Improving Research and Practice Related to Encouraging Awareness of Reduced Fetal Movement and its Subsequent Clinical Management

A thesis submitted to the University of Manchester for the degree of Doctor of Philosophy in the Faculty of Biology, Medicine, and Health

2023

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SCHOOL OF MEDICAL SCIENCES

Contents

Word count: 69,457

List of figures

List of tables

List of abbreviations

AFI	Amniotic Fluid Index
CI	Confidence Interval
COMET	Core Outcome Measures in Effectiveness Trials
COS	Core Outcome Set(s)
CTG	Cardiotocography
EFW	Estimated Fetal Weight
EPOC	Effective Practice and Organisation of Care
FGR	Fetal Growth Restriction
GRADE	Grading of Recommendations, Assessment, Development, and Evaluation
GP	General Practitioner
IPD	Individual Participant Data
ITS	Interrupted Time Series
NHS	National Health Service
NICE	The National Institute for Health and Care Excellence
NICU	Neonatal Intensive Care Unit
NRS	Non-Randomised Study/Studies
ONS	Office for National Statistics
OR/aOR	Odds Ratio/adjusted Odds Ratio
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
RCOG	Royal College of Obstetricians and Gynaecologists
RCT	Randomised Controlled Trial
RFM	Reduced Fetal Movement(s)
RoB 2	Cochrane Risk of Bias Tool for Randomised Studies (version 2)
ROBINS-I	Risk of Bias in Non-Randomised Studies of Interventions
RR/aRR	Risk Ratio/adjusted Risk Ratio
SBLCB(v2)	Saving Babies' Lives Care Bundle (version 2)
UK	United Kingdom
US	Ultrasound
USA	United States of America
WHO	World Health Organization

Abstract

Introduction

Maternal concern about reduced fetal movements (RFM) is a common reason for presentation to maternity care and studies have shown associations between RFM and adverse pregnancy outcomes such as stillbirth and fetal growth restriction (FGR). Despite this, studies of interventions for encouraging awareness of RFM and/or its subsequent clinical management have shown varying results, and systematic reviews of these studies have been inconclusive. Guidelines for RFM vary in quality and are not informed by all the available evidence. This thesis aimed to improve future research and clinical practice related to RFM.

Methods

To achieve the objectives of this thesis, three studies were conducted: 1. A systematic review of interventions for encouraging awareness of RFM and/or improving its subsequent clinical management, considering both randomised and non-randomised studies; 2: Development of a core outcome set (COS) for future studies of RFM, and; 3. A survey of UK-based clinicians' knowledge and practice related to RFM.

Results

Current evidence is insufficient for drawing many definitive conclusions about the effect of interventions for RFM on adverse outcomes. Interventions aimed at encouraging awareness of RFM may reduce neonatal intensive care unit (NICU) admissions and fetal movement counting may lead to decreased maternal anxiety and increased maternal-fetal attachment. COS for studies aimed at encouraging awareness and/or improving its subsequent clinical management were created. A survey of clinicians' knowledge and practice related to RFM showed that although knowledge and practice has improved, there is still a lot of variation in the guidelines that are followed, leading to variation in care.

Discussion

The next step in RFM research should be to conduct international adequately powered trials of (multifaceted) interventions, measuring all outcomes specified by the COS. Variation in clinical practice still exists and may be influenced by the strength of recommendations behind guidelines; better trials will increase the likelihood that future evidence syntheses will be able to make recommendations.

Declaration

No portion of the work referred to in this thesis has been submitted in support of an application for another degree of qualifications of this or any other university, or any other institute of learning.

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Acknowledgements

I would like to thank my supervisors — Alex Heazell, Tanya Walsh & Jo Dumville — for their valued input, feedback, and guidance.

Thank you to all my study co-authors — Valerie Smith, Declan Devane, Sanne Gordijn, Anna Akselsson, Lucy Higgins, Melissa Whitworth & Margaret Fisher — as well as to Ingela Rådestad, Billie Bradford & Brita Winje for providing study data and advice.

This work would not have been possible without everyone who participated in the core outcome set and survey of practice, or without everyone at MFH past and present.

Chapter 1 - Introduction

1.1 Overview

This chapter will provide information about RFM — its definition, how it is managed and studied, and its associated outcomes and risk factors. This chapter aims to provide rationale and context for the rest of the thesis and is not intended to be an exhaustive summary of this area of research. Evidence synthesis will also be discussed, alongside how COS and surveys of practice have been used to improve research and practice, specifically in maternity care.

1.2 Reduced fetal movement

1.2.1 Definition

RFM in pregnancy is defined as a decrease in the strength and/or frequency of a baby's normal pattern of movements in utero.[1] From clinical data, RFM is perceived in 4-15% of pregnancies;[2] this may be based on maternal perception, can be measured using kick charts or other formal counting methods, and/or can be quantified using clinical testing such as auscultation of the fetal heart, cardiotocography (CTG), and/or ultrasound.

1.2.2 Assessment of RFM

Guidance such as that from the Royal College of Obstetricians and Gynaecologists (RCOG) in the UK states that fetal movements should be assessed by subjective maternal perception; this is rated as grade C evidence based on studies that have shown variation between maternally perceived movements and movement seen using ultrasound.[3–5] A 2016 study (n=21) found that these pregnant women perceived between 2.4% and 81.0% of fetal movements detected using ultrasound, and that some movements recorded by the participants in this study were not detected by ultrasound scanning.[6] However, it should be noted that there is no objective test for RFM as testing cannot measure how fetal movement compares to the mother's experience of it before testing.[7] It should also be considered that fetal movement changes over the course of a pregnancy, and can vary based on the time of day, level of activity, food intake, and body position; perception can also be affected by parity.[8]

Most people who are pregnant become aware of fetal movements by 18-20 weeks of pregnancy (with a peak on average between 28 and 34 weeks) and usually learn the pattern of their baby's movements. Recent research has suggested that it may be beneficial to learn the normal pattern of a baby's movements and their frequency and strength, rather than to count movements.[9] Techniques aimed at encouraging awareness of fetal movements have

also been shown to be viewed positively by pregnant women.[10] Using kick charts to measure and define fetal movement is currently not recommended by the RCOG due to the subjective nature of RFM and differences in what is considered normal movement for each fetus.[11]

1.2.3 Outcomes associated with RFM

A recent individual participant data (IPD) meta-analysis of observational studies (n=3,108) demonstrated an association between RFM and late stillbirth, with an adjusted odds ratio (aOR) of 2.33 (95% confidence interval (CI) 1.73 to 3.14).[12] The MiNESS study[13] showed that the odds of stillbirth occurring were higher in the women who reported three or more episodes of RFM (odds ratio (OR) 5.11, 95% CI 3.22 to 8.10) than in those who reported a single episode (OR 2.36, 95% CI 1.69 to 3.30).

A recent systematic review and meta-analysis of 39 non-randomised studies (NRS) demonstrated associations between RFM and stillbirth (OR 3.44, 95% CI 2.02 to 5.88) and small for gestational age (OR 1.37, 95% CI 1.16 to 1.61), with similar effect sizes found for both outcomes when only studies at low risk of bias were included in the analyses.[14] The case for a causal relationship is strengthened by case control studies of placental pathology that have found associations between RFM and maternal vascular malperfusion, placental size, and inflammatory response.[15,16] This relationship is further supported by evidence from low income settings[17] where the association between RFM and stillbirth may be stronger.[18]

Criticism of RFM as a risk factor for adverse outcome is often based around its lack of specificity, and the potential harms of interventions for RFM,[19,20] which is important to acknowledge when considering the findings from trials. Although, these criticisms do recognise the lack of definitive trial evidence in this area and that (at the time these articles were published) evidence from trials in progress was yet to be considered.

1.2.4 Risk factors for RFM

A systematic review and meta-analysis of risk factors for RFM analysed data from 27 studies and identified 12 modifiable and non-modifiable risk factors. [21] Five of these risk factors (anterior placenta, ethnicity (Caucasian v non-Caucasian), oligohydramnios, polyhydramnios, and smoking) were found to be predictive for RFM, with ORs between 1.31 and 4.04 and CIs that did not overlap 1.00. Variation attributed to heterogeneity in these analyses was low, although analyses included between two and five studies. Furthermore, it is important to acknowledge that risk factors for RFM may also be risk factors for outcomes associated with RFM.

1.2.5 RFM and COVID-19

The COVID-19 pandemic may have affected the number of attendances at hospital due to concern about RFM. Research at a single site (n=1,613) suggests that first attendances for concern about RFM may have reduced, though the stillbirth rate was unaffected in this small sample.[22] Further research in this area is needed.

1.3 Evidence synthesis

1.3.1 Overview

Throughout this thesis, evidence synthesis will be used to describe any way of combining the results of multiple research studies to gain a better understanding of the overall effect. Systematic reviews and meta-analysis will be focused on as systematic, methodologically sound, examples of evidence synthesis.

Broadly, systematic reviews include the development of a structured research question and systematic reproducible methods, to reduce bias, and to answer the research question.[23,24] Systematic literature searches are constructed to identify all relevant studies, which are screened according to inclusion criteria, and data are then extracted from the studies that meet these criteria along with important study characteristics. Included studies are assessed to determine their risk of bias. Systematic reviews may or may or not include meta-analysis, a statistical method of combining data from multiple studies.[24]

Although various applications of systematic reviews exist, such as diagnostic test accuracy reviews and prognosis reviews, this thesis will mainly focus on intervention reviews — their methodology, interpreting their results, and their applications.

1.3.2 Types of study to be included in evidence synthesis

1.3.2.1 Considering study design

When deciding which study types should be considered, and therefore included, in any form of evidence synthesis, their design needs to be considered. Study types differ in their advantages and disadvantages, and the usefulness of each study type may vary depending on the research question. Some research questions may not be amenable to certain study designs, for example, when interventions are delivered at a community level or when randomisation is not feasible and/or ethical.

1.3.2.2 Randomised studies

In randomised controlled trials (RCTs), individual participants (or clusters of individual participants in cluster RCTs) are randomly assigned to the intervention group or a control group.[25] The process of randomising people or other 'units' of investigation (such as

hospitals) into groups creates a more rigorous study, meaning results are more likely closer to the true effect (i.e. unbiased).[25]

If randomisation is performed correctly, and provided that the sample size is sufficiently large, then known and unknown confounders (factors that influence the association between the treatment and the outcome)[26] are, on average, equal between groups. Outcomes are then less likely to differ between groups without any intervention.[27] Therefore, randomisation makes it more likely that any observed differences in outcome between treatment and control groups are due to the intervention and not due to differences in confounding factors.[23]

The Cochrane handbook for systematic reviews of interventions states that randomised trials are 'the preferred design for studying the effects of healthcare interventions'.[23] The hierarchy of evidence described by Hess in 2004 categorises RCTs and meta-analysis of RCTs as the strongest evidence to answer effectiveness questions.[28] Systematic reviews of observational studies are categorised as intermediate strength, and unsystematic clinical observations as the weakest level of evidence.[29]

1.3.2.3 Non-randomised studies

Commonly-used NRS designs for evaluating health care innovations which have a comparator group include: quasi-randomised controlled trials, natural experiments, cohort studies (with prospective or retrospective controls), controlled before after studies, (controlled) interrupted time series, and case-control studies.[30,31] Other NRS which are descriptive in design, such as cross-sectional studies, are generally not used to explore questions of intervention effectiveness and as such are not considered further in this thesis.[32] An overview of different study designs is provided in Table 1, and study designs are described further in Chapter 2.

In contrast to RCTs, the allocation of participants to intervention groups in NRS is often influenced by researchers, health professionals, or the participants themselves. Allocation may depend on factors such as the hospital protocol, the care provided by a ward within a hospital, or the treatment preferred by an individual doctor. This lack of randomisation leads to a greater risk of confounding and selection bias, and consequently a lower rank in the hierarchy of evidence than RCTs and systematic reviews of RCTs.[28]

NRS designs, such as cohort studies, obtain data from subsets of a defined population who are, have been, or in the future may be exposed to a factor (or factors) which are thought to influence the likelihood of occurrence of an outcome (such as a disease).[33] NRS designs

allow observation of large numbers of participants over a long period of time and a comparison of the incidence rates between exposed and unexposed groups.

1.3.3 Study design in maternity care

There are specific challenges when conducting RCTs in maternity care, such as the necessary sample sizes, whether the study is externally valid, and appropriate study populations, recruitment, and consent.

Sample size

The outcomes of interest in this field are often rare, for example, the rate of stillbirth in the UK in 2018 was 4.1 per 1000 births.[34] This means that the sample size required to study differences in rates between populations or intervention groups is high — the AFFIRM study aimed to have the statistical power to show a 30% reduction in stillbirth and, as such, recruited over 400,000 women from 37 hospitals.[35] Trials of the requisite size are expensive and time consuming to run, as well as difficult to recruit to. If an adequate sample size is not achieved then this leads to lower statistical power and increases the risk of a type II error – failing to detect an effect when one exists.[36] Type II errors are likely in studies of rare outcomes where sample sizes are small enough that, by chance, the outcome of interest is hardly observed (or not seen at all).[37]

External validity

Additionally, the results from RCTs may not always be externally valid (whether the study is asking an appropriate question and how generalisable or applicable the findings are).[38] This has led to criticism that RCTs are not always useful in showing what the 'real world' effects of an intervention are, only what it achieves under trial conditions.[39]

Which outcomes are measured and how they are measured should also be considered – the definitions used should be appropriate and practical to measure, relevant to clinical practice, and acceptable to trial participants.

Study populations, recruitment, and consent

Following on from this, participants in RCTs for preventative interventions also tend to be more affluent, educated, and healthy than in the general population.[40] In maternity care, this may mean that trial populations do not reflect the pregnant population outside of a trial scenario and so the results do not reflect what is seen in normal practice.

It can also be challenging to recruit people to studies where stillbirth is a main focus, and evidence for the reasons why is limited[41] – minimising attrition can also be difficult, whether this is not preventable (people giving birth outside of study parameters, for example) or whether people no longer wish to take part in a study.

Table 1 – Overview of non-randomised study designs

Study type	Design	Advantages	Disadvantages
Cohort studies[25,42]	Data are obtained and outcomes compared between exposed and unexposed groups. May be prospective, retrospective, or a combination of the two (historically controlled).	Easier and cheaper to conduct than RCTs. Allows matching of exposed and unexposed groups. Eligibility criteria and outcomes can be standardised.	Control and intervention groups may be taken from different populations, increasing risk of confounding. Exposure may also be linked to unknown confounder(s).
Case control studies[25]	Individuals with the outcome of interest are matched to an appropriate group of controls without the outcome, information is then obtained about whether individuals were exposed to the factor of interest.	Faster and easier to conduct than other study types. Fewer subjects needed as only patients with the outcome need to be matched.	May be subject to recall and selection bias. Matching in a way that reduces confounders can be difficult as it requires confounders to be known and measured.
Quasi-randomised controlled trials[25,31]	Individuals, or clusters of individuals, are allocated to intervention or control groups in a quasi-random manner (such as alternation) that should not be known to trial participants or personnel.	Most structurally similar to an RCT. Blinding is possible, unlike other NRS designs.	The method of allocation may still introduce selection bias as it is not completely random.

Before-after study (and controlled before-after study) [25,43,44]	In a before-after study an uncontrolled comparison is made between frequencies of outcomes at two time points (before and after an intervention). If controlled, outcomes can be compared between clusters before and after the intervention, adjusted for outcomes in the control groups at both time points.	Presence of a well-selected control population may protect against the effects of trends or sudden changes.	If not controlled, then relies on the assumption than any observed changes are a result of the intervention. Liable to confounding due to differences in study populations. Selection of a control group is often difficult.

Non-randomised interrupted time series (and controlled interrupted time series)[25,31,44]	Outcomes recorded over a period of time from a single group or several clusters. If controlled, there is a contemporaneous control group.	Design can be useful in guideline implementation research to study the effects of interventions.	Measurements are taken from different populations so confounding needs to be assessed. If not controlled, it is assumed that any changes observed are due to the implementation of the intervention.
Natural experiments[25]	Differences in outcomes before and after the implementation of an intervention (not under the control of researchers) are studied.	May show the effect of an intervention in a 'real world' setting. Can be useful when RCTs are not ethical or feasible.	Study populations are likely to differ due to temporal separation, so results are liable to confounding.

Some NRS designs, such as those that are retrospective in design or those at a population level, may permit large enough sample sizes to study rare outcomes, which is advantageous to studies in maternity care. For the reasons described above, their results may also be more generalisable to a wider population than those from RCTs in some cases. Even so, there is a far higher risk of confounding due to participant allocation as mentioned; imbalances in participant characteristics between treatment and control groups is far more likely than in RCTs.

Well-designed NRS that account for their inherently higher risk of bias (by matching of control groups, or statistical adjustment of analyses, for example) due to a lack of randomisation should be considered as higher quality evidence than those that are poorly designed. In some cases, large, well-designed NRS may more accurately show the results of an intervention in a clinical population than small poorly-designed RCTs. Nonetheless, when considering data from NRS, the higher risk of bias and confounding should always be kept in mind. An area of maternity care for which both study designs have been used will now be discussed.

1.3.3.1 A practical example: induction of labour after 39 weeks' gestation for improving outcomes in advanced maternal age

The 35/39 trial, an RCT comparing induction of labour at 39 weeks' gestation with expectant management in pregnant women over 35 years of age, concluded that induction of labour at 39 weeks had no significant effect on its primary outcome of caesarean section rate and also had no effect on other secondary outcomes such as birth weight, Apgar scores, or NICU admission.[45] However, this trial did not plan to look at any potential effects of induction at 39 weeks on stillbirth or perinatal death — there were only 619 participants, meaning that the trial was underpowered to detect any difference in the rate of these outcomes. These 619 participants were also from a larger cohort of 4,542 who were eligible, as 3,923 declined to participate; if the participants who declined were mainly from certain demographics or socio-economic backgrounds then this may reduce the validity of the trial.

Knight et al. conducted a retrospective study (n=77,327) comparing induction of labour at 40 weeks' gestation with expectant management in pregnant women over the age of 35 — a much larger sample size than the 35/39 trial.[46] Similarly to the 35/39 trial, this study found no significant effect on the caesarean section rate. In contrast, this study found that induction of labour at 40 weeks' gestation may reduce the rate of perinatal death. The 35/39 trial was unable to measure effects on this outcome, which demonstrates that

considering data from NRS as well as RCTs can be beneficial and that RCTs do not always show the true effect of an intervention. Chapter 2 of this thesis will address when RCTs and NRS should be considered in evidence synthesis, and how to include both study types.

In the next section, I will discuss several examples of areas in maternity care that have been informed by systematic reviews, including when data from NRS has been considered alongside data from RCTs.

1.3.4 Systematic reviews of randomised studies in maternity care

1.3.4.1 Electronic fetal monitoring and perinatal mortality

Large cohort studies conducted in the 1970s suggested that the routine use of electronic fetal monitoring led to significant reductions in the rates of both stillbirth and neonatal death. For example, a retrospective before and after study by Johnstone, Campbell & Hughes in Aberdeen in 1978 compared outcomes before and after the introduction of continuous fetal monitoring and found a statistically significant ($p<0.05$) drop in the rate of stillbirth.[47] Analyses were not adjusted for population characteristics; the authors stated that their study could not prove that electronic fetal monitoring reduced fetal death, but that an RCT would likely not be feasible. Despite this, subsequent RCTs were conducted, and did not find significant reductions in perinatal death (and were mostly underpowered to do so).[39] Meta-analysis of the RCT data[48,49] suggested that although routine electronic fetal monitoring results in increased odds of intervention (OR 1.53, 95% CI 1.17 to 2.01 for caesarean section; data from nine studies, n=18,561)[48] it also reduces the risk of neonatal seizures and perinatal mortality (RR 0.21, 95% CI 0.12 to 0.29 for perinatal death in studies outside of the United States; data from seven studies, n=16,892).[49] These reviews were conducted before the creation of GRADE guidelines and as such did not formally consider the certainty of evidence.

1.3.4.2 Delayed umbilical cord clamping

Rabe, Reynolds & Diaz-Rosella conducted a Cochrane review in 2004[50] to investigate the effects of delayed cord clamping compared with early cord clamping in preterm births. Published studies to this point had suggested both advantages and disadvantages associated with this practice.[51,52] The Cochrane review originally included data from seven RCTs, and found that delayed cord clamping was associated with benefits such as less need for blood transfusion and less intraventricular haemorrhage (but this review did acknowledge that most outcomes had wide CIs and that further research was needed). The most recent version of this review (updated in 2019) now includes 48 RCTs, with data available from 40 studies (n=4,844), and concludes that delayed cord clamping may reduce the risk of

perinatal death (before discharge from hospital) in preterm births (RR 0.73, 95% CI 0.54 to 0.98; certainty of the evidence rated as moderate).[53]

1.3.5 Including non-randomised studies in systematic reviews in maternity care

1.3.5.1 Ursodeoxycholic acid for intra-hepatic cholestasis

Grand'Maison, Durand & Mahone published a review exploring the potential effects of ursodeoxycholic acid for treating intra-hepatic cholestasis in pregnancy.[54] Because of an existing Cochrane review of RCTs in which results were inconclusive, the authors opted to include controlled NRS as well as RCTs.[55] Aims of this study were to determine if patients included in NRS were similar to those in RCTs, and to determine whether including NRS data could improve current evidence and inform clinical practice. Results were comparable to the Cochrane review, and interestingly no significant difference was found between the results of RCTs and NRS; however, the NRS were judged to be of poorer quality.

1.3.5.2 Non-clinical interventions for reducing unnecessary caesarean section

A review of non-clinical interventions for reducing unnecessary caesarean section by Chen et al.[56] extracted data from 19 RCTs and ten observational studies (including one controlled before-after study and nine interrupted time series studies); this review was conducted following guidance from the Cochrane Effective Practice and Organisation of Care group which specifies study designs that can be used.[43] By considering evidence from both study types, the authors found moderate to high certainty evidence that some interventions targeting healthcare professionals can reduce caesarean section rates, as well as uncertainty around interventions targeted at women or families. This review was conducted to inform a World Health Organization (WHO) guideline.

1.3.5.3 Induction of labour after 39 weeks' gestation for improving outcomes in advanced maternal age

A 2020 meta-analysis, including data from the studies by Knight et al. and Walker et al. discussed earlier, aimed to determine if induction of labour was associated with increased rates of caesarean births and other adverse outcomes.[57] This study included six RCTs and two NRS. Pooling data from all eight studies, which is not recommended,[42] showed no statistically significant difference in the rate of caesarean section between induction and expectant management (OR 0.97, 95% CI 0.79 to 1.19). Using data from RCTs only, meta-analysis showed a similar effect size with a smaller CI (OR 0.97, 95% CI 0.86 to 1.1). These analyses support the findings of both trials mentioned previously, although perinatal death was not an outcome specified by this review.

1.3.5.4 Caesarean section for breech infants

The Term Breech Trial,[58] an RCT of 2,083 nulliparous women randomised to either caesarean section or vaginal birth for breech presentation, implied that it was safer to perform caesarean section for breech infants and was incorporated into guidelines. This trial has proven controversial, with papers published since that have refuted the findings as the morbidity and mortality seen in the trial cannot be directly attributed to the mode of birth.[59] The Term Breech Trial was also stopped early due to safety concerns, as there were more fetal deaths in the vaginal birth group. A 2015 Cochrane review (n=2,396) included three randomised trials of breech presentation.[60] Meta-analysis of the data showed a reduction in perinatal and neonatal death or severe neonatal morbidity for caesarean section compared to vaginal birth (RR 0.07, 95% CI 0.02 to 0.29, moderate quality evidence), although data in this analysis were only from one RCT in a country with a low perinatal mortality rate. The same effect was not seen in settings with high perinatal mortality (low quality evidence from one study).

NRS were not considered in the Cochrane review and several observational studies have failed to demonstrate the same effect in a normal clinical setting,[61–63] suggesting that results of individual RCTs may lack external validity and the results of the Term Breech Trial may not be applicable in all countries. A 2016 review synthesised data from observational studies, including 1 RCT and 26 NRS.[64] Meta-analysis of data from 14 studies (n=258,953) showed a higher risk of perinatal death in planned vaginal delivery compared with planned caesarean section in breech presentations (RR 4.6, 95% CI 2.6 to 8.1), which is in the same direction as the findings of the Cochrane review. Results from this study should be interpreted with caution as inclusion criteria for study design are not specified and GRADE was not used.

The RCOG guidelines for management of breech presentation, published in 2017,[65] states that planned caesarean section leads to a small reduction in perinatal mortality, citing the Term Breech Trial and Cochrane review as higher quality evidence (level 1+) than the Berhan et al. meta-analysis (level 2++).

From these examples, we can see that data from both RCTs and NRS have been used to inform systematic reviews and guidelines. Using data from larger, high quality NRS may give insight where sufficiently powered RCTs are not available.

1.3.6 IPD meta-analysis

Overview

In IPD meta-analysis, original study data sets are combined and analysed *de novo* rather than

summary effect sizes.[66] The Cochrane handbook states that IPD reviews should be considered when available published data do not permit a high quality review or when an aim of the review is to look at the effects of subpopulations and effect modification.[67] In IPD reviews, each participant is an individual data point meaning that patient characteristics as well as whether each individual patient was in the treatment or control group is recorded alongside outcomes.

Advantages and disadvantages

Advantages of this approach are that it allows each participant's individual characteristics to be taken into account along with their intervention status and corresponding outcome, meaning that if there are participants or subpopulations in which the intervention is more or less effective then this can be explored. An IPD approach also allows standardisation of outcomes across trials and detailed data checking.[66] It also allows trials that are unpublished or incompletely reported to be considered and included and, where data are sufficient, subgroup analyses can be performed to look at the effects of certain characteristics such as age or sex.[68] This is less likely to be feasible when using aggregate data. These analyses should be specified and justified at the protocol stage of the review.

Disadvantages of this approach are that data may be incomplete or difficult to obtain and may also need to be recoded and reformatted, which can be time consuming.[66] A variation of the PRISMA statement has been developed to be more specific to IPD reviews.[67]

IPD meta-analysis in maternity care

In maternity care, IPD meta-analysis has been used to measure the association between maternal going-to-sleep position and stillbirth, allowing an association between supine going to sleep position and late stillbirth to be seen independently of other risk factors, although this was a review of case control studies (RCTs and cohort studies were also searched for) and was not a study of interventions.[69]

An IPD review of timing of birth for twins with growth restriction and growth discordance demonstrated that the risk of stillbirth and neonatal death were higher when one or both twins were growth restricted, as well as with higher levels of discordant growth, but did not find evidence that optimal timing was affected by either of these factors.[70] Previous meta-analysis had only looked at uncomplicated twin pregnancies.

As a final example, IPD analysis was performed to determine optimal timing of birth in pregnancies with preeclampsia; previous reviews had not looked at hypertensive disorders separately and had not found any clear impact on neonatal outcomes.[71] This review used IPD meta-analysis to perform subgroup analyses, for example grouping by blood pressure values, that would not have been possible with aggregate data. The authors found that planned birth on or after 34 weeks' gestation reduced maternal morbidity and the

incidence of FGR, but increased short-term neonatal respiratory morbidity.

1.3.7 Evidence synthesis in studies of reduced fetal movement

In addition to the areas mentioned above, systematic reviews have been conducted to address the lack of consensus in the clinical management of RFM. A Cochrane review of studies of fetal movement counting, first conducted in 2008 and updated in 2015,[72] found 13 studies that met the inclusion criteria. Observational studies were not considered for inclusion in this study, only RCTs and cluster randomised studies. It should be noted that these studies were mostly for the use of Doppler ultrasound and CTG in high-risk pregnancies, and data for RFM specifically were only available from one study. This review concluded that current data are insufficient to inform practice and there is a need for research to evaluate the benefits and risks of strategies to manage RFM, which should include high quality RCTs of sufficient size.

