	0.034	-0.0064
All	0.53	1.5	0.34	-1.9	-0.96	0.29
All + location	2.2	2.2	3.2	-3.0	-1.5	1.8

MEWS maternal early warning score; GA gestational age; CS denotes previous caesarean section; pre-existing denotes pre-existing conditions; x denotes an interaction term.
Figures rounded to two significant figures.
Scaled Brier scores within subgroups do not sum to the overall scaled Brier score.

Appendix Table D6.9 Effect modification of MEWS by ethnic group without adjustment

	MEWS 0		**MEWS >0**	
	N with/without SMM	**OR (95% CI)**	**N with/without SMM**	**OR (95% CI) per 1-unit**
SMM-12h				
Asian	38/64,486	0.65 (0.46-0.92)	59/47,587	1.64 (1.48-1.81)
Black	13/15,521	1.01 (0.62-1.67)	29/12,088	1.71 (1.46-2.01)
White	60/79,340	1.00	79/52,987	1.45 (1.30-1.62)
SMM-24h				
Asian	75/64,486	0.72 (0.57-0.94)	101/47,587	1.44 (1.32-1.58)
Black	25/15,521	1.12 (0.79-1.60)	51/12,088	1.56 (1.37-1.77)
White	121/79,340	1.00	125/52,987	1.32 (1.21-1.45)
SMM-48h				
Asian	126/64,486	0.73 (0.60-0.89)	157/47,587	1.35 (1.25-1.45)
Black	42/15,521	1.04 (0.79-1.37)	74/12,088	1.49 (1.34-1.66)
White	218/79,340	1.00	182/52,987	1.21 (1.12-1.31)

SMM-12 hour: RERI for Asian vs. White -0.40 (-0.19, 0.11), Black vs. White 0.28 (0.16, 0.54)
SMM-24 hour: RERI for Asian vs. White 0.0021 (-0.16, 0.12), Black vs. White 0.30 (0.11, 0.49)
SMM-48 hour: RERI for Asian vs. White 0.0.42 (-0.055, 0.14), Black vs. White 0.30 (0.15, 0.44)

Appendix Table D6.10 Association between receipt of a medical review within two hours and SMM

	Review within 2 hours
SMM-12 hours	*RR (95% CI)*
Adjusted for MEWS	2.02 (1.55-2.63)
Adjusted for maternal prognostic factors	2.04 (1.55-2.67)
SMM-24 hours	
Adjusted for MEWS	1.60 (1.30-1.98)
Adjusted for maternal prognostic factors	1.66 (1.34-2.07)
SMM-48 hours	
Adjusted for MEWS	1.44 (1.21-1.71)
Adjusted for maternal prognostic factors	1.51 (1.27-1.81)

MEWS maternal early warning score. Maternal prognostic factors are those included in the full modified MEWS model (gestational age, maternal age, parity, previous caesarean, pre-existing conditions, plurality, gestational age at booking, ethnicity, and interaction terms between the MEWS and ethnicity, the MEWS and parity, and the MEWS and gestational age). There was no evidence of statistical interaction between receipt of a review within two hours of a MEWS and ethnicity.

Appendix Table D6.11 Net benefit per 10,000 MEWS for antenatal and postnatal observations over 12-hour, 24-hour, and 48-hour time horizons

	SMM-12	SMM-24	SMM-48
Antenatal MEWS			
MEWS 1	0.66	1.2	1.3
MEWS 2	0.54	0.026	0.068
MEWS 3	-1.2	-1.0	-1.7
Postnatal MEWS			
MEWS 1	0.98	0.38	0.17
MEWS 2	0.38	-0.070	-0.80
MEWS 3	0.14	0.073	-0.40
Antenatal Modified MEWS			
MEWS 1	0.89	2.5	6.0
MEWS 2	0.50	0.72	2.9
MEWS 3	-0.13	-0.66	0.091
Postnatal Modified MEWS			
MEWS 1	2.0	1.1	0.0015
MEWS 2	0.60	0.11	-0.65
MEWS 3	0.16	0.054	-0.13

MEWS maternal early warning score; Modified MEWS denotes the model that includes the MEWS with additional predictors (gestational age, maternal age, parity, previous caesarean, pre-existing conditions, plurality, gestational age at booking, ethnicity, and interaction terms between the MEWS and ethnicity, the MEWS and parity, and the MEWS and gestational age). Threshold denotes various levels at which a MEWS may be programmed to trigger an alert. Figures rounded to two significant figures.

Appendix Table D6.12 Net benefit per 10,000 MEWS for ethnic groups in higher resolution

	Asian Bangladeshi	Asian Indian	Asian Pakistani	Black African	Black Caribbean
SMM-12					
MEWS 1	0.95	2.3	0.69	4.8	11
MEWS 2	-0.80	2.5	1.3	4.5	8.2
MEWS 3	-0.45	2.0	1.4	3.0	4.6
SMM-12 Modified					
MEWS 1	2.3	3.5	2.7	6.7	9.4
MEWS 2	0.47	1.7	1.8	3.8	9.9
MEWS 3	0	0.42	1.5	3.1	6.6
SMM-24					
MEWS 1	-2.2	2.5	1.1	7.1	20
MEWS 2	-2.1	0.10	0.20	4.3	13
MEWS 3	-1.7	0.88	0.82	3.0	4.7
SMM-24 Modified					
MEWS 1	1.0	6.4	3.0	9.2	18
MEWS 2	1.1	3.5	2.2	5.6	16
MEWS 3	-1.3	0.34	0.57	1.3	9.7
SMM-48					
MEWS 1	-1.5	0.87	2.2	8.7	18
MEWS 2	-3.5	-1.1	0.12	6.7	16
MEWS 3	-2.6	1.5	0.38	3.8	7.3
SMM-48 Modified					
MEWS 1	-0.051	6.7	4.3	14	25
MEWS 2	1.3	5.5	2.6	6.4	20
MEWS 3	0.26	-0.087	1.1	4.9	14

SMM severe maternal morbidity over 12, 24, or 48 hour time horizons. MEWS maternal early warning score; Modified MEWS denotes the model that includes the MEWS with additional predictors (gestational age, maternal age, parity, previous caesarean, pre-existing conditions, plurality, gestational age at booking, ethnicity, and interaction terms between the MEWS and ethnicity, the MEWS and parity, and the MEWS and gestational age).