Another systematic review was carried out in 2020 to investigate the effects of interventions for RFM; again, only randomised studies were included.[73] This review grouped all studies together when conducting analyses and found 'weak associations' between fetal movement counting and preterm birth, caesarean section, and induction of labour.

1.3.8 Guideline development

The uncertainty found by reviews has an effect on guideline development. The RCOG Green-top Guideline No.57 for the management of RFM in pregnancy[11] was created by searching databases for RCTs, systematic reviews, and other NRS that investigated the effects of clinical management on the outcomes of pregnant people who present to hospital with RFM. The guideline includes 31 recommendations. Of these, one is grade 'A' (based on at least one high-quality or well conducted meta-analysis, systematic review, or RCT); 10 are grade 'B' (based on high quality systematic reviews of case-control or cohort studies, or high quality case-control or cohort studies with consistent results), 9 are grade 'C' (based on well-conducted case-control or cohort studies with low risk of bias and consistent results), and 11 are based on best practice. It is stated that one limitation is that there is a paucity of large scale descriptive or intervention studies because the main outcome of stillbirth is uncommon, and adequately powered studies of different management protocols would require large numbers of participants as mentioned previously in this review. As such, it is stated that the guideline should serve as a broad practical guide for clinical practice rather than a definitive guideline.[11]

If guidelines are not based on high quality evidence then this may lead to uncertainty in clinical practice — as evidenced by hospitals often developing their own guidelines for RFM instead of following national guidelines.[74] However, it should also be considered that high quality evidence may not be available, and so guideline developers must determine whether the creation of guidelines based on lower quality evidence is still worthwhile. Guidance for developing a Green-top guideline, from the RCOG, states that for each research question '*the study type with the least chance of bias should be used*', where RCTs and systematic reviews of RCTs are seen as preferable to data from observational studies (using the grading system described above). When there is no relevant higher quality evidence, guidance states that non-analytic studies (case reports and case series) and/or expert opinion could be used; this would be given a grade 'D'. Where there is no relevant research evidence at all, practice can be recommended based on the clinical experience of the development group, although this is not given a grade in the same way as above – guidance emphasises that these are not evidence-based recommendations and should only be used in the absence of an alternative.[75]

Subsequent to the publication of the RCOG Green-top guideline 57, the results of two large RCTs looking at the management of RFM have been published.[76,77] The Green-top guideline no.57 cites NRS that have aimed to quantify the effects of interventions for RFM[78,79] but have not been considered in a formal synthesis. Therefore, the management of RFM in the UK is not currently informed by all the available evidence. Studies that have employed interventions other than formal fetal movement counting would also be beneficial to consider, such as those aiming to encourage awareness of fetal movement (their pattern and strength rather than formal counting),[76,77] and employing clinical testing such as ultrasound,[80] as well as combinations of these.[81]

Conducting a systematic review including both RCTs and NRS, including all interventions for RFM, and including the most recently published studies will provide a better overview of the effect of interventions for the management of RFM. Furthermore, ensuring that studies all measure the most important outcomes would improve future syntheses.

1.4 Core outcome sets

1.4.1 Overview

COS describe a standardised set of outcomes that should be reported and measured in all studies in a specific area as a minimum.[82,83] COS are often developed using Delphi surveys and consensus meetings, where relevant stakeholders rate the importance of outcomes; COS methodology will be described in Chapter 2.

COS are currently in use across several healthcare fields and aim to address issues with outcome reporting; systematic reviews and meta-analyses often identify inconsistent outcome reporting as a limitation,[84] which makes synthesis difficult and may have a knock on effect onto the quality of guidelines. A Cochrane review categorized 2,535 systematic reviews by the suggested area that needed further evaluation, and 51.9% of these reviews suggested outcome measures.[85]

1.4.2 Uptake of core outcome sets

The uptake of COS varies across different health disciplines; a systematic review found that, of 24 studies measuring COS uptake in RCTs, the percentages of these RCTs that used the full COS varied wildly (from 0-81%).[86] None of the COS included in this review were related to maternity care. A study of 95 trials published in major medical journals between October 2019 and March 2020[87] showed that 98% of these did not use a COS, despite relevant COS existing for 33% of trials; 8 trials in this study were classified as Pregnancy & Childbirth. If COS are not used despite their presence then it is likely that there are other factors affecting COS implementation.

Kirkham et al.[88] assessed the uptake of one of the first COS, the WHO-ILAR COS for rheumatoid arthritis[89] by looking at the outcomes measured by 273 trials since publication of the COS in 1994. The full COS was reported by 116 out of 143 completed trials (81%) and 190 out of 273 trials (70%) identified from a registry, suggesting that there is a willingness to use COS. Uptake of the COS was shown to increase over time, which may explain some of the variation seen in the above review. However, it should also be considered that some trialists may choose not to use it despite being aware of its existence (though most would choose to).[88] It has also been suggested that one of the main barriers to the uptake of COS is trialists' own outcome preferences and choice,[87] even though COS do not restrict the outcomes that can be measured.

A survey of 62 clinical trialists showed that some other key factors lowering the uptake of COS include: poor knowledge about COS, difficulties involved with identifying a relevant COS, and the perception that COS can be restrictive and/or contain too many outcomes.[90] Similar barriers were suggested by Hughes et al.,[86] as well as a lack of patient and key stakeholder involvement. Despite this, a large number of participants in the survey believed that COS can improve outcome reporting (96%) and comparability of findings across trials (86%).[90]

1.4.3 Core outcome sets in maternity care

The CROWN initiative (Core Outcomes in Women's and Newborn Health) lists and

provides links to information about COS in women's and newborn health,[91] which may help trialists to locate relevant COS. A 2017 systematic review found 49 registered COS in women's and newborn health,[91] some examples in maternity care include:

- The COSGROVE study,[92] a COS for trials of prevention or treatment of FGR, was developed after identifying that the evidence at the time was difficult to interpret as there was a lack of consensus on the outcomes that should be measured;
- A COS for evaluation of interventions to prevent preterm birth[93] aimed to address heterogeneity in outcome reporting in this area and created a final set of 13 outcomes (four maternal and nine neonatal);
- The COSNEON[94] COS describes 19 outcomes that should be reported in studies of feeding interventions after FGR;
- The iCHOOSE study, aiming to develop a COS for stillbirth care research,[95] is currently in progress. This COS is also being conducted as a response to inconsistent outcome reporting in this field and intends to be applicable to studies of interventions offered after stillbirth (hospital care, community care, and those for subsequent pregnancies after stillbirth).

There is not currently a COS for studies of RFM; the creation of one would aid future synthesis if it were more likely that all studies measured the same outcomes.

1.5 Surveys of practice

1.5.1 Overview

As mentioned above, guidelines that are not evidence-based, or not based on high-quality evidence, may lead to variation in clinical practice. Surveying clinicians, specifically obstetricians and midwives in maternity care, plus others depending on the survey topic, is one way to gather information on the current state of practice.

Other methods may include ethnography, which may involve observing practice first-hand and/or conducting interviews (although this is resource intensive and usually only gathers information from a limited amount of settings or practices) and surveys of service users.[96] This approach has been used to describe clinicians' practice relating to RFM at two UK maternity units, using observation, interviews, and analysis of policy documents and maternity notes.[97]

Surveys of practice allow researchers to see how practice changes — or stays static — over time, and whether this may be influenced by the publication of trials, systematic reviews

and meta-analyses, and/or the presence or lack of guidelines. However, it is important to note that other factors such as individual beliefs and the guidelines, culture, and resources available to a specific unit or hospital may also have effects on the care provided.

Surveys of practice may also be designed to inform studies of interventions, for example a cross sectional survey of midwives describing practice related to assessing and repairing perineal trauma.[98,99]

1.5.2 Surveys of practice in maternity care

1.5.2.1 Umbilical cord clamping

Delayed cord clamping, mentioned earlier in this chapter, is an area in which systematic reviews have been used to inform practice but also where surveys of practice have been conducted. An online survey of midwives and obstetricians was conducted to gain an overview of clinical practice relating to umbilical cord clamping in Canada, as there were no Canadian practice guidelines.[100] The 2004 Cochrane review on delayed umbilical cord clamping on preterm infants had been published, but no corresponding review for term infants.[50] This survey found that, despite the results of the Cochrane review, the majority of participants did not practice delayed cord clamping in preterm babies, and instead practice was influenced by personal preference and hospital routine.[100]

A similar survey of midwives in Ireland in 2018 also showed variation in practice related to cord clamping, although the majority stated that they would usually delay cord clamping, and highlighted the need for a national guideline.[101]

1.5.2.2 Reduced fetal movement

Surveys of knowledge and practice specific to RFM have also been published. A 2008 survey of UK-based clinicians was carried out to determine whether uncertainty around the definition and management of RFM leads to variation in clinical practice — this study revealed significant variation in knowledge of RFM and its clinical management, and practice that was not always evidence-based.[2] The authors proposed that the creation of a national guideline for the management of RFM may be useful.

Two surveys in Ireland also reported an absence of local guidelines and a lack of consensus for the management of RFM. One of these surveys presented participants with a specific scenario about the management of a patient with concerns about RFM, and concluded that there was a need for national guidelines.[102] The other aimed to look at the effect of recent surveys and intervention studies for RFM, recommending that large prospective studies are needed to determine optimal management.[103] In Australia, a survey of obstetricians in

relation to current practice and views around RFM again demonstrated significant variation in both components.[104]

1.6 Summary

RCTs, and systematic reviews of RCTs, are the gold standard for studying healthcare interventions. Systematic reviews of high quality RCTs are more likely to show the true effect of an intervention than the results of individual studies. However, in maternity care, where important outcomes are rare and it is often unfeasible to conduct adequately powered RCTs, synthesis that includes well-designed NRS may be beneficial.

The management of RFM is one area in which there is still a lot of uncertainty, which leads to uncertainty in guidelines. Presently, the RCOG guideline for the management of RFM is based on limited evidence and states that there is a need for further RCTs to inform practice, but data from several large observational studies have not been synthesized. Published systematic reviews of interventions for RFM have mainly considered evidence from RCTs despite the existence of relevant NRS. Thus, conducting a review of management of RFM, and expanding the inclusion criteria to include well-designed NRS, may help to inform clinical practice.

RFM research would also benefit from the creation of a COS to improve future studies, and synthesis of these studies. An updated survey of practice would show whether uncertainty around guidelines is reflected in clinical practice related to RFM, and whether knowledge and/or practice related to RFM has changed in the last decade.

1.7 Aims and objectives

The work comprising this thesis aims to improve future research and practice related to encouraging awareness of RFM and its subsequent clinical management. The objectives of my PhD are:

- To conduct a systematic review investigating the effectiveness of interventions for encouraging awareness of fetal movement and/or the subsequent clinical management of RFM, including data from RCTs and NRS,
- To create COS for future studies of interventions for encouraging awareness of fetal movement and/or its subsequent clinical management,
- To survey UK-based clinicians in order to describe current knowledge and practice around RFM, and whether this has changed since the 2008 survey.

Chapter 2 - Methodology

2.1 Overview

This chapter will cover the main research methods used in this thesis. First, methods for conducting systematic reviews will be described, with a focus on the types of study that should be included in intervention reviews (where systematic reviews are carried out to address questions on the effectiveness of different interventions) and when some methods may be more suitable than others. Then an overview of COS development will be given, and finally, surveys of practice will be covered.

2.2 Systematic reviews

Systematic reviews aim to collate all the available evidence on a given topic, using systematic reproducible methods to reduce bias, to answer a specific research question.[23,24] The parameters of the research studies which may address this question are then set in terms of eligible study design, participants, and, potentially, interventions. A key stage in systematic reviews is the critical appraisal of all included data, largely to assess the internal validity of studies — whether they answer the research question in a manner free of bias, defined as a systematic error in results due to the design of a study.[105] Systematic literature searches are then constructed to identify all relevant studies, which are screened according to inclusion criteria, and data are extracted from studies that meet these criteria along with important study characteristics. Systematic reviews can inform guidelines and can help decision makers to process large amounts of data from multiple studies. Systematic reviews may or may or not include meta-analysis, a statistical method of combining data from multiple studies,[24] which will be described later.

2.2.1 Systematic reviews of interventions

2.2.1.1 Introduction

Systematic reviews of interventions are performed to estimate the effect of an intervention, or several interventions, on healthcare outcomes. When planning a systematic review of interventions, consideration should be given to the design of included studies and whether they are likely to measure the true effect of the intervention(s).

2.2.1.2 Including data from randomised trials in systematic reviews of interventions

As discussed in Chapter 1, evidence from randomised trials is often seen as the gold standard in systematic reviews as, if designed and conducted well, there is less potential for bias. NRS are inherently more prone to bias due to the lack of randomisation and many

systematic reviews have only considered RCT data because of this. Data from RCTs should be included in intervention reviews as long as the studies have clearly reported mechanisms of group formation, clearly defined inclusion criteria, and described methods of ascertainment of eligible patients and their recruitment.

When considering data from cluster randomised trials, in which 'units' of individuals (such as hospitals) are randomised to interventions rather than the individuals themselves, reviewers should ensure that analyses performed in these studies are appropriate — unit of analysis errors can arise if clustering is ignored and data are analysed as though individuals had been randomised.[106] These errors can lead to CIs and p values that are smaller than they should be, and therefore false positive results that will receive more weight in a meta-analysis than is appropriate.[106]

2.2.1.3 Including data from non-randomised studies in systematic reviews of interventions

Depending on the available evidence, review authors may wish to consider data from NRS in addition to, or in lieu of, data from RCTs. The Cochrane handbook for reviews of interventions states that data from NRS can be included alongside RCT data if both study types address the same research question, although results should be presented and analysed separately.[42] Similarly, Schünemann et al. propose a framework where NRS data are used as a complement to RCT data when high quality data are available from both study types, but recommend that data from NRS are not used if the certainty of evidence from RCTs is high.[107]

Alternatively, data from NRS may be used instead of data from RCTs. Reeves et al. state that data from NRS can be used in studies of interventions when available RCTs do not directly or entirely address the review question.[108] This may include when evidence is needed for interventions that are unlikely to be, or cannot be, studied in RCTs — such as population level interventions for when study participants are likely to strongly prefer an intervention group. The framework by Schünemann et al. suggests that NRS data can be used in the absence of high certainty RCT data, either as a sequence (when RCT data are unavailable or insufficient, for example for long-term outcomes) or replacement (when NRS data provides equivalent or higher confidence in the evidence).[107]

Similarly, the Cochrane Effective Practice and Organisation of Care (EPOC) group state that it may be appropriate to include a wider range of study designs when randomised trials are not available.[43] This guidance does suggest that data from even well-designed NRS may not necessarily add to a review in cases when there is sufficient evidence from

randomised trials, due to higher potential for bias caused by separation (geographical or otherwise) of intervention groups. However, a review of comparisons of the results of NRS and RCTs for interventions in different subject areas, by Deeks et al.,[109] found similar results from each study type in five out of eight included reviews.[110–114] Two included reviews found that effect sizes were generally larger in NRS[115,116] and another found differences that varied in direction.[117]

When deciding whether to include NRS in a review, authors should consider the existing evidence and whether excluding data from NRS will mean that their review is not synthesising all the useful data, or whether including poorly designed NRS will mean that the true effect of an intervention is not being measured.

2.2.1.4 Which non-randomised study designs should be considered in systematic reviews of interventions?

As touched on above, deciding which NRS should be included in reviews is related to validity — how well a study's results represent the true findings among similar individuals to the study participants outside of a study setting.[38] Internal validity is the extent to which the observed results represent the true effect in the population of interest and are not instead determined by methodological errors. External validity, which should only be judged if a trial is internally valid, describes whether the results apply to similar patients in a different setting and therefore whether the intervention can be used in other settings.[38] For example, the results of a trial (with internal validity) examining the effects of an intervention in low-risk pregnancies in a high-income country may not be applicable to populations in other lower income countries.

Guidance from the EPOC group for authors of Cochrane healthcare reviews states that appropriate NRS designs to include in a review may include: non-randomised trials (or non-randomised controlled studies), controlled before-after studies, and interrupted time series (ITS) and repeated measures studies.[43] Including studies without control groups such as uncontrolled before-after studies and cross-sectional studies is 'strongly discouraged' as it is not possible to attribute causation in these study designs.[43] These study designs are also described in Table 1 in Chapter 1.

Among NRS designs, quasi-randomised controlled studies are most analogous to RCTs, with the main difference being how participants are allocated to intervention groups.[31] Reviewers should be mindful of whether bias is likely to have been introduced by inappropriate group formation, for example if participants can influence their own

allocation to intervention groups.

Controlled before-after studies include two study populations, both of which start without the intervention, then at a given time point one population receives the intervention and the other does not. Presence of a control group allows bias that may be introduced by both temporal and spatial separation to be accounted for in statistical analysis, which should be considered when assessing these study types. Uncontrolled before and after studies risk introducing temporal confounding as any effect seen may be due to a change over time,[30,44] and hence should not be considered.

ITS and repeated measures studies are both composed of measurements in different patient populations before and after an intervention.[31] These designs are commonly used for measuring the effects of the introduction of a health-related policy. Again, reviewers should consider whether appropriate statistical analysis has been performed to adjust for differences between control and intervention groups, as otherwise any differences in outcomes cannot be attributed to the intervention. Bias could also be introduced by the timing of measurements; ITS differ from before-after studies as outcomes are measured at multiple time points.[30,44] However, this may help to reduce temporal bias, and for complex health interventions ITS studies may be considered especially useful as characteristics that could lower internal validity can be measured both before and after the intervention was implemented.[118]

A checklist by Reeves, Wells & Waddington[25] can help to classify research evaluating effects of health interventions when considering studies to include in systematic reviews, which may aid in determining the internal validity of a study in terms of inferring causality. The checklist aims to avoid assumptions based purely on study design labels, as these are often ambiguous or describe the analyses rather than the actual design approach. Instead, the checklist encourages review authors to consider how study features may affect the risk of bias and confounding in relation to the research question of interest. This means that considered decisions can be made about relevant study features that shape review inclusion criteria.[25]

Whether NRS are included in a review should be specified when writing the protocol. Authors may wish to state that the decision to include NRS will be considered based on the quality and validity of available evidence from RCTs, based on their risk of bias (including publication bias), inconsistency, indirectness, and imprecision.[107] Alternatively, reviewers could plan for post-hoc analyses to be performed to test for bias introduced by

study design.

In maternity care, rare, serious outcomes (such as stillbirth or hypoxic-ischaemic encephalopathy) are often measured by trials. This means that the sample size and statistical power required to study differences in rates between populations or intervention groups is achieved more easily using observational data obtained from NRS designs. Not including NRS in systematic reviews in these scenarios would exclude a large amount of potentially useful data and would reduce the overall statistical power of a review. Therefore, it may be even more appropriate to include NRS data in systematic reviews in maternity care, even when RCT data are available.

2.2.2 Planning a systematic review

When planning a systematic review, it may be useful to consult the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement — this was originally published in 2009, has since been updated,[24,119] and includes a checklist describing steps that should be taken in order to ensure that all necessary parts of a robust systematic review are reported. A completed version of this checklist is often requested by journals when submitting a systematic review manuscript: steps in the checklist include having well-defined eligibility criteria, describing all information sources used and providing full literature searches, stating how studies were selected, and describing methods used to assess risk of bias in individual studies.[119]

An extension of this, the PRISMA-P (Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols) checklist,[120] can be used when developing and reporting systematic review protocols. Creation of a protocol can help to plan a review as well as enabling transparency — if a protocol is available online before a review is published then readers can see whether inclusion criteria, analyses, and outcomes were pre-specified and adhered to. The PICO model (Table 2) can be used to frame the research question and to determine inclusion and exclusion criteria for the review, which can then inform literature searches and the types of study to be included.

Steps in conducting a systematic review, once the aim and eligibility criteria have been decided upon, will now be described sequentially.

Table 2 – The PICO model

P	Population	The population or patients of interest
I	Intervention	The intervention under investigation (an experimental intervention, may be an exposure in observational studies)
C	Comparison	The intervention in the control group, or no intervention
O	Outcome(s)	The outcome(s) of interest

2.2.3 Constructing search strategies

Literature searches for systematic reviews should aim to identify as many studies as possible that are relevant to the review in question. However, searches with high sensitivity will often have low precision,[121] which can lead to extra time spent screening references.

The Cochrane handbook recommends that search strategies for a systematic review should be constructed with the aid of a librarian or information specialist.[121] Working with such specialists may also be beneficial to review authors when it comes to obtaining copies of including papers and/or translations. Searches need to be thorough, objective, and reproducible,[121] with the aim that they could easily be performed again accurately (were the review updated in future, for example).

When designing search strategies, the review team should first consider the review question — it may help to use the PICO model described above. This will help to collate a list of keywords which can be combined using the OR Boolean operator. These searches can then be combined using the AND Boolean operator (another operator, NOT, is used to exclude certain terms, for example "pregnancy NOT twin"). In PubMed, Medical Subject Headings (MeSH) can also be used. Exclusions can be made based on language and publication date, though this is not often recommended, or factors such as study type and study subject (humans or animals). Search strategies should be reported in full, as opposed to lists of keywords.

2.2.4 Searching databases and screening references

To reduce bias, multiple databases should be searched.[121] For reviews of interventions, the Cochrane handbook recommends searching the Cochrane Central Register of Controlled Trials (CENTRAL) alongside MEDLINE and Embase. PubMed, a free way of searching MEDLINE that also allows searching of records not fully indexed to MEDLINE, is often a useful way of identifying the majority of relevant studies.[122] The Cochrane handbook also suggests running two independent searches at the same time, although the feasibility of this will depend on the time and resources available to the review team.

Other studies have set out to quantify the impact of using specific databases, or combinations of databases, on systematic literature searching. Bramer et al. examined 58 systematic reviews and recommend searching in Web of Science and Google Scholar in addition to MEDLINE and Embase.[123] This study, and others, have concluded that the databases used can substantially affect the percentage of relevant studies that are found and, therefore, the results of the review itself.[123,124] Hand searching, reference checking and contacting study authors should also be performed, which may be a way to overcome the limitations of solely searching online databases.[123] It may also be beneficial to search 'grey', or unpublished, literature using databases such as OpenGrey, to search for preprints using databases such as medRxiv, and to search for trials in progress.

Once searches are complete, any duplicates (references retrieved by one or more databases) can be removed using reference management software such as Mendeley or EndNote. Literature screening should then be performed by at least two study authors, with another being available to help settle disagreements, so that there is a consensus on whether each study should be included in the review or not; this has been shown to reduce errors in study selection, compared with data extraction by a single reviewer.[125] This method should be used both for screening references based on their title and abstract (which is used as a time-efficient method of removing references that are immediately obvious as not relevant) and during full-text screening. Software such as COVIDENCE[126] are available to simplify this process.

2.2.5 Risk of bias assessment

2.2.5.1 Introduction to risk of bias assessment

A vital component of systematic reviews is assessing the risk of bias of the included studies. Bias is defined as a systematic error in estimating the true effect of an intervention as a result of problems with a study's design and conduct.[127] Assessing risk of bias allows reviewers to measure the validity of the included studies, and whether they are likely to be answering the review question. Assessing and labelling the risk of bias of included studies can enable sensitivity analyses (for example, limiting analyses to studies that are not at high risk of bias) and may help with how the results of individual studies should be considered. Choosing the tool for assessing risk of bias for a given study should depend on the study design.

2.2.5.2 Risk of bias assessment in randomised trials

Types of bias that may affect RCTs are: selection bias, performance bias, detection bias, attrition bias, and reporting bias.[105] If performed correctly, randomisation will prevent

selection bias (allocating interventions to participants based on other indications, which can lead to confounding factors not being evenly distributed between groups).[128] The randomisation process could still introduce bias if allocation to treatment groups is not truly random (if based on participants' dates of birth, for example), or if participants or trialists were not blinded to the process. Performance bias (differences between groups in the care that is provided) and detection bias (differences between groups in how outcomes are measured) may be prevented by blinding of study personnel to the treatment and control groups. Attrition bias (differences between groups in withdrawals from a study) and reporting bias (differences between reported and unreported findings) are usually unaffected by study design.[105] The magnitude and direction of bias (under or overestimation of an effect, and by how much) can vary.

The standard approach for assessing risk of bias in RCTs is to use the Cochrane risk of bias tool for randomised trials (RoB 2).[128] RoB 2 can also be used to assess bias in cluster randomised trials, with an additional domain to assess bias arising from the timing of identification and recruitment of participants (bias can be introduced if this happened after randomisation).[106] RoB 2 is structured into five domains, to measure bias arising from: 1. The randomisation process, 2. Deviations from intended interventions, 3. Missing outcome data, 4. Measurement of the outcome, and 5. Selection of the reported result. This assessment gives an overall verdict of 'low risk of bias', 'some concerns', or 'high risk of bias'. Strengths of RoB 2 include its transparency and the development procedure; potential weaknesses include that it does not consider potential bias due to funding and/or conflicts of interest (although it is modifiable, and a Tool for Addressing Conflicts of Interest in Trials is under development), and low inter-rater agreement, which may create problems for review authors.[129]

Other scales and checklists exist for assessing risk of bias in RCTs,[130] however, these are less frequently used due to the rigour of RoB 2.

2.2.5.3 Risk of bias assessment in non-randomised studies

Non-randomised studies of interventions can be assessed for risk of bias using the Risk of Bias in Non-Randomised Studies of Interventions (ROBINS-I) tool, which was developed by Sterne et al.[131] ROBINS-I is generally preferred over other tools for assessing bias in NRS, such as the Downs-Black checklist,[132] and the Newcastle-Ottawa scale[133] which has low inter-rater reliability and/or can be difficult to use.[134] ROBINS-I can be modified before use and consideration of review- and/or study-specific confounders and co-interventions can be pre-specified to conduct robust assessments.

Assessment using ROBINS-I is similar to assessment using RoB 2, in that domains for assessing bias due to deviation from the intervention, missing data, outcome measurement, and result reporting are specified. Differences occur in ROBINS-I when assessing biases that randomisation, when done properly, should protect against, including: whether prognostic variables determine the intervention received by a participant, when participant selection is related to intervention or outcome, or when intervention status is misclassified.[131] Only in exceptional circumstances will NRS be judged as at low risk of bias from confounding; for this to happen the study should be comparable to a well performed randomised trial.[131]

2.2.6 Assessing interventions in included studies

The Cochrane EPOC group recommends describing interventions using the TIDieR Checklist,[135] both at the protocol stage and when extracting data and planning analyses. Use of the checklist may help to decide if interventions are relevant to the review inclusion criteria and may help decide which studies are similar enough to group for meta-analysis. TIDieR is composed of 12 items, such as describing materials and procedures used in the intervention, alongside who provided the intervention and how many times, as well as the theory behind it.

2.2.7 Meta-analysis

2.2.7.1 Introduction to meta-analysis

In meta-analysis, data from several studies are combined with the intent of answering a research question using more than just the results from single studies. Meta-analysis is commonly performed using software such as STATA, R, or RevMan. The usual method is to first calculate a summary statistic for each outcome from each study, and then to combine these summary statistics into a weighted average that takes study size into account.[136]

Advantages of meta-analysis are that it can increase the sample size, and thus statistical power, of an analysis (compared with individual studies), and that it enables calculation of an overall effect size rather than relying on the results of single studies; however, meta-analysis may give incorrect or misleading information if data from dissimilar studies are combined (a common criticism of meta-analysis is that it can 'compare apples with oranges') or if heterogeneity is not accounted for.[137,138] Further to this, researchers also must ensure that, when performing meta-analyses and interpreting the results, study design and the potential for bias should be considered as discussed previously.[139]

The Cochrane Handbook[139] states that there are five types of outcome data that are likely to be used in systematic reviews (dichotomous data, continuous data, ordinal data, counts and rates, and time-to-event data); the effect measure that should be used is dependent on the type of data. For the purposes of this thesis, I will consider dichotomous data, where an outcome can be one of two responses (yes or no, for example for outcomes such as stillbirth), and continuous data (measurements, for example birth weight in grams).

2.2.7.2 Effect measures for dichotomous data

For binary outcomes, risk ratios (RRs) or ORs and their corresponding 95% CIs are most commonly used.[140] Effect measures can be extracted directly from a study manuscript, which is preferred when dealing with estimates from cluster-randomised or crossover trials where adjusted effect estimates should be calculated, or calculated by review authors from raw data using a 2x2 table.[140] If this is not possible, effect measures can also be estimated using logistic regression and other methods of transforming data.[141]

The OR is the ratio of the odds of the event in the intervention group divided by the odds of the event in the control group, where the odds itself is the ratio of the probability that an outcome occurs to the probability that it does not and can be expressed as any number.[142,143] An OR of 1 indicates that the odds of an outcome happening are the same in both groups.

The RR is the ratio of the risk of the event between in the intervention group divided by the risk of the event in the control group, where the risk is the probability that an outcome occurs and is expressed as a decimal or percentage; therefore the RR describes the multiplication of the risk that occurs with implementation of the intervention.[140] An RR of 1 indicates that the risk of an outcome happening is the same in both groups.

When interpreting RRs (and ORs), it is important to consider what this means clinically.[140] For example, an RR of 0.5 could mean that an intervention leads to an outcome happening 40% of the time instead of 80% of the time, or 2% of the time instead of 4% of the time.

2.2.7.3 Odds ratios v risk ratios

ORs and RRs are often conflated, and ORs are usually interpreted as a relative risk.[143] A study looking specifically at the use of ORs in obstetrics and gynaecology[144] found that, in 47 out of 107 included studies, the difference between the OR and the estimated RR was over 20% and was often misinterpreted. This is problematic as, while ORs and RRs for the same data are often comparable, in many cases (such as when events are common) doing

this will make the effect appear larger.[144,145] ORs may be more appropriate when events are rare.[145]

RRs are recommended in syntheses of dichotomous data,[139] and may also be easier to understand as they are more intuitive:[143] an RR of 0.5 shows that the risk is halved and an RR of 2 shows that it has been doubled. Nonetheless, the choice of effect measure to be used may also depend on the available data.

2.2.7.4 Effect measures for continuous data

For continuous data, the mean difference (MD) and standardised mean difference (SMD) are most commonly used. The MD should be used when all studies report the outcome using the same scale, the SMD is appropriate when studies use different scales;[139] this may be relevant in maternity care for outcomes such as maternal anxiety, for which different scales are used in practice (such as the Spielberger state trait anxiety index[146] or the Cambridge worry scale[147]). Different approaches are used when calculating the weight for each effect measure: for the MD the weight given to an individual study is calculated by combining the standard deviation (SD) and the sample size (smaller SDs are weighted relatively higher), for the SMD study weights are calculated by standardising the SDs to a single scale.[139] Either the MD or SMD can then be combined in meta-analysis.

2.2.7.5 Data synthesis

Combining effect measures

Effect sizes will usually be combined in meta-analysis using the random effects method (DerSimonian and Laird inverse variance).[148] Random-effects meta-analysis assumes that all studies are estimating slightly different intervention effects due to variation in trial populations and study design; this involves adjusting the standard errors from each study estimate to incorporate a measure of the heterogeneity seen in the effect sizes seen across studies.[139,148] This approach also allows the inclusion of effect sizes from cluster-randomised trials.

Fixed effects models assume that a common effect is being estimated for a specific population and are generally used when little heterogeneity between studies is anticipated. These models are generally less applicable in studies of interventions where studies are carried out in different populations. Fixed effects models are not used in this thesis and will rarely be seen in systematic reviews in maternity care as trial populations will usually show some degree of heterogeneity; as such, they will not be described in detail here.

Effect measures from RCTs and NRS should be presented and analysed separately to prevent generally larger sample sizes from NRS dominating analyses.[42] Analysing both data types together may also make synthesis less certain compared to analyses that only contain data from RCTs.[31]

It is preferable to include adjusted effect measures in meta-analysis as they usually reduce the impact of confounding[140] and some review authors may choose to only include adjusted estimates, though these are not always available. Adjusted and unadjusted effect measures may be synthesised separately, or, alternatively, shown as subgroup analyses.

Subgroup analyses

Review authors may wish to use subgroup analyses to look at the effect of risk of bias of individual studies. Subgroup analyses may provide rationale for sensitivity analyses, for example, excluding studies at high risk of bias from a meta-analysis.

Subgroup analyses can also be performed for interventions that should not be considered similar in an applied sense. For example, the review of non-clinical interventions for reducing unnecessary caesarean section by Chen et al.,[56] discussed in Chapter 1, split analyses into three groups depending on whether interventions were targeted at women or families, healthcare professionals, or healthcare organisations or facilities as combining data from all three groups would not have provided any data with real world usefulness.

2.2.7.6 Assessment of heterogeneity

Heterogeneity is a measure of the variability in results between studies, which can arise as a result of differences in study design or differences in study populations. Heterogeneity can be classified as clinical due to differences in study populations or treatment types, methodological in terms of study design and conduct, or statistical in terms of variation of effects.[149]

Significant statistical heterogeneity suggests that not all studies are measuring the same thing but does not necessarily mean that the true effect varies.[139] Statistical heterogeneity can be assessed using the Chi-squared statistic, χ^2, as well as the I-squared measure. I-squared is a measure of the proportion (as a %) of the observed variance that reflects differences in effect size; as such, a low p value for I-squared indicates that there is significant heterogeneity and variation in effect sizes between studies is likely due to this heterogeneity, not chance.[150] I-squared does not measure how much the effect size varies across studies.[151]

Significant heterogeneity may imply that studies cannot be considered as from comparable populations. Assessing heterogeneity using I-squared is useful for determining whether subgroup analyses are warranted to explore sources of heterogeneity.

2.2.7.7 Testing for publication bias and small study effects

Publication bias happens when published research does not represent all completed studies.[152] This occurs as studies with significant and/or positive results are more likely to be published than those without, meaning that meta-analysis may be influenced if unpublished studies with smaller and/or statistically non-significant effect sizes have not been included. [153]

Small study effects are a potential sign of publication bias and can be investigated by the creation of a funnel plot (plotting effect estimates from individual studies against their CIs, which is usually a reflection of sample size). This is only recommended for meta-analyses of at least ten studies, as statistical power is low with fewer studies than this.[154,155] An asymmetrical funnel plot, in which smaller studies at the bottom of the plot are missing, may indicate the presence of small study effects.[154]

2.2.7.8 Narrative synthesis

Where meta-analysis is not possible in a systematic review of interventions, the synthesis without meta-analysis (SWiM) reporting guideline can be used to determine how results can be presented.[156] SWiM aims to ensure transparency in the methods used, as narrative synthesis methods are rarely reported, and validity of the findings. This guideline was developed by a group of experienced systematic reviewers and consists of nine items to be reported in the absence of meta-analysis, including alternative synthesis methods such as effect size summaries, combining p values, and vote counting based on direction of effect.[156]

2.2.7.9 Individual participant data (IPD) meta-analysis

IPD meta-analysis is not performed as part of this thesis and, as such, methods will not be described in detail. The Cochrane handbook states that IPD reviews should be considered when available published data do not permit a high-quality review or when an aim of the review is to look at the effects of subpopulations and effect modification.[66] IPD analysis allows each participant's individual characteristics to be taken into account along with intervention status and outcome; this may allow factors that affect outcomes other than the intervention to be identified, such as confounders, and whether interventions work better in some populations than others.

An IPD approach allows standardisation of outcomes across trials and detailed data checking.[66] It also allows trials that are unpublished or incompletely reported to be considered and included and, where data are sufficient, subgroup analyses can be performed to look at the effects of certain characteristics such as age or sex (which is less likely to be feasible when using aggregate data).[157] Disadvantages of this approach are that data may be incomplete or difficult to obtain and may also need to be recoded and reformatted, which can be time consuming.[66] Again, PRISMA guidelines have been developed that are more specific to IPD reviews.[67]

2.2.8 Grading the evidence

2.2.8.1 Introduction to GRADE

GRADE was created by a group of international guideline developers as a response to the perceived shortcomings of the study grading systems that were already in place. GRADE is used to rate the certainty of a body of evidence in systematic reviews (as well as other syntheses such as guidelines and clinical recommendations) that aim to examine the effect of interventions, compared to no intervention, current practice, or other interventions.[158]

Applying GRADE to a review ensures that the strength of the evidence behind the result for each outcome is discussed (some criticisms of systematic reviews have been based on the inclusion of low-quality, and therefore low certainty, evidence that should not inform decision making).[159] GRADE adds transparency to a review and ensures that the studies contributing to an effect measure are considered in detail, rather than focusing solely on the effect estimate itself.

2.2.8.2 Rating the certainty of evidence

The certainty of evidence is defined as "the extent to which we are confident that an estimate of the effect is correct".[160] Overall judgements are made on the level of certainty for the effect measure for each outcome of a review, based on the strength of evidence of studies that contributed to each one. This rating system is based around the hierarchy of evidence referenced in Chapter 1;[28] randomised trials without important limitations are counted as high quality evidence and observational studies that do not have 'special strengths or important limitations' are deemed low certainty. There are four levels of certainty in total (Table 3) and studies may be moved between levels based on criteria such as risk of bias and the effect size found.[160]

From this table, randomised trials with no important limitations should initially be marked as high certainty whereas observational studies with limitations and no 'special strengths' should be categorised as low certainty; however, it is possible for these labels to be changed

based on additional details. The certainty of evidence may be upgraded when based on studies with large effect sizes, when all possible confounding would reduce the effect or increase the effect if none was observed, or when a dose-response gradient is shown.[160,161] Upgrading is contingent on no other GRADE domains being downgraded. The certainty of evidence may be decreased based on five domains: 1. Risk of bias (if risk of bias of the included studies is considered to be significant), 2. Imprecision (if confidence intervals are wide, and/or of if the effect size is based on few studies or few events), 3. Inconsistency, when individual studies show differing effects, 4. Indirectness, when the intervention(s) and/or study population(s) do not directly address the review question, and 5. Publication bias, if it is likely that evidence from unpublished studies is missing.[160,161]

Study design limitations that may reduce the quality of evidence for RCTs are: lack of allocation concealment and blinding, not including all patients in the analysis, and selective outcome reporting; for NRS: the inclusion of an appropriate control population, measurement of exposure and outcome, whether confounding was controlled, and whether follow-up was appropriate.[160]

Table 3 – GRADE definitions of certainty of evidence

Grade	Definition
High	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate	We are moderately confident in the effect estimate: The true effect is likely close to the estimate of the effect, but there is a possibility that it is substantially different.
Low	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
Very low	We have very little confidence in the effect estimate: The true effect is likely substantially different from the estimate of effect

2.2.8.3 Reporting and interpreting GRADE

After grading the evidence, review authors need to ensure that the results are written in a manner that means they will be interpreted correctly. GRADE judgements should be reported in summary of findings tables so that readers can easily find effect sizes and the accompanying certainty of evidence for important outcomes.

Thought should also be given to how to present GRADE ratings in order to ensure that they are understood – simply stating the rating means that the reader is tasked with looking up the definitions and interpreting them.

Santesso et al. created a guideline that aimed to effectively convey the findings of reviews using GRADE assessments,[162] which draws from workshops that identified the importance of statements that incorporated both the GRADE verdict and the size of the effect estimate. A template was then created where the recommended wording is based on the size of the effect estimate and the certainty of the evidence. Standardised wording may be useful, but could also be confusing to people who are unfamiliar. For instance, phrases such as "there may be little to no difference",[162] intended to be used when there is a small important effect with low certainty of evidence, are open to interpretation to the reader; the words 'may' and 'likely' are likely be understood differently in different settings.

When communicating the results of a systematic review and meta-analysis, GRADE and the certainty of evidence should be considered first. The effect estimate and CIs should then be considered in light of this, for example a large effect size with small CIs is an unlikely indication of the true effect if the GRADE rating is very low. Less importance should be given to statistical significance, where the emerging consensus is that this should be devalued in favour of the magnitude of the effect and what this means.[163,164]

2.2.9 Summary of findings tables

As mentioned above, summary of findings tables can be constructed to present the findings of systematic reviews and meta-analyses. This enables readers to easily find the main results for a review, and to display the results for all the main comparisons next to one another.

Cochrane guidance for creation of summary of findings tables suggests that they should include: a description of the population, setting, and comparison that are being addressed; the most important outcomes (up to seven), their associated effect sizes, and the numbers of participants and studies contributing to these effect sizes; and the GRADE assessment for each analysis.[165] Which outcomes are to be reported in summary of findings tables should be specified in the review protocol.

2.3 Core outcome sets

2.3.1 Introduction to core outcome sets

A COS describes a standardised set of outcomes that should be reported and measured in all studies in a specific area as a minimum.[82,83] COS do not restrict the outcomes that can be

measured by individual studies, rather they specify those that should be measured. This means that trials can use a COS and measure additional outcomes that are relevant to their study. As described in the previous chapter, COS have been created for studies in several areas of maternity care.

This chapter will give a brief overview of COS methodology, using the Core Outcome Measures in Effectiveness Trials (COMET) handbook as a guide,[82] as well as describing where there is potential for variation. Detailed methods for the creation of a COS for studies of RFM will follow in Chapter 4. This thesis also focuses on the first stage of COS development: defining 'what' should be measured (meaning the outcomes themselves), rather than the second (defining 'how' to measure these outcomes, for which separate guidance exists).[166]

2.3.2 Developing the question

The COMET handbook recommends a five-step process for the creation of a COS.[82] Similarly to planning a systematic review, the first step should be to define the scope of the COS using PICO to specify which area of health or healthcare the COS applies to. It is recommended that the next step is to establish the need for a COS by checking the COMET database to see whether one already exists.[82] Once a gap for a COS is established, authors can write a protocol for the study, which should be registered with COMET, and the systematic review process can commence.

2.3.3 Identifying relevant outcomes for a COS

2.3.3.1 Using a systematic review

Standard systematic search methods, as detailed earlier, should be followed with the aim to identify all relevant studies so that a list of outcomes measured by these studies can be created. Once all studies are identified, their characteristics should be recorded as well as the outcomes that they measured and how these outcomes were measured (what instruments or scales were used, and the definitions used by the authors). Multiple definitions of the same outcomes can also be combined in a similar manner to the screening process in systematic reviews described previously, this should be performed by at least two reviewers to avoid errors. Definitions should be retained for transparency and for use later in the process.[82] Unlike a 'traditional' systematic review/meta-analysis, data on the number of events for outcomes is not needed; there is also no risk of bias assessment, data synthesis, or GRADE assessment.

2.3.3.2 Using qualitative methods

Qualitative methods such as focus groups and interviews may also be used to identify relevant outcomes; this can help to identify outcomes that are most important to stakeholders (and why these outcomes are important) and ensure that the language used is appropriate for surveys.[167]

As an example of this, the GASTROS study used qualitative interviews after outcomes had been identified by a systematic review, to take patients' perspectives into account and to identify any outcomes important to patients that may not have been identified by literature searches.[168] Whether these approaches are feasible may depend on the time and resources available to the research team, and the experience of researchers.

2.3.4 Creating a core outcome set

2.3.4.1 Planning a Delphi survey

The Delphi survey process provides a way for participants to rate the importance of outcomes. The majority of Delphi surveys are conducted online, increasing the potential for larger sample sizes and greater diversity of respondents. Surveys can be conducted using software such as REDCap[169,170] or DelphiManager.[171] Other advantages of online surveys compared to postal or telephone surveys include: reduced costs, greater ease of digital data collection, and the ability to send automated reminders using an online management system.[172] Most Delphi surveys are conducted in English, which has the potential to restrict the number of participants. Alkhaffaf et al. showed that 315 participants in the GASTROS study used the English language version of the Delphi, compared to 637 participants who used one of seven translated versions.[173] Providing translations in more languages is optimal, although the ability to do this will depend on the resources available and the study team should consider the expected reach of the survey.

2.3.4.2 Rating the importance of outcomes and defining consensus

A scoring system that allows the most important outcomes to be forwarded to the consensus meeting should be used (with outcomes being removed between rounds based on their scores). COMET recommends that a Delphi survey should consist of at least three rounds; most COS have two or three rounds, with rare examples of more than this.[82]

The majority of COS allow participants to rate outcomes using Likert scales, for which each outcome is assigned a numerical value depending on its perceived importance.[82] For example, on a nine-point scale, a score of 1-3 indicated limited importance, 4-6 signifies importance, and 7-9 should be given to critically important outcomes. Seven and five point scales are also in use, the choice of scale used may also depend on the survey software

available; any scale can be programmed in REDCap but Delphi manager only allows a nine point scale.

Criteria for retaining outcomes between rounds, based on their scores, also need to be decided upon. Suggested criteria for 'consensus in' (meaning an outcome is included) are that outcomes are scored between 7 and 9 on a nine point scale by 60%,[174] 70%,[175] or 75%[176] of participants.[82]

2.3.4.3 Recruitment of participants

A crucial step in the development of COS is to determine key stakeholder groups that will be involved. For healthcare interventions these are likely patients and healthcare providers (for example, midwives and obstetricians should be included for COS in maternity care). The involvement of these groups throughout the process should also be considered, i.e. whether stakeholder groups will be involved with developing the COS methods or whether they will only participate in the study. Recruitment should aim to minimise bias by recruiting a large international sample from several stakeholder groups. A small sample may lead to a COS that is an inadequate representation of the importance of outcomes, which in turn may affect uptake, and if the participants in a survey do not provide an adequate representation of each stakeholder group then this may introduce response bias to the survey.[82]

Recruitment strategies can be tailored to the stakeholder groups the study is aimed at. When recruiting healthcare users it may be useful to promote the study in healthcare settings such as clinics, as well as patient organisations and by using social media.[177] It may be beneficial to create a dedicated website and/or social media account(s) for a study to help disseminate information about the COS and to help with recruitment.[178] When providing study information such as participant information sheets, it may help to use plain English and/or to create separate information sheets for professionals and healthcare users for ease of understanding.[178]

Relevant professionals such as clinicians and researchers can be targeted directly and also asked to forward the survey to others who may be interested (snowball sampling). The COMET handbook recommends that, if possible, a "distinguished researcher in the field" should help with recruitment by sending personalised emails[82] and research has also shown that selecting participants based on their publication record may make them more likely to take part.[178]

Views on the importance of certain outcomes are likely to differ between groups,[179] therefore, it is important to include a wide range of participants and to consider their views equally. The criteria for forwarding outcomes between Delphi rounds, or for including outcomes at the consensus meeting, can be created with this in mind — for example stipulating that outcomes must be selected by at least one member of each stakeholder group. This decreases the likelihood that the COS is heavily influenced by one particular group.

2.3.4.4 Retaining participants

One of the main challenges when running a COS is managing attrition of participants between rounds. If there is a lot of attrition, or if attrition affects some stakeholder groups more than others, then the COS may not accurately reflect participants' views.[82] The choice of Likert scale used and how well it is explained may affect participants' understanding and willingness to participate in the study — a five-point scale may be more easily viewed on a smartphone than a nine-point scale, for example. Ensuring that participants understand how the scale works, i.e. whether certain scores mean that an outcome is likely to make the final COS, can also affect attrition as participants may become fatigued and lose interest if rating the same outcomes again and again.[82]

Methods to maintain engagement with a study and increase participant retention include: email reminders (personalised where possible), email and social media updates about the study, and extending deadlines.[178] Responses can be monitored, and these strategies can be applied to specific stakeholder groups if some are showing more attrition than others.[82] However, it should also be considered that interest in a COS is likely to diminish over time and participants may become frustrated if rounds are extended for too long or if there is too much time between rounds.[172]

Delphi surveys containing a larger number of outcomes to rate are also associated with lower response rates.[180] Nevertheless, the amount of outcomes is determined by the systematic review (unless too many similar outcomes that could be combined are included) and should not be edited based on this. Nevertheless, it may be prudent to anticipate whether this is likely and plan reminders and updates accordingly. In a scenario where there are a lot of outcomes, it may be wise not to plan a COS with no more than three rounds and with stricter criteria for removing outcomes.

2.3.4.5 Consensus meeting

The outcomes selected by the Delphi process are forwarded to the consensus meeting, in which stakeholders decide by majority vote which of these outcomes will make up the final

COS. Similar definitions for consensus can be used as described above, and thought should be given as how to ensure that all groups' voices are heard; Potter et al. recommend holding separate meetings as a way to combat this.[181] It is important for the participants at the consensus meeting to be a representative sample of all stakeholder groups that completed the Delphi survey.

2.3.4.6 Reporting the results

The COS-STAR checklist was developed by an international group with experience of COS, whether in their creation, usage, or patient representatives.[182] This checklist aims to aid transparent and complete reporting of COS by providing an 18-item checklist that should be reported as a minimum.

2.4 Surveys of clinical practice

2.4.1 Introduction

Surveys can be used to obtain an overview of clinical practice in a given area, examples in maternity care have been described in Chapter 1. This section will give a brief overview of some methodological considerations when designing surveys, specific methods for developing a UK-based survey of knowledge and practice related to RFM will be described in Chapter 5. The first step should be to design a research question, which can then inform the survey structure and targeting of potential participants, as well as required sample sizes.

2.4.2 Methods

2.4.2.1 Recruiting participants

Previous surveys have recruited participants by sending questionnaires in the post via relevant organisations.[2,103,104] Recruitment may also take place online, via e-mail lists, contacting participants directly, or social media, as described in the COS section of this chapter. Researchers should consider their target audience and which methods of recruitment would be most appropriate, most effective, and easiest to implement. The language used should also be considered for international surveys.

2.4.2.2 Surveying participants

Again, surveys can be conducted using software mentioned previously (such as REDCap or Delphi Manager). It may be beneficial to conduct literature searches to see if the research question has been previously (and recently) addressed;[183] this approach was taken by a survey of practice related to umbilical cord clamping.[100] If a survey has been conducted in the same area of practice, then this can be used as a template questionnaire, while thought should be given as to whether the questions are up to date (for example, if any guidelines

are referred to). If the survey consists of Likert scales or tick boxes then researchers may also wish to add the option for participants to explain their answers.[100]

A major challenge in online surveys is overcoming low response rates, rates may be increased by providing clear instructions to participants and may be also affected by survey length and ease of participation.[184,185] Piloting surveys may help to assess their readability and validity.[185] If a single-round survey is being conducted then attrition does not need to be considered.

2.4.2.3 Analysing responses

Statistical differences between groups (midwives and obstetricians, for example, or other demographic details if collected) in their responses can be assessed using the chi-squared test.[2,100] Results can be described narratively, displayed in tables, or as histograms or other simple charts.

2.4.2.4 Reporting results

Eysenback (2004) developed the Checklist for Reporting Results of Internet E-Surveys (CHERRIES), which was designed to improve the reporting of web-based surveys.[186] Following this checklist allows readers to see details about the target population, namely how representative the sample is, how the survey itself was developed, and how the survey was promoted and accessed. This checklist also encourages survey authors to publish the response rates for their survey and how incomplete responses were treated.

Chapter 3 - Effect of encouraging awareness of reduced fetal movement and subsequent clinical management on pregnancy outcome: a systematic review and meta-analysis

Work from this chapter has been published as:

Hayes, D.J.L., Dumville, J.C., Walsh, T., Higgins, L., Fisher, M., Akselsson, A., Whitworth, M. & Heazell, A.E.P. Effect of encouraging awareness of reduced fetal movement and subsequent clinical management on pregnancy outcome: a systematic review and meta-analysis. *AJOG MFM* (2022) https://doi.org/10.1016/j.ajogmf.2022.100821

DH was responsible for study design, writing the study protocol, literature searches, screening papers according to inclusion and exclusion criteria, data extraction, data analysis, writing the first draft of the manuscript, and subsequent edits.

3.1 Abstract

Background

RFM, defined as a decrease in maternal perception of frequency or strength of fetal movements, is a common reason for presentation to maternity care. Observational studies demonstrate an association between RFM, stillbirth, and FGR related to placental insufficiency but data from individual intervention studies has described varying results. This systematic review and meta-analysis aimed to collate data from RCTs and high-quality NRS to determine whether awareness of fetal activity and management of RFM can reduce the frequency of stillbirth or other important secondary outcomes.

Methods

This review was conducted according to a published protocol (CRD 42018088635). Searches were conducted in MEDLINE, EMBASE, Cinahl, The Cochrane Library, Web of Science and Google Scholar. Guidelines, trial registries, and grey literature were also searched. Risk of bias was assessed using Cochrane Risk of Bias 2 and ROBINS-I for randomised studies and NRS respectively. Interventions were classified using the TIDieR checklist. The primary outcome was stillbirth; secondary outcomes were divided into maternal outcomes (including proportion of induced labours, mode of birth, postpartum haemorrhage, measures of maternal-fetal attachment and maternal anxiety) and neonatal outcomes, including: neonatal death, perinatal death (stillbirth or death within 7 days of birth), small-for-gestational-age

infant, Apgar score <7 at 5 minutes of age, preterm birth (<37 weeks of pregnancy), NICU admission.

Results

1,609 citations were identified; 190 full text papers were evaluated against the inclusion criteria, 18 studies (16 RCTs and 2 NRS) were included. Interventions were classified as: 1) encouraging awareness of fetal movement, or fetal movement counting, 2) subsequent clinical management of combined interventions.

The evidence is uncertain about the effect of encouraging awareness of fetal movement on stillbirth compared with standard care (two studies, n=330,084); pooled OR 0.88 (95% CI 0.77 to 0.99). Interventions for encouraging awareness of RFM were associated with a reduction in NICU admissions and Apgar scores <7 at 5 minutes of age; there were no increases in caesarean section or induction of labour.

The evidence is uncertain about the effect of encouraging fetal movement counting on the proportion of stillbirths when compared with standard care; pooled OR 0.69 (95% CI 0.18, 2.65), data from 3 RCTs (n=70,584). Counting fetal movements may increase maternal fetal attachment and decrease anxiety when compared with standard care. When comparing interventions for encouraging awareness of RFM and subsequent clinical management with standard care (one study, n=393,857) the evidence is uncertain about the effect on stillbirth (aOR 0.86, 95% CI 0.70, 1.05).

Conclusions

The effect of interventions for encouraging awareness of RFM alone or in combination with subsequent clinical management on stillbirth is uncertain. Encouraging awareness of RFM is associated with reduced adverse neonatal outcomes without an increase in interventions in labour. Meta-analysis is hampered by variation in intervention, outcome reporting and definitions. Individual studies are frequently underpowered to detect a reduction in severe, rare outcomes and no studies were included from high-burden settings. Studies in high-burden settings are needed to determine whether interventions can reduce stillbirth.