Appendix Table D6.13 Discrimination according to the c-statistic by ethnicity following imputation of observations with 1-2 missing vital signs with a score of zero

	Overall	Asian	Black	Mixed	Other	White
SMM-12 MEWS	0.65 (0.62-0.68)	0.67 (0.62-0.72)	0.69 (0.61-0.76)	0.69 (0.43-0.95)	0.60 (0.47-0.74)	0.63 (0.59-0.67)
SMM-12 Modified MEWS	0.73 (0.71-0.76)	0.75 (0.70-0.79)	0.77 (0.71-0.82)	0.78 (0.56-0.99)	0.57 (0.40-0.74)	0.70 (0.66-0.73)
SMM-24 MEWS	0.61 (0.59-0.63)	0.61 (0.58-0.65)	0.64 (0.59-0.70)	0.69 (0.51-0.88)	0.60 (0.49-0.70)	0.59 (0.56-0.62)
SMM-24 Modified MEWS	0.70 (0.68-0.72)	0.71 (0.68-0.75)	0.69 (0.65-0.74)	0.72 (0.55-0.88)	0.65 (0.54-0.77)	0.66 (0.63-0.69)
SMM-48 MEWS	0.58 (0.56-0.60)	0.59 (0.56-0.62)	0.62 (0.58-0.67)	0.70 (0.56-0.85)	0.55 (0.47-0.63)	0.56 (0.54-0.59)
SMM-48 Modified MEWS	0.68 (0.66-0.69)	0.69 (0.67-0.72)	0.66 (0.62-0.70)	0.72 (0.61-0.84)	0.71 (064-0.79)	0.64 (0.62-0.66)

SMM severe maternal morbidity over 12, 24, or 48 hour time horizons. MEWS maternal early warning score; Modified MEWS denotes the model that includes the MEWS with additional predictors (gestational age, maternal age, parity, previous caesarean, pre-existing conditions, plurality, gestational age at booking, ethnicity, and interaction terms between the MEWS and ethnicity, the MEWS and parity, and the MEWS and gestational age).

Appendix Table D6.14 Percentage change in Brier score by ethnicity following imputation of observations with 1-2 missing vital signs with a score of zero

	Overall	Asian	Black	Mixed	Other	White
SMM-12 Modified MEWS	0.085	2.1	-2.4	-2.1	-1.0	-0.26
SMM-24 Modified MEWS	0.45	1.1	-1.3	-2.1	-1.0	0.62
SMM-48 Modified MEWS	0.52	1.0	-3.7	-2.0	-0.95	0.50

No findings are shown for the MEWS as this was the baseline from which the modified MEWS was compared. SMM severe maternal morbidity over 12, 24, or 48 hour time horizons. Modified MEWS denotes the model that includes the MEWS with additional predictors (gestational age, maternal age, parity, previous caesarean, pre-existing conditions, plurality, gestational age at booking, ethnicity, and interaction terms between the MEWS and ethnicity, the MEWS and parity, and the MEWS and gestational age).

Appendix Table D6.15 Net benefit following imputation of observations with 1-2 missing vital signs with a score of zero

MEWS	Overall	Asian	Black	Mixed	Other	White
SMM-12 MEWS 1	3.3	2.5	8.9	-0.22	3.2	3.2
SMM-12 MEWS 2	2.1	1.8	6.4	0.95	0.26	1.8
SMM-12 MEWS 3	1.4	1.4	4.7	1.9	0.46	0.78
SMM-24 MEWS 1	4.7	3.3	14	-0.77	4.5	4.4
SMM-24 MEWS 2	2.7	1.8	9.9	0.95	0.66	2.2
SMM-24 MEWS 3	1.8	1.4	5.9	0.95	1.8	1.2
SMM-48 MEWS 1	2.1	1.1	9.1	0.28	-0.07	1.5
SMM-48 MEWS 2	1.6	1.2	5.7	0.77	1.6	1.0
SMM-48 MEWS 3	1.2	1.3	3.2	1.1	-0.079	0.76
Modified MEWS						
SMM-12 MEWS 1	4.5	3.8	12	2.2	0.84	4.2
SMM-12 MEWS 2	2.6	2.4	8.7	2.3	-0.18	2.2
SMM-12 MEWS 3	0.97	1.7	4.2	0.36	0.11	0.73
SMM-24 MEWS 1	7.0	6.2	20	2.3	3.8	6.0
SMM-24 MEWS 2	3.9	3.5	14	1.5	2.0	3.0
SMM-24 MEWS 3	1.5	1.7	6.6	-0.21	2.3	1.4
SMM-48 MEWS 1	3.1	2.7	11	0.59	1.5	2.9
SMM-48 MEWS 2	1.1	1.4	5.8	-0.20	1.8	1.2
SMM-48 MEWS 3	-3.1	1.3	3.2	1.1	-0.079	0.76