3.2 Introduction

3.2.1 Reduced fetal movements

RFM (sometimes defined as absent or reduced fetal movements or ARFM) are defined as a decrease or change in maternal perception of a baby's normal pattern of movements *in utero*.[1] Awareness of fetal movements usually happens by 18-20 weeks of gestation and usually people who are pregnant become aware of the pattern of their baby's movements and the time of day that the baby moves the most.[187] Two Confidential Enquiries into Antepartum Stillbirth conducted ten years apart highlighted the importance of information about fetal movements and a clear plan of management for RFM.[188,189] However, there is no accepted widespread consensus regarding the definition of RFM or its management.[2,104]

A 2005 study found that maternal concerns about RFM lead to presentation at hospital in up 15% of pregnancies,[190] though it should be noted that most included studies were from high income countries. Around 70% of these pregnancies have a normal outcome but RFM are associated with adverse outcomes such as stillbirth and FGR.[191] Case control studies have consistently demonstrated an association between RFM and stillbirth after 28 weeks' gestation.[192–194] An individual participant data meta-analysis with data from five studies (n=3,108) reported an adjusted OR (aOR) of 2.33 (95% CI 1.73 to 3.14) for stillbirth with a decreased frequency of fetal movement in the last 2 weeks.[12] It is important to recognise that some study designs may suffer from recall bias from asking about perception of RFM after a pregnancy has already ended in a stillbirth; still, these studies show similar effects across different populations, supporting the potential for a common aetiology. Several studies have demonstrated links between RFM and placental pathology, particularly those relating to maternal vascular malperfusion[15,16,195] which are linked to adverse outcome. This provides a mechanistic link between RFM, FGR and stillbirth.

The association between RFM and stillbirth is thought to represent fetal compensation in cases of insufficient nutrient transfer and hypoxia, which may be caused by placental insufficiency (where the placenta cannot meet the metabolic demands of the fetus) or other fetal stressors, in an attempt to conserve energy and oxygen consumption.[8,196]

Perception of RFM may be affected by other risk factors for adverse outcomes. A systematic review of 27 observational studies that aimed to explore risk factors associated with RFM identified that anterior placenta, ethnicity, oligohydramnios, polyhydramnios, and smoking may be predictive of RFM.[197] The association between RFM and other maternal factors such as body mass index (BMI) and parity is also still unclear.[198]

Criticism of RFM as an indicator of adverse outcome is based on its low specificity (as stated above, most RFM pregnancies will have a normal outcome), meaning that interventions based on maternal perception of RFM alone may lead to unnecessary clinical interventions such as induction of labour or caesarean section.[199] A diagram demonstrating how these interventions might work, as well as potential harms, plus confounding factors that may alter their effectiveness is shown in Appendix 7.1.

3.2.2 Studies of interventions for RFM

The broad aim of interventions focused on RFM should be to identify those pregnancies in which RFM is a symptom of underlying fetal compromise and to prevent adverse outcomes that would otherwise arise as a result via subsequent clinical management, while at the same time not doing any harm. Interventions can be split into two categories: 1) those that aim to encourage awareness of the pattern, strength, and/or frequency of fetal movements and/or fetal movement counting by clinicians, other healthcare professionals, or in people who are pregnant and 2) those that employ subsequent clinical management when there is concern about RFM to identify fetal compromise.[9,200,201] Studies may employ one or the other approach, or a combination.

In high income settings, several large randomised trials have shown insufficient evidence of an effect of interventions on the proportion of stillbirths.[200,202] The 2015 Cochrane review of interventions for fetal movement counting for assessment of fetal wellbeing (date of the last literature search the 31st May 2015) included data from five randomised controlled trials (RCTs) (n=71,458) but reported ongoing uncertainty about the potential benefits or harms of formal fetal movement counting.[203] A 2016 review including both randomised and non-randomised studies (NRS) included data from 16 studies and also reported no clear evidence of harms or benefits for interventions to raise maternal awareness of RFM.[204] A 2020 systematic review and meta-analysis of five randomised trials of fetal movement counting reported a RR of 0.92 (0.85 to 1.00) for perinatal death and 0.94 (0.71 to 1.25) for stillbirth; these analyses used data from two and three trials respectively and the certainty of the evidence was not assessed using GRADE.[73] One RCT of a combined intervention for encouraging awareness of RFM and its subsequent clinical management was included in this review; but in general, studies of clinical management of RFM have not been the focus of systematic reviews due to a lack of RCTs in this area.

3.2.3 Current UK guidance and management strategies

Current UK guidance from the NHS and the National Institute for Health and Care Excellence (NICE) regarding RFM is to contact a midwife or maternity unit if your baby is

(or babies are) moving less than usual or not at all.[205,206] Guidance with respect to clinical management is variable. In the UK, the Royal College of Obstetricians and Gynaecologists (RCOG) Green-top Guideline 57,[11] in place since 2011, states that there is 'insufficient evidence to recommend formal fetal movement counting'. Guideline evidence was given a 'B' rating, meaning that it is based on high quality observational studies only. It is stated that pregnant women should be advised to be aware of their baby's movement patterns; this is given a 'C' rating as it draws from studies rated 2+ (high quality cohort studies with low risk of confounding and moderate probability of a causal relationship).

Ultrasound scanning is recommended, but only in presentations with RFM after 28 completed weeks of gestation where the perception of RFM persists or in the presence of risk factors for stillbirth or FGR. This recommendation is given a 'B' rating as it is based on a prospective cohort study rated as 2+.[207]

In recent years, several RCTs and NRS measuring the effect of interventions for RFM have been conducted and their results published; this research effort could be due to the ongoing uncertainty shown by systematic reviews and guidelines. Consequently, the management of RFM (where management is defined as encouraging awareness of RFM and/or its subsequent clinical management) is not currently informed by all the available evidence. Conducting a systematic review including both randomised and non-randomised studies will not only provide an updated view of available evidence but will also maximise the pool of evidence that has so far been synthesised.

3.2.4 Aims and objectives

The primary objective of this systematic review is to determine whether encouraging awareness of RFM and/or the subsequent clinical management of pregnancies with RFM affects adverse maternal or perinatal outcomes, when compared to other management strategies or no management.

Secondary objectives are:

- to determine whether there is an optimal management strategy for RFM pregnancies
- to determine if some management strategies are more effective than others
- to describe the state of current evidence and identify gaps in the literature

3.3 Methods

3.3.1 Review protocol

The protocol for this review was registered with the International Prospective Register of Systematic Reviews (PROSPERO) on 16/10/2020 (CRD 42018088635).[208] The published protocol can be seen in Appendix 7.2. The PRISMA Statement was followed in the reporting of this systematic review and meta-analysis.[24]

3.3.2 Inclusion criteria and search strategy

We included studies of any interventions that aimed to encourage clinician or maternal awareness of RFM in pregnancy and/or any interventions for the subsequent clinical management of RFM. Interventions may comprise clinical training, information campaigns, or instructions to be aware of or to count fetal movements during pregnancy. Information may be given in the form of leaflets, videos, training sessions, or other material. Interventions may be delivered alone or in combination.

Studies were included if they reported data from singleton pregnancies after 24 completed weeks of gestation, with data on those who presented at least once in a hospital setting. Included definitions of RFM are those based on maternal perception and/or confirmed by clinical assessment of fetal activity. The gestational age threshold has been set at 24 completed weeks as this is consistent with the definition of stillbirth in the UK (from 1992 to present).[209]

Study types considered for inclusion on this review were randomised controlled trials (RCTs), quasi-randomised controlled trials and some NRS: to be eligible, non-randomised controlled studies needed to have a clearly reported mechanism of group formation, clearly defined inclusion criteria, and described methods of ascertainment of eligible patients and their recruitment. NRS designs that fit these criteria may include cohort studies with prospective or retrospective controls, controlled before-after studies, or interrupted time series studies. These study designs allow interventions at both the individual and organisational level to be included. Cross-sectional studies, case control studies, and cohort studies without clearly defined comparator groups were not included as their internal validity was considered too poor for any exploration of intervention effectiveness.

The following electronic bibliographic databases were searched: MEDLINE, EMBASE, Cinahl, The Cochrane Library, Web of Science and Google Scholar. Guidelines, trial registries, and grey literature were also searched. Studies were included irrespective of their publication status and language of publication; the date of the last search was 20th January 2022. Search strategies are included as Appendix 7.3.

3.3.3 Outcomes of interest

The primary outcome of this review is stillbirth, defined as the death of a baby before birth and after 24 weeks of gestation, or as described by the authors (as definitions may vary between study populations and over time). Secondary outcomes were divided into maternal and neonatal outcomes. Maternal outcomes were: proportion of induced labours, mode of birth, postpartum haemorrhage, measures of maternal-fetal attachment and maternal anxiety using any standardised scale, time taken to present to hospital after perceiving RFM, and measures of delayed presentation with RFM. Neonatal outcomes were: neonatal death (death of a baby during the first 28 days of life), perinatal death (stillbirth or death within 7 days of birth), small-for-gestational-age infant (birthweight <10th percentile or the threshold used in the study if different), Apgar score (<7 at 5 minutes of age), preterm birth (<37 weeks of pregnancy), NICU admission, umbilical artery pH <7.05 or BE >-12 (indicating neonatal asphyxia[210]).

3.3.4 Study selection and data extraction

Titles and abstracts of studies retrieved using our search strategy were screened by two authors independently (DH and AH) to see if they met the inclusion criteria, disagreements were resolved by consulting a third author. Full texts were obtained for included studies where possible and a standardised, pre-piloted form was used to extract data. Data were extracted by two authors independently (combinations of DH, MW, LH and AH) and discrepancies were amended through discussion. Studies in progress were also eligible for inclusion.

Where possible, study protocols were obtained for more information on study design to determine whether data for all pre-specified outcomes were reported. Attempts were made to contact study authors via email if a protocol was not available, if any characteristics of the intervention were unclear, or to enquire about unpublished data for secondary outcomes. TIDieR checklists[135] were used to extract information from each study about the nature of the intervention and to record details such as intervention fidelity.

3.3.5 Assessment of risk of bias

Risk of bias was assessed for randomised controlled trials using the Cochrane Risk of Bias 2 (RoB 2) tool;[211] for non-randomised studies the ROBINS-I tool was used.[131] For assessment of confounding, which is especially important in NRS, we considered key confounders to be: estimated birthweight centile, maternal body mass index (BMI), deprivation index, maternal ethnicity, fetal sex, gestation at birth, maternal age, gravidity and/or parity, and stillbirth rate in the study population. Two authors independently

assessed risk of bias and consultations took place in the case of any disagreements. Input of a third reviewer was planned if needed but was not required.

3.3.6 Assessment of heterogeneity and sensitivity analyses

Heterogeneity can be classified as clinical due to differences in study populations or treatment types; methodological in terms of study design and conduct or statistical in terms of variation of effects. Statistical heterogeneity was assessed using methods outlined in Chapter 10 of the Cochrane Handbook.[139] Significant statistical heterogeneity suggests that not all studies are measuring the same outcome but does not necessarily mean that the true effect varies.[139] The Chi-squared statistic, χ^2, [as] as well as the I-squared measure, was calculated to assess whether any differences in effect sizes between studies are likely due to chance; a low p value indicates that there is significant variation due to heterogeneity and variation is unlikely to be due to chance.[150] Heterogeneity was classified as low (I^2 = 0–40%), moderate (I^2 = 41–60%), substantial (I^2 = 61–80%), or considerable (I^2 = 81–100%).[23]

Sensitivity analyses were planned (if there were sufficient numbers of included studies) to determine whether effect sizes are influenced by risk of bias (for example, excluding studies at high risk of bias in meta-analysis to see if effect sizes differ) and to determine whether studies that did not exclude multiple pregnancies and congenital anomalies have a significant effect on the overall estimates. Analyses were also planned to look at the effects of including unadjusted effect size estimates.

3.3.7 Data synthesis

Interventions were broadly classified using the categories in the review protocol (CRD 42018088635)[208] and studies assessing similar populations and interventions were grouped for analyses — more detail is given in Appendix 7.4.

Adjusted effect estimates were presented from included studies where possible. When adjusted values were unavailable, for binary outcomes we calculated ORs and their corresponding 95% CIs. Where adjusted and unadjusted estimates were reported, we presented the adjusted effect estimates (aORs). Where adjusted and unadjusted estimates were provided for the same outcome and intervention grouping, these were displayed as subgroups on the forest plot.[212]

Binary data were combined using the random effects method (DerSimonian and Laird inverse variance[148]). For continuous outcomes, the standardised mean difference (SMD) was calculated along with corresponding 95% CIs using the mean difference or

standardised mean difference where outcomes were measured on different scales. Effect estimates for randomised and non-randomised studies were calculated separately.

When studies had zero events for an outcome in both the intervention and comparator group then they were not included in analyses. A correction of 0.5 was added if there was one group with zero events. Where synthesis was not possible, data from individual studies are reported. Data from secondary outcomes are only reported when available.

3.3.8 GRADE

GRADE[158,160] was used to determine the certainty of the body of evidence by assessing study design, inconsistency of results, indirectness of evidence, imprecision, and publication bias. This assessment reflects the extent to which we are confident that the estimate is certain for any given finding, and was carried out for all comparisons for the outcomes of stillbirth, perinatal death, and neonatal death. Evidence from randomised studies starts out as high certainty, evidence from NRS starts out as low certainty; [213] this can then be upgraded or downgraded after assessing the characteristics of included studies.[214]

3.4 Results

3.4.1 Literature search and characteristics of included studies

From literature searching we identified 1,609 citations. These were screened on the basis of their titles and abstracts and 190 full text papers were obtained and evaluated against our inclusion criteria, resulting in 18 included studies (

Figure 1 – PRISMA flow diagram). These studies are described in Table 4 and excluded papers that were screened as full text are described in Appendix 7.5. Additional data, study protocols, and/or further detail about the study were obtained from three authors.[146,215,216]

In total, 16 RCTs and two NRS were included. Of the RCTs, 12 focused on interventions aiming to encourage fetal movement counting and/or awareness of fetal movement in pregnant women and/or healthcare professionals, three focused on the subsequent clinical management of RFM after identification, and one employed a combination of these. Of the NRS, one focused on comparing interventions to encourage maternal awareness of RFM and the other focused on the subsequent clinical management of RFM after identification.

One ongoing trial was identified; a multicentre cluster RCT comparing measurement of the cerebroplacental ratio in RFM with standard care in otherwise low risk RFM pregnancies.[217]

3.4.2 Risk of bias

Nine of the 16 included RCTs were rated as at low risk of bias overall; the other seven RCTs were rated as at high risk (**Error! Reference source not found.**). Concerns were mainly due to deviations from the intended intervention,[37,77,146,200,202] where intervention fidelity was low in some studies, and were also due to the adequacy of the randomisation process.[200,218–221]

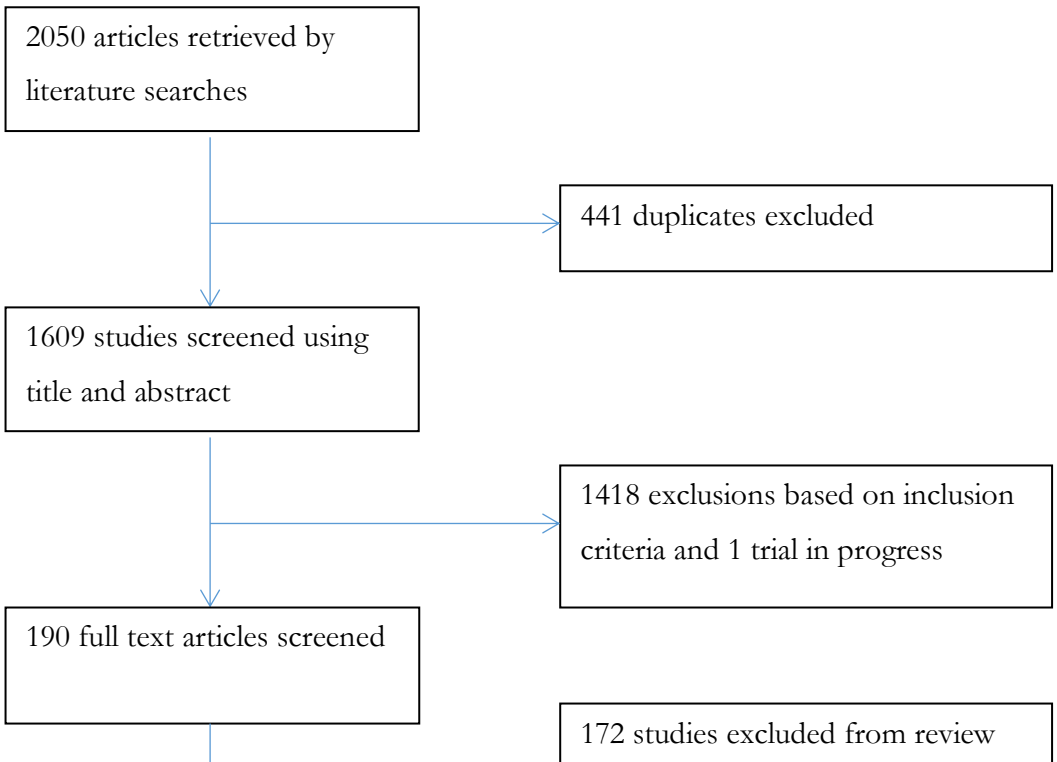


Figure 1 – PRISMA flow diagram

Table 4 – Characteristics of included studies

Study	Study design	Population	RFM management in intervention group	RFM management in control group	Recurrent RFM	Outcomes
Randomised studies						
Abasi, Tafazoli & Esmaeili 2010[218]	RCT comparing fetal movement counting to standard care	**BMI:** not stated **Gestation**: 28-32w **RFM**: kick chart **Risk**: low (obstetric problems excluded) **Timeframe**: n/s n= 83	Pregnant women given training on fetal movement recording, asked to count fetal movements for one month daily after breakfast for half an hour	Standard care (no training given, no fetal movement counting)	No information	Maternal-fetal attachment
Akselsson et al. 2020[9]	Cluster RCT comparing Mindfetalness to standard care	**BMI:** 24.3 in intervention, 24.4 in controls	Leaflet about fetal movements given at 24 weeks' gestation and a lecture was held for midwives. Women were asked	Routine care at obstetric clinics.	No information	Stillbirth (after 32 weeks' gestation).

	across 78 maternity clinics in Sweden	**Gestation:** >24w **RFM:** maternal perception **Risk:** mixed **Timeframe:** Nov 2016 to Jan 2018 n= 39,865	to practice Mindfetalness from week 28 until birth; women were instructed to lie on their sides for 15 minutes per day and monitor fetal movements, seeking care if they were worried about fetal wellbeing. Monthly newsletters sent.			5 min Apgar <7, 5 min Apgar <4, BW <10th centile, CS, NND <27 days, NICU admission, PTB <37w, SGA <10th centile
Armstrong-Buisseret et al. 2020[222]	RCT comparing standard care with standard care plus an additional blood test	**BMI:** n/s **Gestation:** 36-41 w **RFM:** maternal perception **Risk:** mixed **Timeframe:** Mar-Dec 2018 n=216	CTG and ultrasound for all presentations with RFM, women with abnormal CTG were not recruited. All women had blood samples taken and were offered expedited birth at 37+0 if their sFlt-1:PlGF ratio was above 38.	All women had CTG and ultrasound at presentation as part of standard care. Women with abnormal CTG were not recruited.	29/107 in the control group and 27/109 in the intervention group presented more than once	Stillbirth (fetal death recorded after 36 weeks) 5 min Apgar <7, CS, EmCS, IoL, NICU admission, NND, perinatal death, SGA (INTERGROWTH and GROW), UA pH<7.05.

Delaram & Jafarzadeh 2016[146] / Delaram & Shams 2016[223]	RCT comparing fetal movement counting with a control group	**BMI:** average 24.82 (2.66) in control group, 24.22 (3.23) in intervention **Gestation:** >28w **RFM:** kick chart **Risk:** mixed **Timeframe:** n/s n=208	Fetal movement counting from 28 weeks' gestation; women were asked to lie in the left lateral position and count fetal movements every morning for half an hour, kick charts were shown to care providers at weekly visits up to 37w.	Standard care, no formal fetal movement counting	No information.	Stillbirth (fetal death after 28 weeks) Apgar score (mean), BW, FGR, maternal anxiety, PTB
Flenady et al. 2021[77]	Stepped wedge cluster RCT	**BMI:** 21% >30 in intervention, 18.8% in control **Gestation:** ≥28w **RFM:** maternal perception	Education package provided to clinical site teams to raise RFM awareness and management, materials such as posters and pens provided as well as an elearning programme. Mobile phone app for women.	Standard care, brochure about RFM given during pregnancy, management according to recommended guidelines		Stillbirth (from 28 weeks' gestation) 5 min Apgar <7, BW <2500g, CS, IoL. NICU admission, SGA

		Risk: mixed **Timeframe** n=290,219				
Gibby 1988[219]	RCT comparing fetal movement counting to a control group	**BMI:** n/s **Gestation:** >33w **RFM:** kick chart **Risk:** low **Timeframe:** n/s n=33	Cardiff count to ten chart given, advised to use daily, if 10 movements were not perceived in ten hours then women were asked to call the hospital	Standard care, no formal fetal movement counting		Maternal anxiety
Gómez et al. 2007[37]	RCT comparing the count-to-ten kick chart with a new method	**BMI:** over 30 excluded **Gestation:** >30w **RFM:** kick chart **Risk:** all high risk	Latin American Center for Perinatology (CLAP) fetal movement chart; four 30 minute periods per day of fetal movement counting, 10 or more movements per day considered reassuring.	Count-to-ten method of fetal movement counting, record the elapsed time from the first to the tenth movement each day. 10 movements in under 2 hours considered reassuring.	No information	Intrauterine fetal death after 28 weeks, NND

		Timeframe: Oct 1999 to March 2000 n=1400				
Grant et al. 1989[200]	Cluster RCT on the use of Cardiff count-to-ten charts versus standard care	**BMI:** n/s **Gestation:** >28w **RFM:** kick chart **Risk:** mixed **Timeframe:** ten weeks in 1987 n=68,654	Daily fetal movement counting using a modified Cardiff "count-to-ten" chart. Women were instructed to contact hospital if no movements on a single day or <10 movements in 10h on 2 successive days. Clinicians were asked to respond to RFM as they deemed appropriate.	Standard care. Women were told that their care was not changing. Clinicians were told about the trial. Women could raise concerns about RFM and kick charts could be given when indicated.	No information	Stillbirth (antepartum fetal death after 28 weeks)
Güney & Uçar 2019[224]	RCT to determine the effect of fetal movement counting on	**BMI:** n/s **Gestation:** 28-32w **RFM:** kick chart	Fetal movement counting using the Cardiff count-to-ten method	Standard antenatal care		Maternal-fetal attachment

	maternal-fetal attachment	**Risk:** low (high risk excluded) **Timeframe:** Jan – May 2016 n= 100				
Heazell et al. 2013[225]	RCT comparing standard and intensive management of RFM.	**BMI:** 25 (18-50) **Gestation:** ≥36w, mean 38^{+6} (36^{+0} to 41^{+1}) **RFM:** maternal perception **Risk:** mixed **Timeframe:** Oct 2011 to Aug 2012 n=120	CTG in all women. US for head circumference, abdominal circumference, femur length, liquor volume, UA Doppler, EFW. hPL measured, <0.8 MoM considered low. Abnormal results led to expedited birth by the most appropriate method.	CTG in all women. EFW, liquor volume, umbilical artery Doppler if the criteria for US were met (2+ attendances with RFM, >37w gestation, symphysis fundal height <10^{th} centile)	This was an indication for further testing in the control group but numbers were not given.	Stillbirths after 36 weeks' gestation BW ≤10^{th} centile, CS, IoL, NICU admission, umbilical artery pH ≤7.1

Liston, Bloom & Zimmer 1994[226]	RCT looking at the effects of FMC on anxiety	**BMI**: n/s **Gestation**: >28w **RFM**: fetal movement counting **Risk**: low **Timeframe**: Jan-June 1988 n=613	Use of a modified Cardiff count to ten chart – note each fetal movement felt and record time taken for the tenth movement. US biophysical profile if ten movements not perceived.	Standard care, women were given charts and instructed to record sleep times	No information	Stillbirth after 28 weeks Maternal anxiety
Mikhail 1991[227]	RCT comparing fetal movement counting methods	**BMI:** n/s **Gestation:** 28-32w **RFM:** fetal movement counting **Risk:** low **Timeframe:** n/s n=213	Two fetal movement counting groups using Sadovsky and Cardiff charts	No fetal movement counting		Maternal-fetal attachment

Neldam 1980[228]	Prospective randomised controlled trial	**BMI**: n/s **Gestation**: n/s **RFM**: maternal perception and fetal movement counting **Risk**: n/s **Timeframe**: 1st Sept to 31st Dec 1978 n=2250	Fetal movement counting once a week until 32 weeks' gestation, then 3x a week. Instructions to contact hospital if <3 movements per hour perceived after 2 hours of monitoring. CTG, US, blood tests for these cases, could lead to CS, observation, or discharge,	No formal instruction to count fetal movements but women were always asked whether they felt movements. CTG and blood tests if fewer movements perceived, treatment then decided by the obstetrician in charge.		Stillbirth, defined as intrauterine death in fetuses weighing >1500g without congenital malformations. All occurred after 32 weeks.
Norman et al. 2018[202]	Stepped wedge cluster randomised trial	**BMI:** 21.8% obesity in intervention group, 20.3% in control group **Gestation:** <24w **RFM:** maternal perception	e-learning package for all clinical staff about the importance of RFM and how to manage it, plus a leaflet for pregnant women (usually given at 20 weeks). Management plan for presentations with RFM after 24 weeks given to all hospitals.	No RFM information given to staff or parents. Data from 33 hospitals so no information on clinical management protocols.	Numbers not given but recurrent RFM was an indicator for birth.	Stillbirth after 24 weeks' gestation (or >500g if gestation unknown) 5 min Apgar <7, BW <2500g, CS, EmCS, IoL, NICU admission, NND, perinatal mortality, PTB, SGA

		Timeframe: Jan 2014 – Dec 2016 n=385,552				
Saastad et al. 2011 & 2012[229,230]	Multicentre RCT	**BMI:** 12.5% obesity in intervention group, 10.7% in controls **Gestation:** >28w **RFM:** kick chart **Risk:** mixed **Timeframe:** Sept 2007 to Nov 2009 n=1076	Pregnant women received an information brochure, including instructions on how to use a fetal movement chart, and counted fetal movements from 28 weeks of gestation using a modified count to ten method	Standard care according to Norwegian guidelines		Perinatal death Apgar score <4 at 1 and 5 min, BW, EmCS, maternal anxiety, NICU admission, SGA <10th centile, PTB
Thomsen 1990[221]	Prospective randomised trial	**BMI:** n/s **Gestation:** >29w	Daily fetal movement counting using modified Cardiff count to ten chart. Participants instructed to contact hospital if	Oestriol and hPL measured at 33, 36, 39, 41 weeks and then twice weekly. CTG,	No information	Stillbirth, not defined

		RFM: kick chart **Risk:** low (no obstetric complications or miscarriages) **Timeframe:** n/s n=1112	fewer than ten movements recorded in five hours, birth expedited if fetal jeopardy indicated. If movement less than half of usual then present at hospital the next morning for CTG, blood test, examination.	physical examination, repeat analyses if results were below the 2.5% reference limit.		Apgar score <7 at 1 and 5 minutes, FGR <5th centile, umbilical artery pH <7.5
Non-randomised studies						
Awad et al. 2018[80]	Retrospective observational study	**BMI:** n/s **Gestation:** >26w **RFM:** maternal perception, confirmed in hospital (those with normal movements were discharged)	CTG on admission, biophysical profile for all patients before discharge	CTG on admission, biophysical profile if CTG was non-reactive and/or oligohydramnios or FGR.	158 women in Mt Sinai group and 73 in Windsor group had normal movements in triage	Stillbirths after 26 weeks (8 on arrival excluded) CS No stillbirths in women discharged after CTG and biophysical profile, 1 stillbirth out of 19 in women not scanned in intervention

		Risk: mixed **Timeframe:** Jan-Dec 2012 n=579				
Wackers et al. 2018[231]	Prospective cohort study	**BMI:** n/s **Gestation:** >24w **RFM:** maternal perception **Risk:** mixed **Timeframe:** April-Nov 2015 n=140	Information booklet regarding fetal movements given to women at 24 weeks' gestation	Information booklet regarding fetal movements given to women at 28 weeks' gestation		Time to present with RFM
Randomised studies in progress						
Damhuis et al. [217]	Multicentre cluster RCT	**BMI:** n/a **Gestation:** 37^{+0} to 46^{+1} w **RFM:** maternal perception	Cerebroplacental ratio measured, expedited birth recommended if ratio is low	Standard care. Cerebroplacental measured but results not revealed.		Stillbirth, neonatal mortality, Apgar score <7 at 5 min, umbilical artery pH <7.10, emergency birth will be measured as part of a composite adverse outcome.

		Risk: low (EFW >10th centile) **Timeframe:** recruitment ongoing				

BMI, body mass index; n/s, not stated; RFM defined as either maternal perception or by using a kick chart

BW, birthweight; EmCS, emergency caesarean section; IoL, induction of labour; NICU, neonatal intensive care unit; NND, neonatal death; PTB, preterm birth; SGA, small-for-gestational-age

Table 5 – Overall risk of bias for randomised studies using Cochrane RoB2

Study	Risk of bias judgement due to:					
	Randomisation process	Deviations from the intended intervention	Missing outcome data	Measurement of outcomes	Selection of reported results	Overall
Abasi, Tafazoli & Esmaeili 2013[218]	High	Some concerns	High	Low	Low	High
Akselsson et al. 2020[9]	Low	Some concerns	Some concerns	Low	Low	Low
Armstrong-Buisseret et al. 2020[222]	Low	Some concerns	Low	Low	Low	Low
Delaram & Jafarzadeh 2016[146]	Low	High	Low	Low	Low	High
Flenady et al. 2021[77]	Low	High	Low	Low	Low	High
Gibby 1988[219]	High	Some concerns	Some concerns	Low	Low	High
Gómez et al. 2007[37]	Some concerns	High	Low	Low	Some concerns	High
Grant et al. 1989[200]	High	High	Some concerns	Low	Low	High
Güney & Uçar 2019[224]	Low	Low	Low	Low	Low	Low
Heazell et al. 2013[225]	Some concerns	Some concerns	Low	Low	Low	Low
Liston, Bloom & Zimmer 1994[226]	Low	Low	Low	Low	Low	Low
Mikhail 1991[227]	Some concerns	Low	Low	Low	Low	Low
Neldam 1980[220]	High	Some concerns	Low	Low	Low	High
Norman et al. 2018[202]	Low	High	Low	Low	Low	High
Saastad et al. 2011[232]	Low	Some concerns	Low	Low	Low	Low
Thomsen 1990[221]	High	Low	Low	Low	Low	High

Table 6 – Overall risk of bias for non-randomised studies using ROBINS-I

Study	Risk of bias judgement due to:							
	Confounding	Selection of participants	Classification of interventions	Deviations from intended interventions	Missing data	Measurement of outcomes	Selection of reported result	Overall
Awad et al. 2018[80]	Critical	Low	Low	Moderate	N/I	Low	Low	Critical
Wackers et al. 2018[231]	Moderate	Low	Low	Moderate	Low	Low	Low	Moderate

Of the two NRS, one study was rated as at moderate risk of bias[231] and the other at critical risk[80] (**Error! Reference source not found.**). All NRS were judged to be of at least moderate risk of bias for confounding, due to differences between study groups in key confounders or because some of our pre-specified confounding factors (such as stillbirth rate in the study population) were not measured. Concerns for other domains were mostly low.

3.4.3 Analyses

Random effects meta-analyses were performed throughout, as such, each pooled result presented is an average effect and should be interpreted in this manner rather than as representing a common effect.[233] On the forest plots, 'favours intervention' indicates that the likelihood of adverse outcome is lower in the intervention group, and 'favours comparator' indicates that it is lower in the comparator group. Raw data for analyses are shown in Appendix 7.6.

3.4.3.1 Interventions for encouraging awareness of fetal movement [group one]

Encouraging awareness of RFM compared with standard care (two RCTs; 330,084 participants)

Data were available from two RCTs; Akselsson et al. (n=39,865) compared the Mindfetalness intervention, aimed at encouraging maternal awareness of RFM, with standard care; this study was rated as at low risk of bias.[9] Flenady et al (n=290,219) compared an intervention comprising of encouraging awareness of RFM in clinicians and pregnant women with standard care, this study was rated as at high risk of bias.[77]

Adjusted effect estimates were available from both studies: Akselsson et al. adjusted for maternal age, parity, country of birth, and smoking – the estimate used is detailed in each section; Flenady et al. performed a multivariable analysis adjusted for time, clustering, and hospital effects (baseline risk factors were evenly distributed and adjusting for these in the model made no significant difference).

Primary outcome

Stillbirth

The evidence is uncertain about the effect of encouraging awareness of RFM on stillbirth when compared with standard care; pooling aORs from both studies gave an aOR of 1.19 (95% CI 0.96 to 1.47; I squared 0.0, p=0.929). The aOR from Akselsson et al. was adjusted for country of birth. Raw data were also used to calculate ORs, displayed as a subgroup on the forest plot (Figure 2). Evidence is of very low certainty, downgraded once for

imprecision as the CI fails to exclude important benefits and harms as well as no effect, once due to risk of bias (one study contributing most of the weight of the analysis was rated as being at high risk of bias), and once for indirectness as evidence is from high income countries only.

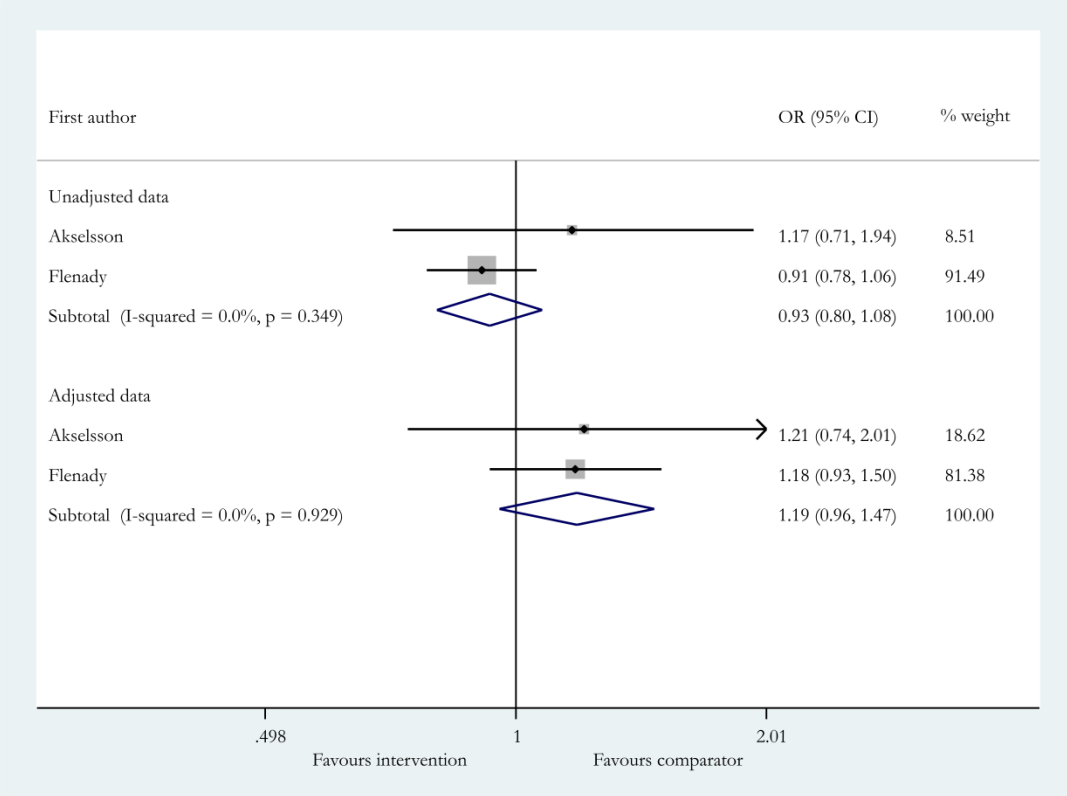


Figure 2 – Stillbirth for interventions encouraging awareness of reduced fetal movement

Neonatal death

The evidence is uncertain about the effect of encouraging awareness of RFM on neonatal death when compared with standard care; pooling aORs from both studies gave an aOR of 0.80 (95% CI 0.54 to 1.20; I squared 0.0, p=0.780). The aOR from Akselsson et al. was adjusted for country of birth. Raw data were also used to calculate ORs, displayed as a subgroup on the forest plot (Figure 3). Evidence is of very low certainty, downgraded once for imprecision as the CI includes both benefit of the intervention and standard care, once for risk of bias as above, and once for indirectness as above.

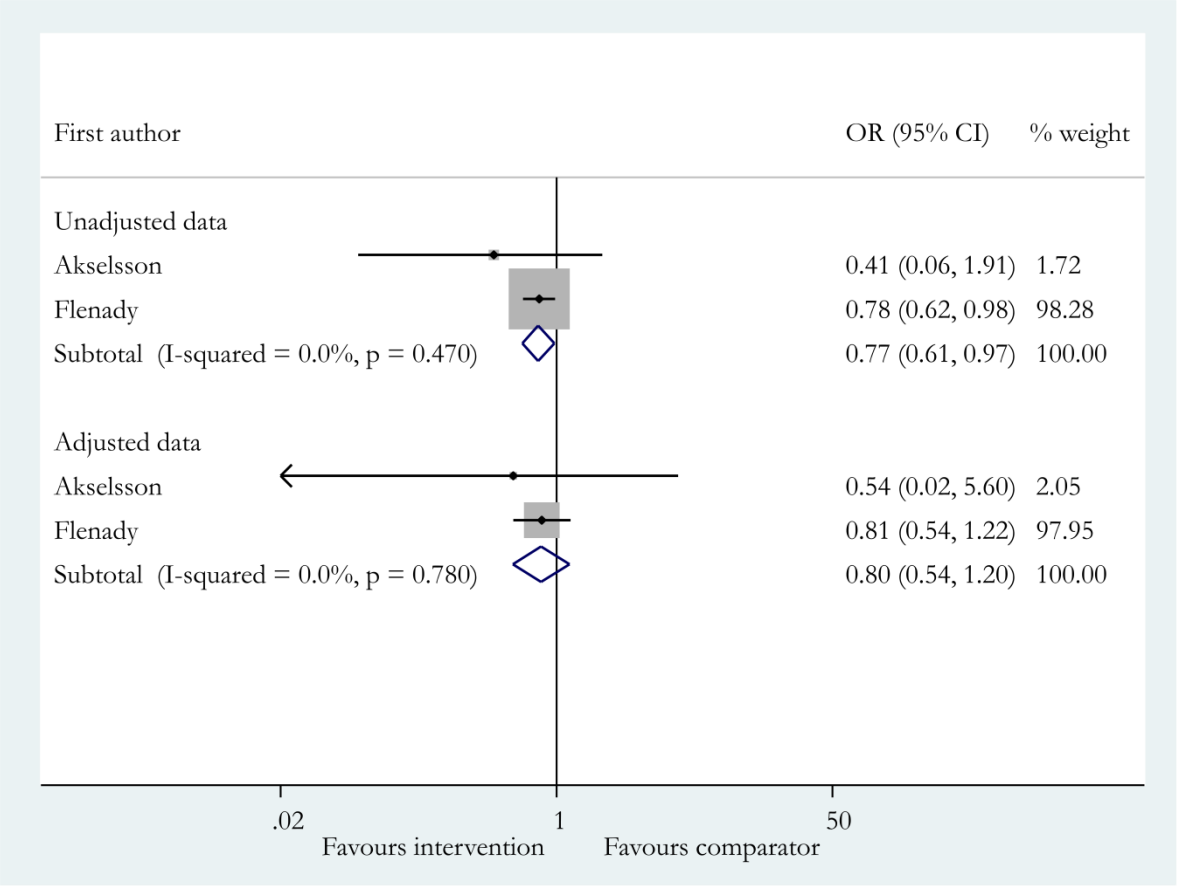


Figure 3 – Neonatal death for interventions that aimed to encourage awareness of RFM

Perinatal death

There is insufficient current evidence of a difference in the effectiveness of encouraging awareness of RFM when compared with standard care; pooling ORs calculated using the raw data from both studies gave an OR of 0.88 (0.78 to 1.00). Flenady et al. also reported an aOR of 1.07 (95% CI 0.86 to 1.31) for perinatal death; both estimates are shown in Figure 4. An aOR was not available from Akselsson et al. as perinatal death was not a prespecified outcome for this study.

Evidence is of low certainty, downgraded once as one study contributing 94% of the weight to the analysis was rated as at high risk of bias, and once due to the indirectness of the evidence (included studies are from high income countries only).

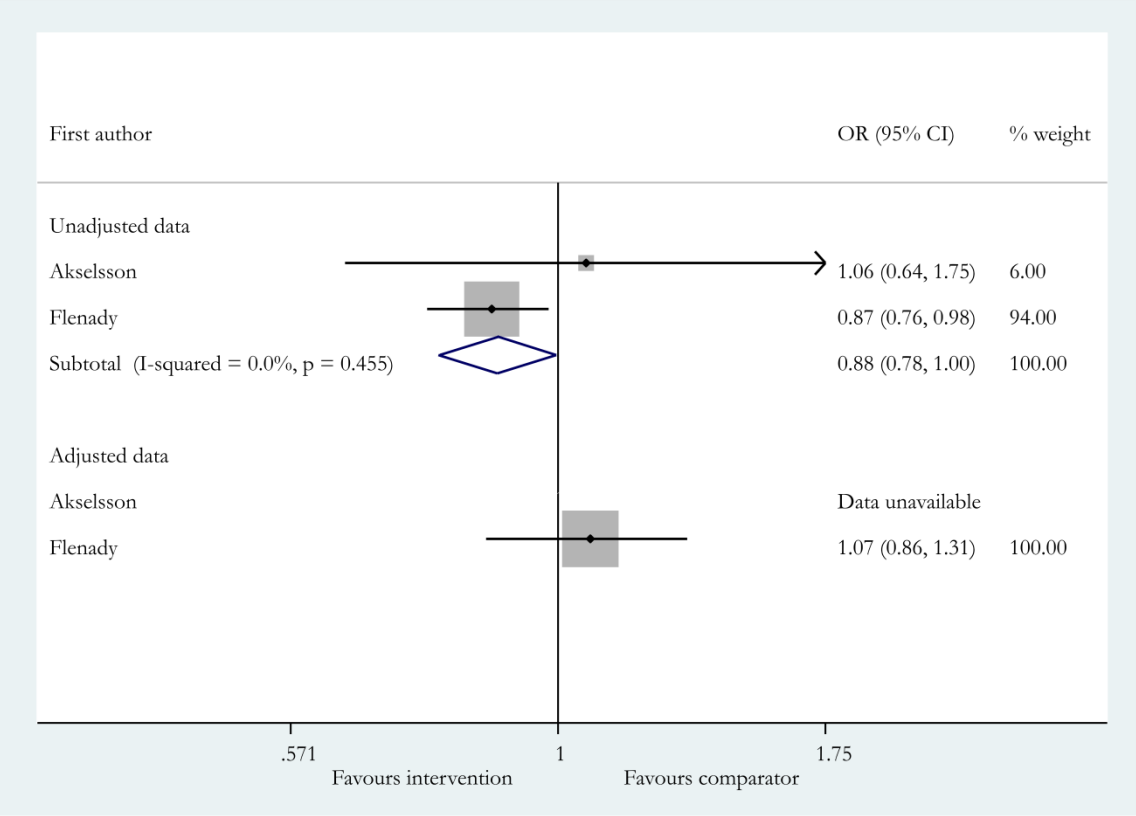


Figure 4 – Perinatal death for interventions that aimed to encourage awareness of RFM

Other secondary outcomes

Interventions for encouraging awareness of RFM were associated with a reduction in NICU admissions; there may also be reductions in Apgar scores <7 at 5 minutes of age, caesarean section, and induction of labour (Figure 5). Adjusted ORs were used for all comparisons except for Apgar scores <7 at minutes of age, where these were not available. As ORs and aORs did not differ significantly for all outcomes, and to make the forest plot easier to read, subgroup analyses for adjusted and unadjusted data are not shown.

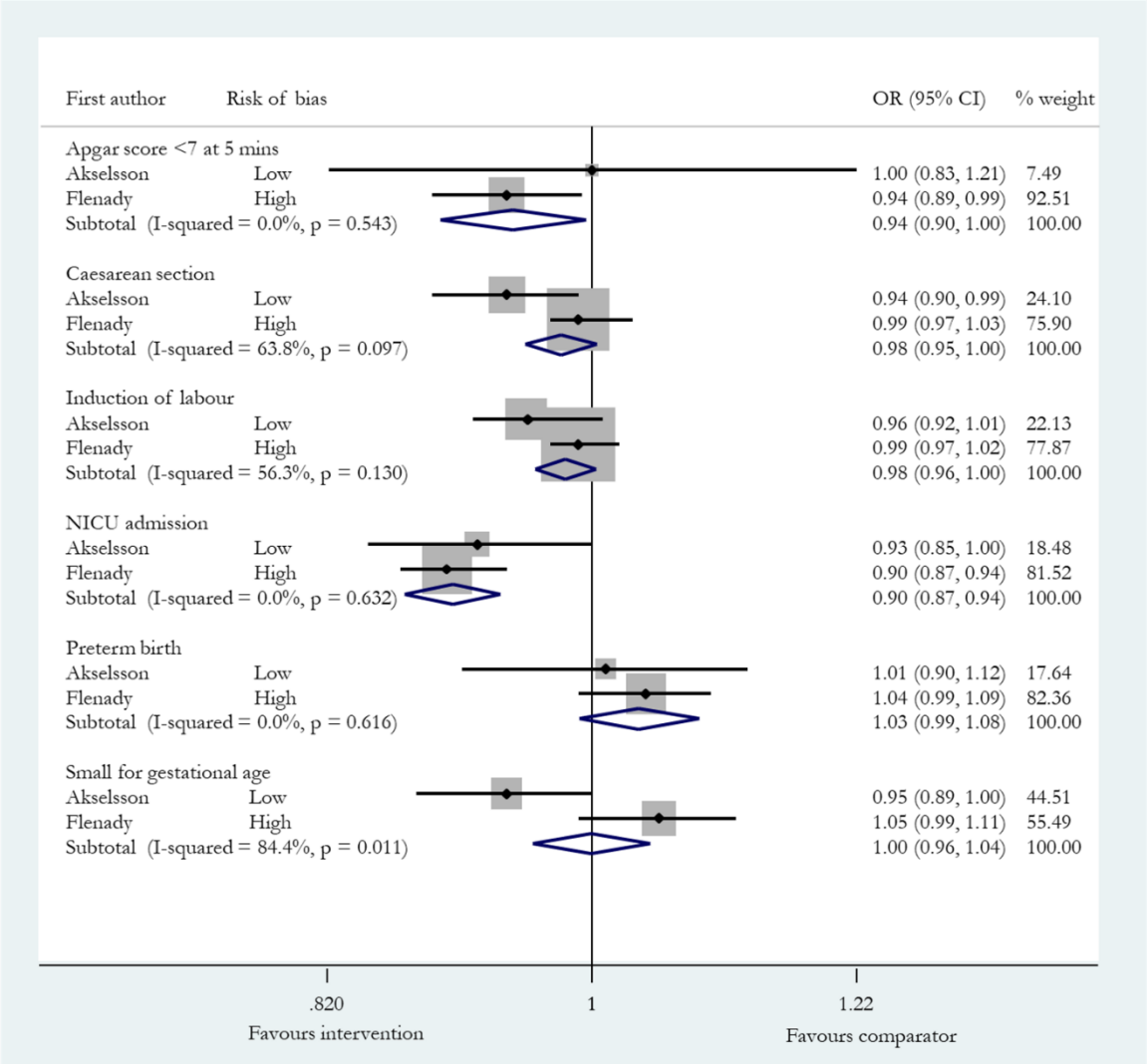


Figure 5 – Secondary outcomes for interventions that aimed to encourage awareness of RFM

Encouraging awareness of RFM at different gestational ages (one NRS; 140 participants)

One NRS (n=140) rated as at moderate risk of bias compared introducing an intervention aimed at encouraging maternal awareness of RFM at 24 weeks' gestation with introduction at 28 weeks.[231]

Primary outcomes

None of our primary outcomes were measured.

Secondary outcomes

We found no current evidence for differences in maternal presentation times to hospital after perceiving RFM between the two groups (Table 7).

Table 7 – Effect sizes from studies comparing encouraging awareness of RFM at 24 weeks' with at 28 weeks' gestation

Study	Wackers[231]
Outcome	OR (95% CI)
Maternal time taken to present to hospital after perceiving RFM >24h	0.98 (0.52 to 1.92)
Maternal time taken to present to hospital after perceiving RFM >48h	0.08 (0.10 to 0.62)

Note: ORs calculated from raw data using intention-to-treat rather than per protocol data

Encouraging fetal movement counting compared with standard care (8 RCTs; 72,212 participants)

Eight RCTs compared encouraging fetal movement counting with standard care (as defined by each study); four were rated as being at low risk of bias,[224,226,227,229] the other four as high risk.[200,218,220,223] Further details of these studies, including the kick charts used by each study as well as descriptions of standard care where available, can be seen in Table 4. None of these studies presented adjusted effect estimates.

Primary outcomes

Stillbirth

Five of our eight included studies measured stillbirth as an outcome, two of which[223,229] recorded no stillbirths and were not included in the analysis.

The evidence is uncertain about the effect of encouraging fetal movement counting on the proportion of stillbirths when compared with standard care, pooling data from three RCTs (n =70,584)[200,220,226] gave an OR of 0.69, 95% CI (0.18 to 2.65) (I squared 53.1%). Evidence is of very low certainty, downgraded three times: once due to imprecision (the 95% CI fails to exclude important benefit or harm), once due to the inconsistency of the evidence due to clinical heterogeneity (study populations and definitions of standard care across these populations are likely to differ), and once as two studies (contributing to over 70% of the weight of the analysis) were at high risk of bias.

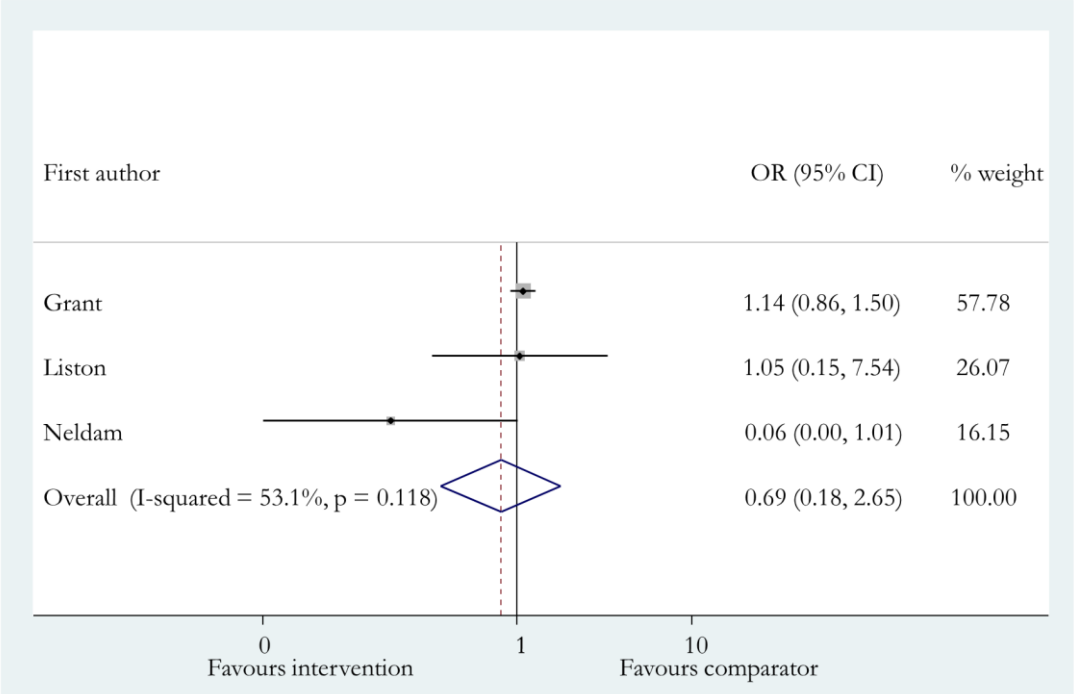


Figure 6 – Stillbirth for interventions encouraging fetal movement counting

Neonatal death

No studies presented data on neonatal death.

Perinatal death

One randomised trial comparing FMC with standard care reported this outcome; Saastad et al. recorded no perinatal deaths in a study with 1,076 participants.[229]

Other secondary outcomes

Three randomised studies (n=406) presented data for maternal-fetal attachment; two studies[218,227] used the Cranley MFA scale, the third[224] used the MAAS (Condon) scale.

Maternal-fetal attachment scores may be higher, indicating greater attachment, in fetal movement counting groups compared with standard care; meta-analysis gave a pooled SMD of 1.22 (95% CI 1.01 to 1.43; I squared 48.0%, p=0.146) (Figure 7 –).

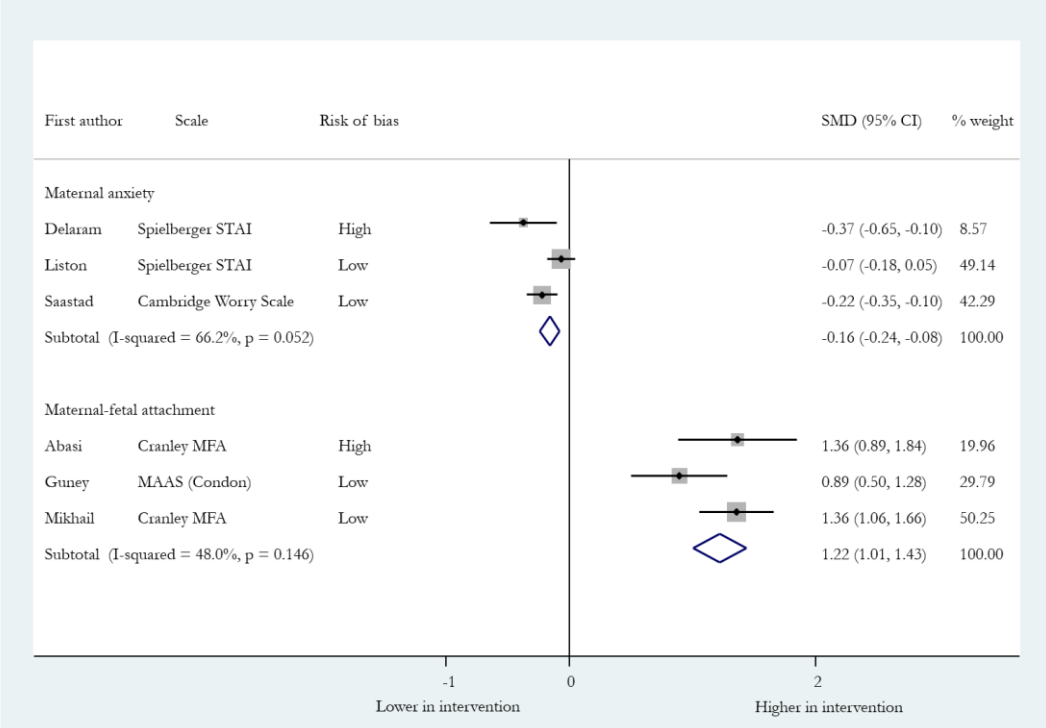


Figure 7 – Maternal anxiety and maternal-fetal attachment for interventions encouraging fetal movement counting

Three randomised studies (n=281) presented data on maternal anxiety measured using the Spielberger state trait anxiety index (STAI), trait scores[223,234] or the Cambridge worry scale.[147] Another RCT could not be included in this analysis as it presented only p values and no data.[219] Pooling data from three studies suggested that maternal anxiety scores during pregnancy may be lower in those offered fetal movement counting compared with those who were not offered this, indicating lower levels of anxiety; pooled SMD of -0.16 (95% CI -0.24 to -0.08; I squared 66.2%, p=0.052) (**Error! Reference source not found.**).

Data from randomised studies comparing encouraging fetal movement counting to standard care for other outcomes are shown in Table 8. There is insufficient evidence of an effect on secondary outcomes from Saastad et al. as CIs are wide; there may be no effect on NICU admission as there is less imprecision around this effect estimate.

Table 8 – Fetal movement counting v standard care – randomised studies

Study	Delaram[223]	Liston[226]	Saastad[229]
Outcome	OR (95% CI)		
5 min Apgar score <4			0.19 (0.01 to 4.07)
Caesarean section (all)			0.92 (0.57 to 1.48)
Emergency caesarean section			1.72 (0.50 to 5.19)
NICU admission			1.08 (0.65 to 1.80)
Small for gestational age	None in study	None in study	0.98 (0.64 to 1.50)
Preterm birth	None in study	None in study	0.81 (0.44 to 1.48)

Note: all ORs calculated using raw study data

Comparing two fetal movement counting methods (one study; 1,400 participants)

One RCT compared the effectiveness of two different approaches to fetal movement counting charts (CLAP and count-to-ten) in high risk pregnancies.[37] This study was judged as at high risk of bias due to deviations from the intended intervention and no primary or secondary outcome data relevant to the review were reported.

Fetal movement counting compared with hormone analysis (1 study; 1,112 participants)

One RCT in a low risk obstetric population compared fetal movement counting from 29 weeks' gestation to blood tests for oestriol and hPL starting at 33 weeks.[221] Both interventions could lead to cardiotography (CTG) testing and expedited birth.

Primary outcomes

Stillbirth

The evidence is uncertain about the effect of fetal movement counting on stillbirth when compared with hormone analysis. OR of 3.67 (95% CI 0.15 to 90.17). Evidence is of very low certainty; findings were downgraded once for imprecision (data from one study with one stillbirth; confidence intervals fail to exclude important benefit or harm), once as the study is at high risk of bias due to concerns about the randomisation process, and once due to indirectness as the study was carried out in a low-risk population.

Other secondary outcomes

Data for secondary outcomes are shown in Table 9. There is no current evidence of an effect for fetal movement counting compared to hormone analysis on most secondary

outcomes due to imprecision — CIs are wide, generally include benefits and harms, and the study was classed at being at high risk of bias.

Table 9 – Secondary outcomes for Thomsen et al. [221]

Outcome	OR (95% CI)
Apgar score <7 at 1 minute	1.70 (0.93 to 3.11)
Apgar score <7 at 5 minutes	2.45 (0.45 to 13.44)
Caesarean section*	1.21 (0.82 to 1.78)
IUGR (birthweight below 5th centile)	1.11 (0.60 to 2.06)
Umbilical artery pH <7.15	0.78 (0.53 to 1.15)

Note: all ORs calculated from raw data

*includes data from women who were partially compliant with FMC in FMC group and three women who did not give a blood sample in the test group

3.4.4 Interventions for the subsequent clinical management of RFM [group two]

Universal ultrasound screening for RFM compared with ultrasound when indicated (one NRS; 579 participants)

One NRS compared universal CTG and ultrasound screening with universal CTG and ultrasound (for biophysical profile) only if indicated.[235] This was a retrospective observational study with 579 participants, who all self-reported RFM after 26 weeks of gestation, and was rated at critical risk of bias due to confounding.

Primary outcomes

Stillbirth

The evidence is uncertain about the effect of universal ultrasound screening on the proportion of stillbirths in RFM pregnancies compared with ultrasound when indicated; OR 0.53 (95% CI 0.05 to 5.86). Evidence is of very low certainty, downgraded once due to serious and critical risk of bias in these studies and once due to imprecision (95% CIs fail to exclude important benefits or harms). No further outcomes relevant to the review were reported.

Universal ultrasound screening plus blood tests compared with standard care (two RCTs; 336 participants)

One RCT in women presenting with RFM after 36 weeks' gestation compared intensive management (ultrasound scan, serum human placental lactogen (hPL), induction of labour if indicated) with standard care; this was described as a feasibility study (n=120).[225] A

second RCT (n=216) in women presenting with RFM after 36 weeks' gestation compared standard care and a biomarker blood test (sFlt-1/PlGF) with standard care alone, where the result of the blood test determined whether expedited birth was offered.[236] Both studies were rated as at low risk of bias.

Primary outcomes

Neither study recorded any stillbirths or neonatal deaths, therefore analyses were not performed for any primary outcomes.

Secondary outcomes

Secondary outcome data relevant to this review are shown in Table 10. These data were not pooled due to the different blood tests employed by each study.

Table 10 - Secondary outcomes in randomised trials – universal ultrasound plus blood tests v standard care

Study	Armstrong-Buisseret[236]	Heazell[225]
Outcome	OR (95% CI)	
Apgar score <7 at 5 minutes	0.98 (0.06 to 15.90)	
Birthweight <10th centile		0.39 (0.13 to 1.20)
Caesarean section (for RFM)	2.97 (0.11 to 73.78)	0.45 (0.13 to 1.57)
Emergency caesarean section	0.81 (0.35 to 1.90)	
IoL (for RFM)	0.80 (0.43 to 1.48)	**2.87 (1.32 to 6.22)**
NICU admission	0.98 (0.24 to 4.03)	0.31 (0.03 to 3.08)
SGA[1]	4.73 (0.99 to 22.41)	
SGA[2]	2.28 (0.89 to 5.84)	
Umbilical artery pH <7.05	9.17 (0.49 to 172.44)	0.31 (0.03 to 3.01)
Outcome	SMD (95% CI)	
Maternal anxiety		0.146 (-0.212 to 0.505)

Note: not all outcomes were presented by both studies. All effect sizes calculated from raw data. Bold text indicates statistical significance

[1] Using INTERGROWTH-21st as birthweight standard; [2] Using GROW as birthweight standard

3.4.4.1 Combined interventions for encouraging awareness of fetal movement and its subsequent clinical management [group three]

Encouraging maternal awareness of RFM and subsequent clinical management compared with standard care (one RCT, n=393,857).

Norman et al. conducted a stepped wedge RCT in 33 hospitals comparing education of pregnant women and clinicians, along with a clinical management plan including CTG and US for all presentations with RFM, with standard care.[202] This study was rated as being at high risk of bias due to low adherence to the intervention.

We used data from this study from a corrected version of the online supplementary appendix[237] where possible, therefore numbers and effect sizes may differ from those in the original publication. Odds ratios are adjusted for maternal age, number of babies in the pregnancy, and year.

Primary outcomes

Stillbirth

The evidence is uncertain about the effect on stillbirth after 24 weeks' gestation when comparing this combination intervention with standard care (aOR 0.86, 95% CI 0.70 to 1.05). Evidence is of very low certainty, downgraded once as the study was rated as at high risk of bias, once as the CI fails to exclude important benefits or harms as well as no effect, and once due to indirectness as this is a single study in a high income setting.

Neonatal death

Data for neonatal death from Norman et al. were not used as this outcome was not pre-specified in the study protocol and data were added after review as supplementary information, in which the authors reported that "analyses arising from these data are additionally unlikely to be as robust as the data in the main tables".

Perinatal death

The evidence is uncertain about the effect on perinatal death between the intervention and standard care, this study presented an aOR of 0.95 (95% CI 0.81 to 1.12). Evidence is of very low certainty, downgraded once due to study limitations (rated as at high risk of bias), once due to imprecision, and once due to indirectness as described above.

Secondary outcomes

Secondary outcomes reported by Norman et al. are shown in Table 11. There are statistically significant increases in the number of Apgar scores <7 at 5 minutes, caesarean section, emergency caesarean section, and NICU admission and statistically significant reductions in induction of labour and the proportion of SGA babies, however, conclusions that can be drawn from these results are limited by the high risk of bias.

Table 11 – Combined interventions for randomised studies

Norman et al. [202]	
Outcome	aOR (95% CI)
5 min Apgar <7	**1.12 (1.07 to 1.18)** (unadjusted data)
Caesarean section (all)	**1.15 (1.12 to 1.18)**
Emergency caesarean section	**1.09 (1.08 to 1.11)**
Induction of labour	**0.81 (0.78 to 0.84)**
NICU admission	1.05 (1.00 to 1.10)
SGA (<10th centile)	0.93 (0.86 to 1.02)*
Preterm birth	1.00 (0.95 to 1.04)

Note: aORs from the intention to treat analysis are shown where available. ORs were calculated using raw data. Some outcomes include multiple pregnancies and missing data. Bold text indicates statistical significance.

*after 40 weeks' gestation

3.4.5 Comparing results from randomised and non-randomised studies

No comparisons between randomised and non-randomised studies for similar interventions were possible.

3.4.6 Other planned analyses and changes from protocol

We planned on presenting data as RRs, but due to the available data (adjusted estimates were available as ORs only) we decided to present all data as ORs to minimise potential confusion created by using two different effect estimates.

Planned sensitivity analyses were not possible due the number of studies at overall low risk of bias. Tests for small study effects were also not possible due to the low number of included studies in each comparison. The majority of studies did not present adjusted effect estimates but these were used where possible. Other intervention comparison groups, such as hormone analyses, were added after extracting data from all studies.

A summary of findings for comparisons looking at stillbirth, neonatal death, and perinatal; death is shown in Table 12.

Table 12 - Summary of findings table

Outcome	No. of studies	Intervention (n, events/non events)	Comparator (n, events/non events)	Effect size	Certainty of evidence (GRADE)	Notes
GROUP ONE						
Encouraging awareness of fetal movement compared with standard care						
Stillbirth	2	345/159,434	396/169,909	aOR 1.19 (95% CI 0.96 to 1.47)	Very low	
Neonatal death	2	135/159,644	188/170,117	aOR 0.80 (95% CI 0.54 to 1.20)	Very low	
Perinatal death	2	480/159,299	584/169,721	OR 0.88 (95% CI 0.78 to 1.00)	Low	
Encouraging fetal movement counting compared with standard care						
Stillbirth	3	101/32,850	110/37,523	OR 0.69 (95% CI 0.18 to 2.65)	Very low	Two studies with no events not included in analysis
Neonatal death	0	n/a	n/a	n/a	n/a	
Perinatal death	0	n/a	n/a	n/a	n/a	One study reported no events
Encouraging fetal movement counting compared with hormone analysis						
Stillbirth	1	1/500	0/611	OR 3.67 (95% CI 0.15 to 90.17)	Very low	
GROUP TWO						
Universal ultrasound screening compared with ultrasound when indicated						
Stillbirth	1	1/280	2/296	OR 0.53 (95% CI 0.05 to 5.86)	Very low	One study with no events not included in analysis
GROUP THREE						
Encouraging maternal awareness and subsequent clinical management compared with standard care						
Stillbirth	1	466/141,014	841/251,536	aOR 0.86 (95% CI 0.70 to 1.05)	Very low	
Neonatal death	1	n/a	n/a	n/a	n/a	Data not used, see text
Perinatal death	1	753/115,262	1,454/224,859	aOR 0.95 (95%CI 0.70 to 1.05)	Very low	

3.5 Discussion

3.5.1 Summary

This is the most comprehensive systematic review and meta-analysis of the literature regarding intervention studies for RFM, and takes into account both randomised studies and the most appropriate NRS while still employing strict inclusion criteria. It contains information from 16 RCTs and 2 NRS, compared with prior reviews that have focused solely on interventions for fetal movement counting and only included RCTs.

3.5.2 Effects of interventions and clinical context

Current evidence is insufficient for measuring the effects of interventions for encouraging awareness of RFM or interventions for encouraging fetal movement counting on perinatal death (including stillbirth and neonatal death as individual outcomes), when compared with standard care. This may be in part due to the relative rarity of these severe outcomes in high-resource settings and the size of the trials that have measured them rather than the interventions themselves; trial design and sample sizes will be discussed in more detail later on.

The results of our meta-analysis indicate that interventions for encouraging awareness of RFM may lower NICU admissions. NICU admission is a more common outcome than perinatal death, so it may be that our sample size is more likely to detect an effect on this outcome. From a clinical standpoint, lower NICU admissions, lower frequency of Apgar scores <7 at 5 minutes, and no increases in other outcomes indicates that the effects of these interventions are all acting in the same direction along the proposed clinical pathway. Alternatively, it may be that acting on presentations with RFM is able to reduce the number of babies that end up in NICU (i.e. those that are unwell but not at immediate risk of death) but not always save those babies that are at immediate risk of death as RFM is too late an indicator.

However, these numerical results should not be considered in isolation and the risk of bias of the included studies for the effects of encouraging awareness on NICU admission should be taken into account. Data from Flenady et al. contributed most of the weight to this analysis; this study was rated as at high risk of bias due to very low adherence to the intervention (54% of participants in the intervention group were registered to download the app and only 9.4% downloaded it). This could mean that NICU admissions would be lowered further if adherence were higher and we are not seeing the true effect of the intervention, but it could also connote that the intervention would be difficult to implement successfully outside of a trial setting.

Our analyses also show that interventions for encouraging fetal movement counting may result in higher maternal-fetal attachment and lower maternal anxiety when compared with standard care. Again, the risk of bias of the included studies needs to be addressed and whether these trials did not show the true effect of the intervention or whether it will always be difficult to achieve high fidelity with interventions such as these. It should also be considered whether the degrees of difference seen in the standardised measures are clinically different.

Criticism of fetal movement counting and awareness of fetal movements has focused on the potential harms,[20] which have not been found by this review (albeit using limited data). Studies that have found low Apgar scores may be due to standardised intervention programmes that expedite birth at a given gestation.[202] If awareness of fetal movements leads to a positive experience of pregnancy, as has been demonstrated by the Mindfetalness trial,[10] then it can be argued that awareness or counting of fetal movements should not be discouraged as long as there is a clinical protocol in place when there is concern about RFM that prevents unwarranted intervention. Importantly, there have been few studies of the subsequent clinical management of RFM, and no conclusions can be drawn as to whether ultrasound screening or blood tests of placental markers are likely to be of benefit.

3.5.3 Strengths and limitations

This review is strengthened by being conducted in accordance with a published protocol and as such we were able to critically appraise the existing literature and to identify gaps in outcome reporting. This review builds on others in the area such as those by Mangesi et al.[203] and Bellussi et al.[73] by widening the inclusion criteria for both study design and the types of intervention that were included, as well as extracting data for a larger range of outcomes. At the same time, we have maintained the validity of this review by only including robust study designs, only comparing interventions that we judged as similar using the TIDieR checklist, and applying GRADE to our findings, not all of which have been done by previous reviews. We were also able to obtain a significant amount of unpublished data in order to conduct analyses that would otherwise not have been possible.

Importantly, many of the included studies were not adequately powered to measure the effects of their interventions on this review's primary outcome of stillbirth. We aimed to combine data from several studies to achieve larger pooled samples, anticipating that this was more likely to have sufficient power to yield sufficiently precise estimates to answer the research question. Despite including seven studies with 795,104 participants, the numbers

of events for stillbirth in this review were still relatively low, leading to potential fragility of the meta-analyses. Furthermore, we were not able to formally synthesise data for most of our secondary outcomes due to large variation between published studies in terms of their design and the outcomes that were measured (or reported), to make any comparisons between different interventions for the same outcome, or to examine whether intervention effectiveness differs across study populations. This heterogeneity impedes synthesis and means that there may be effects of interventions in terms of our secondary outcomes, but which cannot be comprehensively investigated. Included studies also varied in the composition of their comparator groups, the protocols for care of RFM pregnancies in these groups, and other key characteristics such as population stillbirth rate (discussed below). Due to the small number of studies per comparison, we were not able to formally investigate how study design and characteristics are linked to intervention effectiveness.

We were limited by the available evidence from non-randomised studies, as most studies identified by our searches that were otherwise relevant did not meet our inclusion criteria due to their study design. Several uncontrolled before and after studies have been conducted to measure the effect of guideline implementation for RFM on adverse outcomes.[201,216,238] These studies were not included as their design means that it is not possible to attribute any differences in outcome to the intervention.

Our analyses were also limited by drawing evidence from high income countries only; consequently, all analyses were downgraded as there is no evidence to signify whether these interventions would have the same effectiveness in lower income countries. The majority of research to date on interventions for RFM has been conducted in high resource countries in which the burden of stillbirth is lower. Knowing the effectiveness of interventions in low and middle income countries is important as the incidence of stillbirth in these countries is higher and the association between RFM and stillbirth may also be stronger; a meta-analysis of studies in low and middle income settings estimated that the OR for stillbirth in pregnancies with RFM compared to those without is between 6.74 and 14.13 (compared with an estimated OR of 2.33 described in high income countries for RFM in the two weeks before birth).[12,18]

3.5.4 How should the effectiveness of interventions be measured?

3.5.4.1 Considerations for study design

It must be considered whether randomised trials are the easiest or most effective way to study interventions for RFM. The relative lack of trials in this area may reflect the difficulties associated with, and the resources required for, conducting a trial where any

effects that are seen can be reliably shown to be a result of the intervention, or it may be a reaction to the results of published trials that have not demonstrated reductions in fetal death. There are also difficulties in designing trials that are sufficiently powered to detect differences in rare outcomes.

When considering sample size, a 2015 Confidential Enquiry showed that there was suboptimal management of RFM in 25% of antepartum stillbirths.[188] If an intervention were 50% effective in reducing stillbirth in these pregnancies, then that would reduce antepartum stillbirth by 12.5%. Using these numbers and the current UK stillbirth rate of 4.2 per 1000, a trial would require over 230,000 participants in each arm (which has not been achieved by any of our analyses even when studies are combined). However, consideration should also be given to the expected reach of and adherence to the intervention, and the number of cases with adverse outcome that i) will present with RFM who otherwise would not have done or where the time to present will be reduced, and ii) where this outcome can be prevented by appropriate clinical management. Thus, measurement of the time taken to present to hospital with RFM as a study outcome would help to determine the extent to which the intervention has been taken up by the population, and therefore whether it is likely to reduce adverse outcome if an effective clinical management protocol is in place.

Our assessments of risk of bias and GRADE demonstrate that the majority of published RCTs suffer from issues with adherence to the stated intervention, in terms of the percentage of the intervention group that the intervention reaches as well as limitations in how this is measured. For example, Norman et al. classified adherence as a binary variable based on whether four out of five aspects of the AFFIRM intervention were adhered to, which is unlikely to be an accurate measure (this then informed whether clusters were classed as part of the intervention group or not). Up to 10% of women in some control clusters counted fetal movements in the study by Grant et al., which could have reduced any measured effect of the intervention or diluted the estimate of effect. In the My Baby's Movements trial only 54% of the intervention group were registered to download the app, and only 9.4% downloaded it. Low adherence will severely limit the potential effectiveness of any intervention and may also reflect the acceptability of any interventions. Furthermore, it should be noted that implementing interventions without knowledge of their acceptability could lead to lower than anticipated adherence.

Non-randomised study designs may be an easier way to achieve the necessary sample sizes, but these are not without their own issues. None of the included NRS were rated as at low

risk of bias and none accounted for all our pre-specified confounding factors (especially stillbirth rates before and after the intervention), which was the main factor that lowered the certainty of the evidence in our stillbirth analysis. However, NRS, if done well (and most importantly if adequately controlled), could be a useful approach as temporal separation (e.g. before and after the implementation of a guideline or change in practice) may create more distinction between intervention and control groups and also may be a more accurate reflection of standard care in the control group in the case of retrospective studies.

One potential answer to the problems described above, which also allows the effect of an intervention in multiple settings to be seen, is to conduct trials that international and conducted across multiple centres. This approach will be used in a study to address uncertainty surrounding an intervention for palate surgery[239] and a similar model would allow for larger sample sizes and allow potential variation by country and income setting to be seen.

Trials in low- and middle-income countries may also be useful settings to test the effects of interventions for RFM as there is a higher chance that effects on severe outcomes (e.g. stillbirth and neonatal death) can be seen due to their higher incidence; current evidence suggests that harms of the interventions are not likely to be seen — while this is yet to be tested in lower resource settings. Interventions for awareness and kick counting are easiest to implement and come with fewer associated costs, and are likely to improve knowledge of RFM, which is highly variable; a systematic review found that the proportion of women who were aware of RFM as a 'danger sign' ranged from 3.1% to 62.3% in included studies from low-income countries.[18]

Sufficiently large trials would also improve future syntheses of these studies by increasing the sample sizes for meta-analysis, increasing the possibility that conclusions can be drawn. The results of individual studies should be interpreted with caution, especially when making recommendations or changes to guidelines, as their design and hence the levels of certainty in their estimates may be more important than the results themselves.

3.5.4.2 Interventions for RFM

Awareness interventions have mostly focused on encouraging fetal movement counting. Recent research has suggested that changes in the frequency and/or strength of fetal movements are a better indicator of stillbirth than arbitrary alarm limits which usually focus on counting a certain number of movements and are not tailored to the usual strength or frequency of movements in individual pregnancies.[13] It then needs to be ensured that

concerns regarding RFM are taken seriously and acted upon in a clinically appropriate manner.

Studies employing interventions after a presentation at hospital with RFM should consider the prognostic accuracy of clinical tests such as ultrasound — the accuracy of which for predicting stillbirth has been shown to be lacking.[240] More information on the accuracy of placental biomarkers for RFM is needed; these have been shown to be effective in early detection of preeclampsia[241] and two small scale studies suggest that this approach is likely feasible.[225,236] The created logic model (Appendix 7.1) shows how interventions for encouraging awareness of RFM and interventions for the subsequent clinical management of RFM are linked as well as other factors (such as characteristics of the study population and the expected reach of the interventions) that may affect whether or not the true effect of an intervention is shown by a study.

Ideally, interventions for RFM should be multifaceted as there is interdependence between interventions focused on the awareness of RFM and improving its subsequent clinical management; interventions to encourage and raise awareness can only reduce the incidence of adverse outcomes if combined with effective clinical management. Likewise, clinical management can only prevent fetal death in the event of timely presentation with RFM. Our included studies of clinical interventions have reported stillbirths that were identified in RFM pregnancies on presentation; some of which may have been preventable if there was a reduction in fetal movement over time.

Interventions also need to be as wide-reaching and as practically achievable as possible; for example, those women at higher risk of adverse outcome due to socioeconomic factors, are often those who are less able and/or more reluctant to go to hospital if they suspect something is wrong. This discrepancy was exemplified by women born in Somalia in the Mindfetalness trial were at higher risk of adverse outcomes and were significantly less likely to present to hospital with RFM.[242]

Ultimately, the link between RFM, placental insufficiency, and stillbirth is well established; the challenge is whether this link can be modified and demonstrated by trials.

3.5.4.3 Care bundles

Although outside the scope of this review, interventions for RFM may also be effective as part of a care bundle — a set of between three and five evidence-based practices which are performed with an aim to increase the quality of care.[243] Recently the Saving Babies Lives Care Bundle showed a 20% reduction in stillbirth rate over the course of the study in a

cohort of 463,630 births (aRR 0.80; 95% CI 0.70-0.91);[244] the Safer Baby Bundle is also being evaluated in Australia.[245]

3.5.5 Stillbirth rates in included studies

It is vital that future studies also account for population stillbirth rates. Where possible, stillbirth rates were recorded from the study, or population stillbirth rates at the time of the study were looked up using sources such as the WHO website (Table 13). There was wide variation in these rates due to the study settings and years in which they took place, from 23.7 per 1000 (India, 2007) to 2.6 per 1000 (Australia, 2013).

Changes in population stillbirth rates over the course of a trial may affect findings. Studies by Flenady et al. and Norman et al. have shown decreases in stillbirth rates over the course of a trial. When combined with stillbirth rates that are lower than in the general population, this could mean that any decreases in stillbirth rate associated with the interventions themselves are difficult to detect.

Notably, in several large trials (such as those by Akselsson et al. and Grant et al.) the study stillbirth rates (in both the control and intervention groups) were lower than the population rates during the study period. Lower stillbirth rates in the trial population when compared to the general population, potentially due to trial effects, may be an important factor in limiting whether effects of the intervention are seen. Enhanced adherence to clinical practice guidelines for RFM may be one reason for this observation; it is plausible that hospitals may make a concerted effort to follow national guidelines if they are part of a trial, whereas guidelines in individual maternity units have been shown to vary in quality.[74] This increased fidelity, leading to better outcomes, has been suggested in trials in other areas of healthcare.[246] Lower stillbirth rates may also be a result of the trial populations themselves — we have included trials of singleton pregnancies without congenital anomalies and, as such, stillbirth rates in trial populations are expected to be lower. Furthermore, stillbirth rates are higher in minority ethnic groups, which are under-represented in clinical trials,[247] or from deprived backgrounds. Critically, Akselsson et al. found higher incidences of adverse outcomes in women born in Somalia compared to those in Sweden; the differences between the groups were smaller in women who were randomised to the intervention.[242] The 'ideal' control group in a trial would be one that adequately reflects the general population in terms of stillbirth rate and where usual clinical practice is adhered to.

Table 13 – Population stillbirth rates in included studies

Study	**Timeframe**	**Country**	**Stillbirth rate**			**Study stillbirth definition**
			Population	Control	Intervention	
Akselsson et al. 2020	Aug 2016 – June 2018	Sweden	2.7-2.5 (WHO)	29/20,197 1.4 per 1,000	33/19,606 1.7 per 1,000	All > 32w
Armstrong-Buisseret et al. 2020	2018	UK	4.1 per 1,000 (ONS); 3.0 per 1,000 (WHO)	0/107	0/109	36-41w
Awad et al. 2017	2012	Canada	2.9 per 1,000 (WHO)	2/296 6.8 per 1,000	1/280 3.6 per 1,000	All >26w
Delaram & Jafarzadeh 2016	Aug 2012 – Aug 2013	Iran	7.7-7.9 per 1,000 (WHO)	0/108	0/108	All >28w
Flenady et al. 2021	2016-2019	Australia	2.4 and 2.7 per 1,000 in 2016 and 2018 respectively (WHO)	367/150,079 2.0 per 1,000	312/140,140 2.2 per 1,000	Stillbirth from 28 weeks
Gómez et al. 2007	Oct 1999-March 2000	Peru	13.6 in 2000 (WHO)	0/700	0/700	All >30w
Grant et al. 1989	1986-1987	Mostly UK, 3 Swedish centres, 1 NI	UK 5.3-5.0 (ONS)	100/36,131 2.8 per 1,000	99/31,549 3.14 per 1,000	All >28w
Heazell et al. 2013	Oct 2011-Aug 2012	UK	5.2-4.9 per 1,000 (ONS); 3.7-3.5 per 1,000 (WHO)	0/58	0/60	Measured after 36 weeks

Kapaya et al. 2020	June-Nov 2016 and July-Dec 2018	UK	4.2 and 4.4 per 1,000 in 2018 and 2016 respectively (ONS)	0	0	After 24 weeks
Liston, Bloom & Zimmer 1994	Jan 1986-June 1988	Canada	5.6 per 1,000 in 1990 (from study)	2/380 5.2 per 1,000	0/176	All >28w
Lobb 1985	1977	UK	6.5/1,000 (from study)	66/13,612 4.85 per 1,000	27/6,558 4.12 per 1,000	All >28w
Neldam 1980	Sept 1978 to Dec 1978	Denmark	5.8 per 1,000 (from study)	8/1,117 7.2 per 1,000	0/1,125	All >32w
Norman et al. 2018	2014-2016	UK	4.7-4.4 per 1,000 (ONS); 3.2-3.3 per 1,000 (WHO)	528/157,164 3.36 per 1,000	771/227,089 3.40 per 1,000	All >24w
Saastad et al. 2011	Sept 2007 - Nov 2009	Norway	3.1 to 3.3 per 1,000 (WHO)	0/532	0/544	All >28w
Thomsen 1990	1990 (year of publication used)	Denmark	No data	0/611	1/500	All >29w

Notes: only studies where stillbirth was measured as an outcome are included in this table. Population stillbirth rates may be higher than study populations if twin pregnancies and malformations were included. The UK definition of stillbirth changed from fetal death after 28 weeks' gestation to after 24 weeks in 1992. Data for population stillbirth rate taken from the WHO, and the Office for National Statistics (ONS) for UK-based studies, when possible. If these were not available then study stillbirth rate is presented.

3.5.6 Evidence synthesis in RFM research

Consideration should be given to further improvement of evidence synthesis as well as of improving the quality of individual studies.

To ensure that the most important outcomes are measured by all studies, which will increase the likelihood that meta-analysis of these studies can be performed, the creation of a COS would be beneficial. COS are currently available for use in other areas of maternity care research such as preeclampsia[248] and FGR;[92] the development of COS for use in studies for raising awareness and/or evaluating the clinical management of RFM will be described in Chapter 4; this aims to make future syntheses easier and to reduce the need for authors to obtain unpublished data.

Individual participant data (IPD) meta-analysis may also be useful for obtaining data on other outcomes and for investigating the effect of participant characteristics on interventions, as effectiveness may differ in population subgroups such as in the Mindfetalness trial.[242] This approach has been useful in exploring the findings of observational studies, an IPD meta-analysis showed that the risk of stillbirth was highest in women reporting RFM in the last two weeks between 28-32 weeks' gestation (aOR=6.98) compared to 33-36 weeks' gestation (aOR=3.48) and 1.95 after 37 weeks' gestation. Thus, gestation when perceiving RFM may also be important in relation to studies of interventions.[12] An IPD review is planned to investigate the effects of interventions for improving detection of fetal movement awareness and management on stillbirth rates.[249]

3.6 Conclusions

Using evidence from both randomised and non-randomised trials, it is uncertain whether interventions to encourage maternal awareness of fetal movements over and above standard care affect the rate of stillbirth or perinatal death. Intervention studies for RFM have shown wide variation in adherence to the interventions and differences in population stillbirth rates, which may affect whether the true effect of the intervention is measured. Research into interventions for RFM is still necessary as people who are pregnant are likely to present with valid concerns about their babies' movements. Thus, high-quality controlled studies including those from low-resource settings are needed to provide evidence of the effectiveness for clinical management strategies for presentations for RFM.

Chapter 4 - Development of a core outcome set for studies of reduced fetal movement

The core outcome set protocol has been published as:

Hayes, D.J.L., Devane, D., Dumville, J.C., Smith, V., Walsh, T. & Heazell, A.E.P. Development of a core outcome set (COS) for studies relating to awareness and clinical management of reduced fetal movement: study protocol. *Trials* (2021) **22**(1): 1-6.

The manuscript for the core outcome set has been prepared for submission to BJOG.

DH was responsible for study design and writing the study protocol, literature searches and study screening, creation and maintenance of the survey, recruiting participants, correspondence with participants, writing the first draft of the manuscript, and subsequent edits.

4.1 Abstract

Background

Concerns regarding RFM are reported in 5-15% of pregnancies and RFM are associated with adverse pregnancy outcomes including and stillbirth. Studies have aimed to improve pregnancy outcomes by evaluating interventions to raise awareness of RFM in pregnancy, evaluating interventions for the clinical management of RFM, or both. As shown in Chapter 3, there are no COS for studies of RFM, limiting subsequent synthesis of trial data. This study aims to create COS for use in research studies that aim to encourage awareness of RFM and/or evaluate interventions for the clinical management of RFM.

Methods

A systematic review of the literature was conducted to identify outcomes used in controlled randomised and non-randomised studies aiming to raise awareness of RFM (using techniques to encourage awareness, fetal movement counting, information leaflets, or mobile phone applications), and/or to improve the clinical management of RFM.

An international Delphi consensus process was carried out whereby stakeholders rated the importance of the outcomes identified in the systematic review in i) awareness and ii) clinical management studies. The preliminary lists of outcomes were discussed at consensus

meetings at which two COS (one for awareness and one for management) were agreed upon.

Results

Round one was completed by 128 participants (40 parents, 19 researchers, 65 clinicians) from 16 countries, of which 66% completed all three rounds of the survey. 50 outcomes were identified by the literature review and voted on in round one; 52 outcomes were voted on in two lists in rounds two and three. 66 outcomes were voted on at the final consensus meeting by 17 participants from eight countries. The final COS for studies aiming to encourage awareness of RFM consists of eight outcomes (four maternal and four neonatal), the final COS for studies aiming to improve the subsequent clinical management of RFM includes ten outcomes (two maternal and eight neonatal).

Conclusions

These COS will provide researchers with the minimum set of outcomes that should be measured and reported in studies that aim to quantify the effects of interventions relating to encouraging awareness and/or improving the subsequent clinical management of RFM.

4.2 Introduction

4.2.1 Reduced fetal movement and adverse pregnancy outcome

RFM is usually defined as a subjective decrease or change in a baby's typical pattern of movements *in utero*; [1] current guidance in the UK and Australia is for anyone who is pregnant to contact a midwife or maternity unit if their baby is moving less than usual or not at all.[11,250] Most people who are pregnant become aware of fetal movements by 18-20 weeks' gestation, the pattern of their baby's movements, and the time of day that the baby moves the most by 28 weeks' gestation.[187] Awareness of fetal activity is recognised as one component of maternal-fetal attachment.[251]

Maternal concern regarding RFM leads to a presentation at hospital in 5-15% of pregnancies.[2] Around 70% of these pregnancies have a normal outcome,[191,252,253] but observational studies have recurrently demonstrated that RFM are associated with adverse pregnancy outcomes, including FGR and stillbirth, supporting the potential for a common aetiology.[254,255] Case-control studies have consistently demonstrated an association between reduced frequency and strength of fetal movements and stillbirth after 28 weeks' gestation;[13,193,194] this effect has also been seen in low-income settings.[18] It is thought that RFM may be an attempt by the fetus to conserve energy and oxygen consumption in cases of insufficient nutrient transfer and hypoxia, which in turn may be caused by placental insufficiency or other fetal stressors.[8,196,256]

4.2.2 Studies of interventions for reduced fetal movement

Studies have aimed to improve pregnancy outcomes by evaluating interventions that raise maternal and/or clinical awareness of RFM, such as encouraging awareness of the pattern, strength, and frequency of fetal movements, or kick counting,[76,200] and/or by evaluating clinical management interventions, for example, interventions comprised of further monitoring and/or clinical testing such as CTG or ultrasound to identify whether RFM is an indicator of an underlying condition that may warrant further clinical intervention or even expedited birth.[201,202]

Despite the association between RFM and adverse pregnancy outcomes, a COS for studies evaluating interventions that aim to encourage awareness of RFM and/or studies evaluating the clinical management of RFM does not currently exist. Lack of a COS means that studies often measure and report different outcomes, and employ different definitions for these outcomes, hindering meta-analysis of studies — as shown in Chapter 3. A COS describes a standardised set of outcomes that should be measured and reported in all studies in a specific area as a minimum;[82] COS are currently in use across several healthcare

fields, including maternity care.[92,257,258] It is anticipated that developing a COS will ensure that the most important and relevant outcomes, as agreed by stakeholder consensus, are measured, thus optimising the synthesis of individual studies. This will further facilitate data synthesis and interpretation of the evidence based on prioritised outcomes.

4.3 Methods

4.3.1 Aims and objectives

This study aimed to develop COS for measurement and reporting in studies that aim to encourage awareness of RFM and/or evaluate the clinical management of RFM. Adoption of these COS will ensure consistent and relevant outcome measurement and reporting in studies encouraging awareness and/or evaluating the clinical management of RFM, which may lead to more robust results, improved wellbeing in pregnancy, and may also be applicable in clinical practice. The COS apply to controlled randomised and non-randomised study designs, addressing the research question described in Table 13.

The objectives of this study were:

1. To systematically review the outcomes included in intervention studies for raising awareness of RFM and/or evaluating its clinical management;

2. To develop a consensus on a preliminary COS using these outcomes via the Delphi survey;

3. To develop definitive COS for use in all future intervention studies aimed at raising awareness of RFM and/or evaluating the clinical management of RFM, via an international consensus meeting with key stakeholders;

4. To disseminate and promote the use of these COS.

4.3.2 Study design

The COS development project was registered with the Core Outcome Measures in Effectiveness Trials (COMET) initiative (http://comet-initiative.org/Studies/Details/928) on the 24th of September 2020. The study protocol was developed and published[259] in accordance with the COMET handbook[82] and can be seen as Appendix 7.6. Ethical approval was obtained from the University of Manchester Research Ethics Committee (Ref: 2021-11160-18073) and consent was obtained from all participants before they completed the survey.

4.3.3 Stage 1: Systematic review

A systematic review of the literature was conducted to identify outcomes measured in studies of interventions where the intervention is designed to encourage awareness of RFM and/or evaluate the clinical management of RFM.

4.3.3.1 Inclusion criteria

The target population was people with non-anomalous singleton pregnancies after 28 weeks' gestation; this threshold was chosen over other definitions of stillbirth to facilitate international comparisons.[260] We included controlled randomised and non-randomised studies with clearly reported mechanisms of group formation, clearly defined inclusion criteria, and clearly described methods of ascertainment of eligible patients and their recruitment; these are robust designs for studying the effects of interventions and the types of study that the COS should be used in, therefore we were interested in the outcomes measured by these studies. Studies were included regardless of their publication status and language of publication.

4.3.3.2 Literature searches

The following databases were searched: Medline, Medline (In-Process and Other Non-Indexed Citations), Embase, EBSCO CINAHL Plus, the Cochrane Central Register of Controlled Trials (CENTRAL), the Cochrane Pregnancy and Childbirth's Trials Register, and the Cochrane Database of Systematic Reviews. Other trial registries such as clinicaltrials.gov, WHO ICTRP, and the EU clinical trials register were searched, as well as databases such as OpenGrey (www.opengrey.eu), Joanna Briggs Institute (www.joannabriggs.edu.au), and the National Institute for Health and Clinical Excellence website (NICE; www.nice.org.uk) to find unpublished studies. Reference lists of included papers were reviewed for additional studies.

Studies identified by the literature searches were independently screened for inclusion by two study authors using our study inclusion criteria (Table 14). Disagreements were resolved by consulting a third author. The following data were extracted from included studies: study aim, location of the study (country and city), details of the study population, study setting (e.g. secondary or tertiary hospital), description of the intervention and comparator, and a list of outcomes reported in the study as well as how they were measured (e.g. if a standardised scale was used).

Pregnancy, labour, and birth outcomes were extracted with their corresponding definitions where possible. Outcomes were grouped as maternal or neonatal and then into domains within these categories. Different definitions or ways of measuring the same outcome (such

as stillbirth recorded at different gestational ages) were grouped into single outcome measures; this was facilitated by discussions between members of the study team. The final list of outcomes was used in stage two of the COS development process

Table 14 – Study inclusion criteria for the systematic review

Population	Singleton pregnancies presenting at least once in a maternity care setting after 28 weeks' gestation
Intervention	Any intervention aimed at raising awareness of RFM and/or evaluating the clinical management of RFM
Comparator	Any other intervention described above or no intervention
Outcome	Any maternal or fetal outcomes
Study design	Controlled randomised and non-randomised studies with clearly reported mechanism of group formation, clearly defined inclusion criteria, and described methods of ascertainment of eligible patients and their recruitment

4.3.4 Stage 2: Online international Delphi survey

4.3.4.1 Online survey

A sequential three-round electronic international Delphi study was conducted using REDCap (version 10.1.2)[261] including key stakeholders to produce a preliminary COS. Each round remained open for at least 14 days. In rounds two and three, frequent reminder emails were sent to participants who had not yet responded after 14 days (unless they stated that they no longer wished to participate). Reminder emails were automated at first, and then personalised emails were used to help combat attrition. Data from each round were analysed and presented to participants in the next round (described in more detail below). Attrition rates for each round were also assessed. All participants' contact information remained confidential.

The Delphi survey and following consensus meeting allowed the possibility of producing either one COS (for all studies relating to encouraging awareness and/or evaluating the clinical management of RFM) or two COS (one for studies encouraging awareness of RFM and another for studies evaluating the clinical management of RFM). Whether one or two were produced depended on whether there was significant overlap or similarity in the final outcomes in the two lists and followed the precedent set by other COS in maternity care that have started by running two surveys simultaneously and then voted on whether one COS should be produced.[92,262]

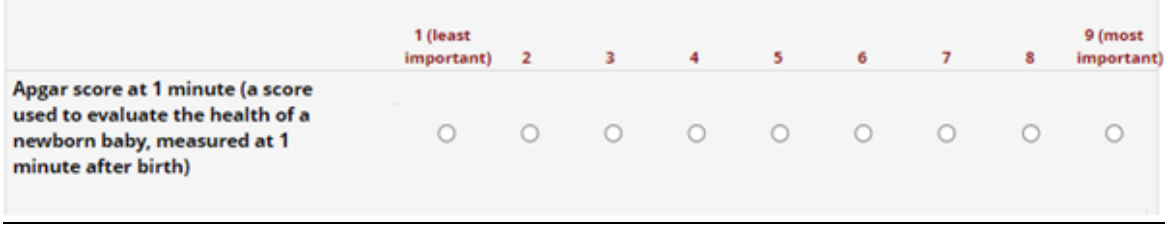
4.3.4.2 Participants

We invited people from all stakeholder groups, aiming for at least 15 people from each of the following three groups to ensure adequate representation and to enable us to have a large enough pool of participants at the end of the survey to contact about the consensus meeting (based on the levels of attrition seen in COS in women's and newborn health).[91] Eligible participants were: 1. Researchers, research funders, and policy makers who are actively involved in work related to RFM; 2. Clinicians (midwives, obstetricians, neonatologists, GPs/family physicians) with experience of clinical management of RFM; 3. Parents: anyone who is or who has been pregnant and their partners if applicable. We recruited participants through professional organisations, electronic discussion lists, and patient organisations or charities. Authors of all included studies were invited to participate; we also encouraged snowball sampling, whereby we requested that participants forward the survey to others who they considered eligible to participate.

Participants of the Delphi survey received all information regarding the study as part of the invitation email or included with the link to the survey on social media. Consent to take part in the survey was ensured by requiring participants to click an 'I agree to take part' box before gaining access to the survey. All personal data of participants was solely accessible to members of the research team and all survey responses were confidential. Participants had the right to withdraw at any point.

4.3.4.3 Round one

Round one collected demographic data including nationality, age, stakeholder group, and role. Participants were presented with a list of all outcomes identified from the systematic review and were asked to rate the importance of each using a nine point Likert scale (Figure 8). On this scale, a score of 1-3 indicates limited importance, 4-6 signifies importance, and 7-9 is used for critically important outcomes. Participants were prompted to add additional outcomes that they felt were important but were not included in the preliminary list. Suggested outcomes were included in round two if they were mentioned by at least two participants. All outcomes from round one were forwarded to round two.



	1 (least important)	2	3	4	5	6	7	8	9 (most important)
Apgar score at 1 minute (a score used to evaluate the health of a newborn baby, measured at 1 minute after birth)	○	○	○	○	○	○	○	○	○

Figure 8 – Example survey question using the nine-point Likert scale

4.3.4.4 Round two

Feedback was provided to all who participated in round one: for each outcome, participants received their scores from the first round and a graphical representation of the percentages of each group who voted for each score for each outcome (Figure 9). All feedback provided to participants was anonymised.

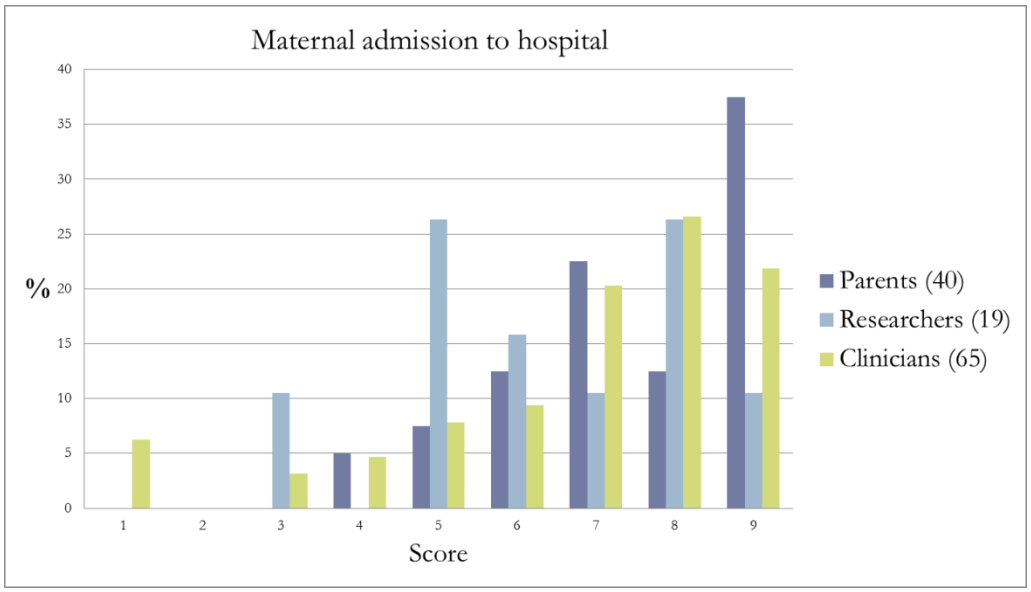


Figure 9 – Example feedback provided to participants

All participants who completed the first round were asked to re-score all outcomes using the same nine-point Likert scale, including any additional suggested outcomes from round one, in light of their and others' ratings.

In round two, participants were asked to rate the importance of each outcome to studies of i) interventions aiming to encourage awareness of RFM and ii) interventions aiming to improve the clinical management of RFM (Figure 10). Outcomes were presented in two corresponding lists and ratings for the two lists were reviewed and analysed separately.

Standardised consensus criteria were applied to the results from round two and were used through rounds two and three to reach the preliminary list of outcomes to be included (Table 14). Outcomes that were not scored by participants were not included in analyses or consensus definitions.

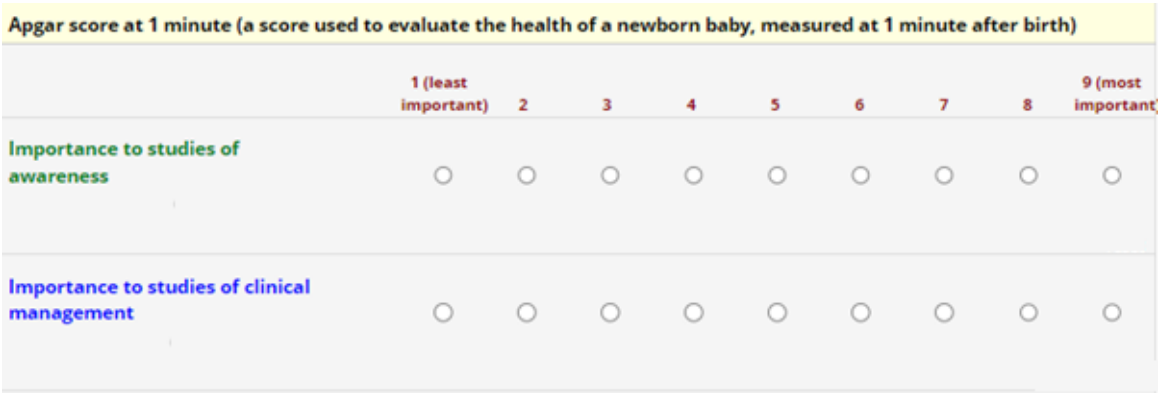


Figure 10 – Example question from round two

Outcomes were included in round three if they are rated as 'consensus in' or 'no consensus' using the consensus criteria outlined in Table 15; those rated as 'consensus out' were removed. Outcomes were removed from lists i) and ii) of the survey individually based on their ratings in each list. We also assessed the rates of attrition from each round and whether participants changed their scores based on the feedback they receive.

Table 15 – Consensus criteria for outcomes

Definition	Criteria
Consensus in	Scored as 7-9 by 70% or more of all participants, including at least one from each stakeholder group, and as 1-3 by less than 15% of participants
Consensus out	Scored as 1-3 by over 70% of participants and as 7-9 by less than 15%
No consensus	Any other combination of scores

4.3.4.5 Round three

Round three only included participants who completed round two. Participants were again provided with feedback and asked to re-rate the outcomes retained from round 2 in the same way as in round 2, in two separate lists for i) RFM awareness studies and ii) RFM clinical management studies using the 9-point Likert scale. The consensus criteria were again used to determine which outcomes are retained in each distinct outcome list following this round and forwarded to the consensus meeting. Those defined as 'consensus out' and 'no consensus' were removed. Round three included a question asking if participants were willing to take part in the final consensus meeting, and if they consented to being contacted.

4.3.5 Stage 3: Consensus meetings

Two initial consensus meetings were held at different times of day to facilitate international participation. These meetings were held online as planned, to maximise attendance and due to the ongoing COVID-19 pandemic. These meetings included a presentation of the findings of the Round 3 Delphi, including the final list of outcomes by category (i.e. awareness and clinical management) and how they were voted for by each stakeholder group. This information was also sent to participants before the meeting. The presentation was followed by a timed discussion and a vote on each outcome for each list. Outcomes were included if voted for by at least 70% of participants. A third meeting was then held to discuss and vote on any outcomes that were included at one meeting only. The consensus panel was made up of at least three representatives from each stakeholder group.

4.3.6 Other analyses

Median scores for each outcome in rounds two and three were compared between stakeholder groups for each round, to see if any stakeholder groups scored outcomes significantly differently between these rounds.

4.3.7 Changes from the protocol

Participants were given the option to provide feedback at the end of round three. Two consensus meetings were held to accommodate participants from all time zones. Due to this, a third meeting was planned if outcomes chosen by each meeting were significantly different. To combat attrition, rounds were open for longer than originally anticipated and multiple reminder emails were sent if necessary. Due to the change in survey structure between rounds one and two we did not look at whether participants' scores changed between these rounds and participants were not given descriptive statistics.

4.4 Results

4.4.1 Systematic review

Systematic literature searches identified 1,125 studies, which were screened based on their titles and abstracts. Relevant papers were also identified via keyword searches detailed in section 4.3.3.2., by screening reference lists, and from the list of included papers in Chapter 3. This process led to the extraction of 225 outcomes from 28 studies. After duplicate outcomes from different studies (or those that were considered similar) were removed or combined, 50 different outcomes (24 maternal outcomes and 26 neonatal outcomes) were forwarded to round one of the survey, shown in Table 16.

Table 16 – Outcomes in round one of the Delphi survey, organised by domain

Maternal outcomes	**Neonatal outcomes**
Maternal health	*Birthweight*
Maternal admission to hospital	Birthweight
Maternal admission to intensive care	Small for gestational age
Antepartum haemorrhage	*Gestation at birth*
Maternal health status postpartum	Gestational age at birth
Maternal health status six months postpartum	Post-term birth
Intrapartum infection	Preterm birth
Postpartum infection	*Labour*
Length of maternal stay in hospital	Abnormal fetal heart rate
Maternal hypertension	Spontaneous onset of labour
Obstetric cholestasis	Respiratory distress
Postnatal depression	*NICU admission*
Prelabour rupture of membranes	Neonatal intensive care unit admission
Postpartum haemorrhage	Neonatal intensive care unit admission after 37 weeks' gestation
RFM knowledge and information	Use of therapeutic cooling for babies admitted to neonatal intensive care unit
Acceptability of information on RFM	Use of mechanical ventilation
Maternal concern about RFM	*Perinatal hypoxia*
Maternal knowledge of RFM	Apgar score at 1 minute
Mode of birth	Apgar score at 5 minutes
Caesarean section	Hypoxic ischemic encephalopathy
Induction of labour	

Instrumental vaginal birth	Meconium aspiration syndrome
Vaginal birth	Neonatal acidaemia
Maternal–fetal attachment	*Perinatal death*
Maternal-fetal attachment	Neonatal death
Maternal anxiety	Perinatal death
Maternal anxiety	Stillbirth
Presentation with RFM	*Other fetal outcomes*
Duration of RFM before presenting to hospital	Dysmaturity score
Number of presentations at hospital with RFM	Need for intubation
	Neonatal resuscitation
	Neonatal seizures
	Oligohydramnios
	Severe neonatal depression

4.4.2 Delphi survey

Round one was completed by 128 participants, 31% of which were parents (n=40), 15% were researchers (n=19), 51% were clinicians (n=65), and 3% chose 'other' when responding (n=4). Of these 128 participants, 80 were from the UK (33 from England, 4 Wales, 2 Scotland, 1 Northern Ireland; 40 did not specify which country), 11 from Zimbabwe, 10 from Ireland, 6 from Australia, 4 from Sweden, 4 from the USA, 3 from New Zealand, 3 from the Netherlands, 2 from Canada, 2 from India, 1 from Austria, 1 from Turkey, and 1 from Uganda.

Two new outcomes were added after round one after being suggested by two or more participants: healthcare costs (additional costs due to extra visits or scans) and maternal wellbeing (maternal mental health throughout pregnancy, including the birth experience and whether any trauma was experienced). A flow chart showing how outcomes moved through the process can be seen in Figure 11.

Round two was completed by 77% (99/128) of participants who completed round one, of whom 30% were parents (n=30), 19% were researchers (n=19), 47% were clinicians (n=47), and 3% fell under the 'other' category (n=3). No outcomes met the 'consensus out' criteria after round two and so all 52 outcomes were forwarded to round three.

Round three was completed by 85% (84/99) of participants who completed round two: 31% were parents (n=26), 23% were researchers (n=19), 44% were clinicians (n=37), and 2% 'other' (n=2). After round three, 23 outcomes were rated as 'no consensus' for studies aiming to encourage awareness of RFM, and 15 outcomes were voted as 'no consensus' for studies aiming to improve the clinical management of RFM. No outcomes were rated as 'consensus out'. This left 29 and 37 outcomes respectively to be voted on at the consensus meetings (Table 17).

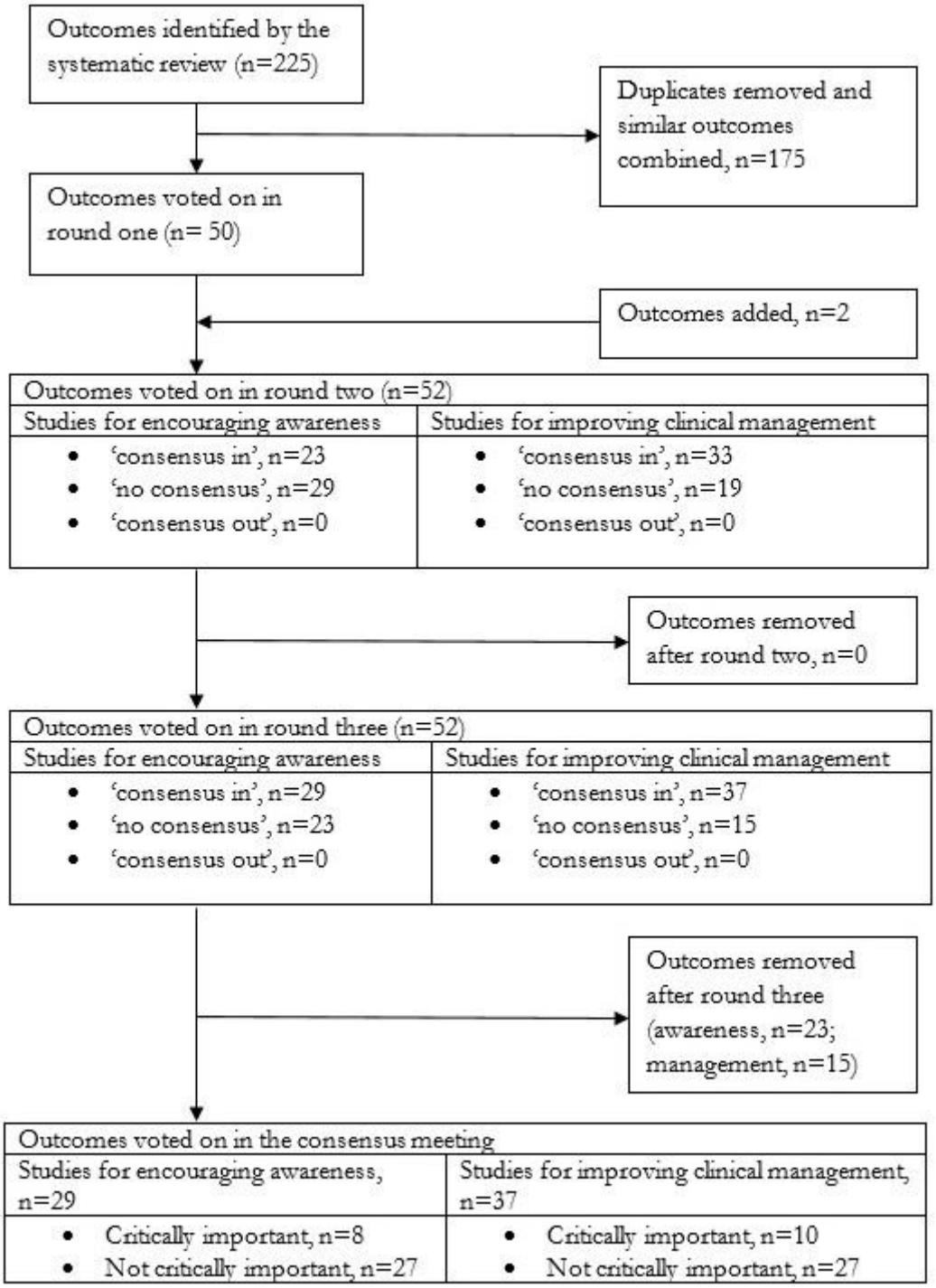


Figure 11 – Flow chart for the Delphi process

Table 17 – Consensus for all outcomes after round three

	Studies aiming to encourage maternal awareness	Studies aiming to improve clinical management
	Maternal outcomes	
Consensus in	*Maternal health* Maternal admission to hospital Maternal wellbeing *RFM knowledge and information* Acceptability of information about RFM Maternal concern about RFM Maternal knowledge of RFM *Mode of birth* Caesarean section Induction of labour Vaginal birth *Maternal anxiety* Maternal anxiety *Presentation with RFM* Duration of RFM before presenting to hospital Number of presentations with RFM	*Maternal health* Antepartum haemorrhage Intrapartum infection Maternal hypertension Maternal admission to hospital Maternal wellbeing *RFM knowledge and information* Acceptability of information about RFM Maternal concern about RFM Maternal knowledge of RFM *Mode of birth* Caesarean section Induction of labour Vaginal birth *Maternal anxiety* Maternal anxiety *Presentation with RFM* Duration of RFM before presenting to hospital Number of presentations with RFM
No consensus	*Maternal health* Antepartum haemorrhage Intrapartum infection Length of maternal stay in hospital	*Maternal health* Length of maternal stay in hospital Maternal admission to intensive care Maternal health status postpartum

	Maternal admission to intensive care Maternal health status postpartum Maternal health status 6 months postpartum Maternal hypertension Obstetric cholestasis Postnatal depression Postpartum haemorrhage Postpartum infection Prelabour rupture of membranes *Mode of birth* Instrumental birth *Maternal-fetal attachment* Maternal-fetal attachment	Maternal health status 6 months postpartum Obstetric cholestasis Postnatal depression Postpartum haemorrhage Postpartum infection Prelabour rupture of membranes *Mode of birth* Instrumental birth *Maternal-fetal attachment* Maternal-fetal attachment
Consensus out	None	None
	Neonatal outcomes	
Consensus in	*Birth weight* Small for gestational age *Labour* Abnormal fetal heart rate Respiratory distress *Perinatal hypoxia* Apgar score <7 at 5 minutes Hypoxic ischemic encephalopathy Meconium aspiration syndrome Neonatal acidaemia	*Birthweight* Birthweight Small for gestational age *Labour* Abnormal fetal heart rate Respiratory distress *Perinatal hypoxia* Apgar score <7 at 5 minutes Hypoxic ischemic encephalopathy Meconium aspiration syndrome Neonatal acidaemia

	Perinatal death Neonatal death Perinatal death Stillbirth *NICU admission* Neonatal intensive care unit admission Neonatal intensive care unit admission after 37 weeks' gestation *Gestation at birth* Gestation at birth Preterm birth *Other neonatal outcomes* Need for intubation Need for resuscitation Neonatal seizures Severe neonatal depression	*Perinatal death* Neonatal death Perinatal death Stillbirth *NICU admission* Neonatal intensive care unit admission Neonatal intensive care unit admission after 37 weeks' gestation Use of therapeutic cooling for babies admitted to intensive care Use of mechanical ventilation *Gestation at birth* Gestation at birth Post-term birth Preterm birth *Other neonatal outcomes* Need for intubation Need for resuscitation Neonatal seizures Severe neonatal depression *Other outcomes* Healthcare costs
No consensus	*Birthweight* Birthweight *Labour* Spontaneous onset of labour *NICU admission*	*Perinatal hypoxia* Apgar score <7 at 1 minute *Labour* Spontaneous onset of labour *Other fetal outcomes*

	Use of mechanical ventilation Use of therapeutic cooling for babies admitted to intensive care *Gestation at birth* Post-term birth *Perinatal hypoxia* Apgar score <7 at 1 minute *Other fetal outcomes* Dysmaturity score Oligohydramnios *Other outcomes* Healthcare costs	Dysmaturity score Oligohydramnios
Consensus out	None	None

4.4.3 Consensus meetings

Overall, 17 participants (three parents, five researchers, and nine clinicians) from eight different countries (Australia, England, Ireland, the Netherlands, New Zealand, Uganda, USA, and Zimbabwe) attended one or more of the consensus meetings. We judged that outcomes included in the COS lists for studies aiming to encourage awareness and studies aiming to improve management were sufficiently different and, as such, a vote on combining the lists was not held and two COS were created.

After two meetings, consensus was reached on six outcomes for studies aiming to encourage awareness of RFM (duration of RFM before presenting to hospital, maternal knowledge of RFM, number of presentations with RFM, neonatal death, perinatal death, and stillbirth) and four outcomes for studies aiming to improve the clinical management of RFM (induction of labour, neonatal death, perinatal death, and stillbirth). Votes were held on four outcomes for studies aiming to encourage awareness of RFM (acceptability of information about RFM, induction of labour, gestation at birth, and NICU admission) and eight outcomes for studies aiming to improve the clinical management of RFM (caesarean section, birthweight, gestation at birth, hypoxic ischaemic encephalopathy, NICU admission, NICU admission after 37 weeks, preterm birth, small-for-gestational-age) at the third meeting respectively, two of which were selected for the COS for awareness and six for management; the final COS are shown in Tables 18 and 19.

Table 18 – Outcomes chosen for the COS of studies aiming to encourage awareness of RFM

Maternal outcomes	**Neonatal outcomes**
Acceptability of information about RFM	Gestation at birth
Duration of RFM before presenting to hospital	Neonatal death
Maternal knowledge of RFM	Perinatal death
Number of presentations with RFM	Stillbirth

Table 19 – Outcomes chosen for the COS of studies aiming to improve the clinical management of RFM

Maternal outcomes	**Neonatal outcomes**
Caesarean section	Birthweight
Induction of labour	Gestation at birth
	Hypoxic ischaemic encephalopathy
	Neonatal death
	NICU admission
	Perinatal death
	Preterm birth
	Stillbirth

4.4.4 Other analyses

Wilcoxon signed rank tests were performed, using the median scores for each stakeholder group for each outcome, to determine if there were statistically significant differences in the ways groups scored outcomes between rounds. This analysis was only performed for round two and three scores due to the change in survey structure after round one. Median scores were higher, indicating greater importance attributed to each outcome, for all groups in round three (Table 20).

Table 20 – Comparisons between round 2 and round 3 scores for each stakeholder group

	No. of scores				
Stakeholder group	**Higher in R3**	**Lower in R3**	**Same in R3**	**Z**	**p**
Parents	25	11	68	2.244	0.02
Clinicians	11	25	68	2.373	0.02
Researchers	31	11	62	3.043	0.002

Although median scores were significantly different between rounds, this only translates as small increases; scores for each stakeholder group were either the same or within one point on the Likert scale for rounds two and three (the only exceptions being neonatal

depression for management studies, scored as 6 in round three and 7.5 in round two for researchers, and dysmaturity score for awareness studies, scored as 7 in round three and 5.5 in round two by researchers). Median scores for all outcomes in rounds two and three are shown in Appendix 7.7.

4.5 Discussion

4.5.1 Main findings

We have developed separate COS for studies aiming to encourage awareness of RFM and for studies aiming to improve the clinical management of RFM using robust methods and following a pre-defined protocol, including an international sample of participants from multiple stakeholder groups. The final COS for studies aiming to encourage awareness includes eight outcomes (four maternal and four neonatal), for studies aiming to improve the clinical management of RFM the COS stands at ten outcomes (two maternal and eight neonatal).

Studies planning on employing combined interventions, i.e. with components aimed at encouraging awareness of RFM and its subsequent management, as recommended in Chapter 3, should measure outcomes specified by both lists.

4.5.2 Strengths and limitations

This COS process followed COMET guidance and a well-established method for reaching consensus. Participants represented each of our desired three stakeholder groups throughout the Delphi survey and at the consensus meeting, which ensured that the views of parents were heard alongside researchers and clinicians. Voting at the consensus meeting was anonymous and electronic. Participants were from 16 countries, including both high and low resource settings — this is higher than the median number of countries involved in the development of COS (based on a review of 281 COS published before 2018).[263] The rate of attrition from round one to round three was 34%, in line with the range of 21% to 48% seen in a review of COS in women's and newborn health.[91]

A large proportion of our respondents (44%) were clinicians, although this was split between midwives and obstetricians. Parents represented almost a third (31%) of our sample overall and at the end of round three. Ideally, there would have been more balance between groups — for example, 23% of participants were researchers, yet many of the clinicians who took part have also published research related to RFM and/or have worked on COS development. This imbalance may be a result of how the survey was programmed: it was only possible to select one response from parent, clinician, or researcher to make

analyses and feedback clearer and easy to interpret. Adding more options or encouraging the use of the available free text boxes would have also been useful in allowing us to see the make-up of clinicians, e.g. how many respondents were neonatologists or primary care doctors.

Clinicians were also in the majority at the consensus meetings (9/17 participants, 53%) which had the potential to impact the final COS. To combat this, we ensured that there was parent representation at the initial and final meetings (2/7 participants, 29%, at the final consensus meeting were parents) and made sure that parents' voices were heard at these meetings by the use of an independent chairperson who did not vote on outcomes. The discrepancy between groups was due to the number of people who indicated that they would like to take part — far more of which were clinicians than parents or researchers. We were also unable to reimburse participants for their time, which could have increased participation (especially as the meetings were held over the summer when people may need childcare).

We reached our targets for recruitment and the consensus meeting. The survey was only provided in English, which has the potential to restrict the number of responses;[173] however, we were limited by the time and resources available. This is perhaps reflected in the larger number of responses from the UK and other English-speaking countries. Ideally, we would have been able to reach more participants from a greater number, and range, of countries — especially lower resource settings. Holding multiple consensus meetings online has both its advantages and disadvantages; on one hand, this facilitated international attendance, but on the other hand it creates the need to consolidate the results from both meetings and could mean that discussions would have been different if all participants were in the same room.

We used techniques recommended by the COMET handbook to reduce attrition such as sending personalised emails from a distinguished researcher in the field, and extending deadlines,[82] allowing us to minimise attrition and to reach our desired sample sizes. Most attrition in our survey happened between rounds one and two (23% of participants were not retained), most likely due to a change in the structure of the survey (from a single list to two separate lists for awareness and management) and the associated time taken to do this; in round three we were able to retain 85% of participants who completed round two. Feedback from some participants (who completed the survey) indicated that they found the survey quite time consuming due to the number of outcomes, which may explain the larger degree of attrition between rounds one and two when this change was made. Due to this

change we were also unable to examine whether attrition bias — when participants do not respond because their scores are different from others' — was present.[82]

A two round Delphi survey, without the changes between rounds, may have made for a more streamlined and efficient process, which in turn may have reduced attrition. We did not use any qualitative methods to identify outcomes alongside the systematic review, instead asking participants during the first round of the survey to suggest additional outcomes. Holding a focus group with key stakeholders before the Delphi survey could have improved this process, ensured that all important outcomes were included in the survey from the start, and again reduced the length of the Delphi process.

4.5.3 Feedback from the Delphi survey and consensus meeting

Feedback collected at the end of round three suggested that the survey could have been further improved by adding clearer explanations of each study type and how the outcomes measured by each may differ, and by using an alternative to the nine-point scale. It may have also been beneficial to use less stringent criteria for removing outcomes after round two, or to place more emphasis on what the scores meant in relation to keeping outcomes, as all outcomes were retained.

Summary graphs provided to participants may have affected the way stakeholder groups voted, as scores were significantly different for all groups between rounds two and three. Yet, this did not translate as large changes in median scores (+/- 2 or more) for any outcomes, so is unlikely to have had a substantial effect on the outcomes that were voted to the preliminary COS.

Feedback from parents included that taking home a live baby was often seen as the most important outcome and all others were viewed as secondary to this, especially those relating to maternal health as parents may prioritise their baby's health over their own. Parents were also unsure about the meaning of some outcomes despite the lay definitions that were used. This was an oversight on our part in not consulting a lay person when writing these definitions, which should have been done to ensure the survey was as accessible as possible and emphasises the importance of this.

At the consensus meeting, consideration was given as to how outcomes were linked — those in the hypoxia pathway domain, for example. This was one reason why NICU admission was selected, as these outcomes often lead to admission to the neonatal unit. Discussions also centred around how morbidity needed to be measured as well as mortality to account for potential harms of interventions, and the best outcomes for quantifying this as well as which outcomes could be measured in the majority of settings globally.

Composite outcomes were also brought up and whether voting for mode of birth as a composite outcome would have been different from voting on each component equally; however, there are additional challenges when considering these in meta-analyses (for example, components may differ across trials and how to weight these outcomes would also need to be considered).

Participants often found it difficult to consider outcomes without corresponding definitions or knowledge of how they would be measured and reported. Nonetheless, this did not prevent outcomes without standardised definitions, such as acceptability of information about RFM, or those that could be reported in a number of ways, such as gestation at birth, from being selected for the final COS.

4.5.4 Future work

4.5.4.1 Implementation and dissemination

The final part of this project will involve disseminating and ensuring implementation of the COS. The COS will be published in an open access journal to ensure maximum reach, making the COS available in the COMET and CROWN databases, and disseminating the COS at national and international conferences where possible. These COS will also be shared with clinical trial registries, maternity service users, and people who took part in the survey.

4.5.4.2 How to measure outcomes

This COS has been developed to determine the outcomes that should be measured by future studies of RFM, not how or when to measure them, and further work is needed to make these recommendations. A guideline for how to select outcome measurement instruments has been created by Prinsen et al., and includes criteria for determining the best measurement properties such as validity, internal consistency, and reliability.[166]

Specific to this COS, consideration should be given as to whether outcomes such as gestation at birth and birthweight are reported as continuous or categorical outcomes, as this affects how they can be used in systematic reviews and meta-analyses, overlap between some of our outcomes (such as gestation at birth and preterm birth), and how to measure outcomes that may manifest as long term symptoms or signs such as hypoxic ischaemic encephalopathy — trials such as TRUFFLE and INFANT have managed this by first publishing the short term outcomes and then measuring long-term outcomes after a two year follow-up periods.[264,265] Some of our outcomes, such as acceptability of information about RFM and maternal knowledge of RFM are not frequently measured and so there are

no consensus definitions or ways to measure them. Definitions of outcomes in our final COS used in the studies identified by our literature review are included as Appendix 7.8.

4.5.5 Conclusions

Following on from research into the management of RFM identified by the Stillbirth Priority Setting Partnership, which prioritised the question "Which investigations identify a fetus which is at risk of stillbirth after a mother believes she has experienced reduced fetal movements?",[266] COS have now been created that should be used in the evaluation of interventions to raise awareness of RFM and/or for the clinical management of RFM. These COS provide researchers with a minimum set of outcomes that should be recorded, facilitating comparisons of interventions. We have taken steps to ensure that the views of parents are adequately represented in this study and the final COS.

Chapter 5 - A UK based survey of midwives and obstetricians' knowledge and practice regarding reduced fetal movement

5.1 Abstract

Introduction

A 2008 survey of UK clinicians found significant variation in both knowledge of RFM, such as how it should be defined, and its clinical management (the role of fetal movement counting and clinical testing). There is a lack of consensus on how RFM pregnancies should be managed clinically, in part due to a lack of evidence. A survey of UK midwives and obstetricians was conducted to test the hypothesis that knowledge of RFM and clinical practice concerning RFM pregnancies has changed in the time since the 2008 survey due to updated RCOG guidelines and the publication of several large trials of interventions.

Methods

A cross sectional online survey of UK-based midwives and obstetricians was conducted, collecting demographic information and surveying participants' knowledge of and attitudes towards RFM, the acceptability of definitions of RFM, participants' clinical practice related to RFM, and the knowledge of conditions associated with RFM. Participants were recruited by contacting relevant organisations (such as the Royal College of Midwives and the British Maternal Fetal Medicine Society), authors of studies about RFM, and social media. Consent was obtained from all participants.

Results

The survey was responded to by 387 participants (293 midwives, 91 obstetricians, and 3 sonographers), 70.0% of which completed all questions in the survey. Maternal perception of reduced movement lasting 12 hours was the preferred definition of RFM; definitions of RFM based on 'alarm limits' are less popular and kick charts are rarely used in routine antenatal care. 98% of participants were aware of guidelines for the management of RFM in their hospital, but responses indicated that not all units followed the same guidelines. Participants found it hard to respond to questions about the clinical management of RFM without knowledge of other risk factors, although, in line with national guidelines, almost all clinicians would offer CTG testing to all presentations with RFM.

Conclusions

Since the 2008 survey, attitude has shifted towards definitions of RFM based on maternal perception being the most useful. Guidelines for RFM are now in place in almost all hospitals but still show variation. Guidelines that are not evidence-based may be harder to implement and lead to inconsistencies in clinical practice.

5.2 Introduction

5.2.1 Background

Concerns about RFM in pregnancy, defined as a decrease or change in a baby's normal movements *in utero*,[1] result in presentation at hospital in up to 15% of pregnancies[267]. Maternal perception of RFM is associated with adverse pregnancy outcomes such as stillbirth and FGR, as previously described in this thesis.[192–194]

A survey of UK-based midwives' and obstetricians' knowledge and management of women presenting with RFM, conducted in 2008, found significant variation in both knowledge of RFM and practice relating to its subsequent clinical management.[2] Similar surveys have been conducted in Ireland[103,268] and Australia,[104] and have also demonstrated variation in responses.

The UK survey (n=233; 129 obstetricians and 94 midwives) found that participants disagreed about definitions of RFM; maternal perception of decreased movements for 24h was the most accepted, by 73.6% of obstetricians and 80.9% of midwives. Definitions based on the number of movements were less popular, although <10 movements total in 12h was accepted by 65.9% of obstetricians and 57.4 % of midwives. Only 70% of obstetricians and 74% of midwives said that their institution had guidelines for the subsequent clinical management of RFM in pregnancy, whilst the majority of participants indicated that they would offer CTG testing, with subsequent ultrasound scanning depending on risk status.

5.2.2 Current UK guidance

Defining RFM

The RCOG Green-top Guideline 57 for RFM[11] states that there is "no universally agreed definition of RFM" and that fetal movements should be assessed by subjective maternal perception, which is rated as grade C evidence due to studies showing variation between maternally perceived movements and movement seen using ultrasound.[3–5]

Encouraging awareness of RFM and presenting to hospital

Current advice regarding RFM from the NHS is to contact a midwife or maternity unit if your baby is moving less than usual or not at all.[205] NICE guidance for antenatal care recommends that doctors and midwives should discuss babies' movements with people who are pregnant after 24 weeks' gestation, and advise them to contact maternity services in the event of any concerns about movement, or if RFM is perceived after 24 weeks.[269] RCOG guidance states that there is insufficient evidence to recommend formal fetal

movement counting during pregnancy, for example via the use of kick charts or other methods, but advises being aware of babies' individual pattern of movements and contacting a maternity unit if there is concern after 28+0 weeks of gestation.[11]

Subsequent clinical management of RFM

There is a lack of consensus on how these pregnancies where RFM is reported should then be managed clinically, in part due to a lack of evidence. NICE guidance for managing RFM recommends following the NHS Saving Babies' Lives Care Bundle Version 2 (SBLCBv2),[270] which contains a checklist based on the RCOG guideline. The RCOG guideline states that a CTG should be performed to exclude fetal compromise after 28+0 weeks' gestation and that ultrasound scanning should be performed if perception of RFM persists or if there are other risk factors for adverse outcome.[11] However, recommendations within the RCOG guideline, such as these, are generally based on evidence rated as 'B' or 'C', meaning that underpinning data are from high quality cohort studies or systematic reviews of these studies, rather than high quality randomised trials or systematic reviews and meta-analyses of trials.

5.2.3 How knowledge and practice might have changed

Recently published trials of interventions to prevent adverse outcomes in RFM pregnancies, such as those by Akselsson et al.[9] and Flenady et al.,[77] focus on being aware of the normal pattern, strength, and frequency of fetal movements and presenting to hospital in cases of deviations from this, rather than kick counting using pre-specified 'alarm limits', which may have increased support for definitions of RFM based on maternal perception. In the interval between this initial survey the RCOG guideline has been updated and reviewed, which may have influenced practice.

In spite of updated guidelines, the systematic review and meta-analysis detailed in Chapter 3 of this thesis showed wide variation in terms of what was considered as standard care at different study sites, both in terms whether awareness of fetal movements was encouraged in all pregnancies (via information leaflets, kick counting, or other methods), and in terms of protocols for the subsequent clinical management of presentations with RFM. The ongoing presence of variation suggests that national guidelines are still not followed at all hospitals, a finding that is corroborated by two reviews of UK clinical practice guidelines regarding RFM;[74,271] this may be a result of the variety in the strength of recommendations described above.

A survey of UK midwives and obstetricians was conducted to test the hypothesis that knowledge of RFM and clinical practice concerning RFM pregnancies has changed over the past decade as a result of updated guidelines, and to highlight areas of practice that could be improved.

5.3 Methods

5.3.1 Aim

This study aimed to survey UK-based health professionals to describe their knowledge of and clinical practice relating to RFM, to determine whether knowledge and/or practice has changed since the 2008 survey, and whether this can be attributed to guidelines or studies that have been published during this time.

5.3.2 Objectives

1. To survey UK-based health professionals about their knowledge of RFM and their experience of clinical practice related to encouraging awareness of RFM and its subsequent clinical management;

2. To see if responses by midwives and obstetricians differ;

3. To compare responses with a previous survey to determine if there have been changes over time;

5.3.3 Design

This was a cross sectional UK-based survey of midwives and obstetricians, structured similarly to a 2008 survey by Heazell et al. to facilitate comparisons with this survey, and with additional questions based on current UK guidelines.

The survey was created using REDCap software[170] and was tested for functionality before it was available online. The survey was open and online; anyone with the link to the survey was able to participate and survey responses were captured automatically, to easily maximise reach and to reflect how research is now conducted. Participants were able to save their answers and return to the survey using a unique code, and were able to submit incomplete responses. The survey was available online for approximately four months (June-September 2022). The study protocol can be found as Appendix 7.9 and at https://figshare.manchester.ac.uk/articles/online_resource/RFM_survey_of_practice_protocol_docx/19467242/1 (uploaded 30th March 2022).

The survey had five sections: 1. Demographics of participants, including whether they work part or full time, their area of practice, years of experience, and whether they work for

the NHS or privately; 2. Asking pregnant women about RFM, knowledge of and attitudes towards fetal movement counting; 3. Definitions of RFM and their acceptability; 4. Clinical management of RFM pregnancies, and; 5. Knowledge of associations of RFM with adverse outcomes and other characteristics.

Participants were asked to elaborate on their answers, providing reasoning and justifications where appropriate. A five-point scale (strongly agree, agree, unsure, disagree, strongly disagree) was used for questions that ask about the acceptability of definitions of RFM or its management. The survey questionnaire is included as Appendix 7.10.

5.3.4 Scope

The purpose of this survey was to describe knowledge and practice relating to RFM in the UK, to identify areas in which knowledge is lacking or variable, or in which practice could be improved, but also to give an overview of these areas and how much they are influenced by the current guidelines. Responses may not be applicable to other countries or income settings; this may be an avenue for future research.

5.3.5 Participants and sampling

Anyone who is currently practising, or has practised, as a midwife or obstetrician in the UK was eligible to take part. There were no inclusion or exclusion criteria based on other demographic criteria. We aimed for a sample size of 200 to facilitate comparisons with the 2008 survey, including people from all countries of the UK (and as many areas as possible within these countries). As the response rate for the previous survey was fairly low (30% for clinicians and 34% for midwives), no upper limits were applied on the number of potential participants that were approached.

Participants were recruited by contacting relevant organisations (such as the Royal College of Midwives and the British Maternal Fetal Medicine Society) and asking them to disseminate the survey to their members, the survey was also advertised via social media (Twitter, Facebook, and Instagram). Additionally, we contacted authors of studies about RFM who are based in the UK and encouraged participants to forward the survey to others who were eligible.

Participants were provided with an information sheet describing the study and its aims, and what participation would entail. Consent to take part in the survey was ensured by requiring participants to click an 'I agree to take part' box before gaining access to the survey.

5.3.6 Analysis

Descriptive statistical analysis was performed using STATA Version 14[272] and the Chi-squared test or Fisher's exact test was used to assess statistical differences in responses between groups; a p value of <0.05 was considered as statistically significant.

5.3.7 Changes from the protocol

We were unable to investigate whether factors such as country of residence or the presence of guidelines were linked to participants' responses.

5.3.8 Ethical approval

Ethical approval was not required for this study as members of the public were not recruited and personal identifiable information was not collected. Participants received all information about the study, including information about data storage, when they were invited to take part and consent was obtained from participants. All responses to the survey were confidential and no personal identifiable information was collected. Participants were able to withdraw at any point.

5.4 Results

5.4.1 Participants

Overall, 387 people (293 midwives, 91 obstetricians, and 3 sonographers) responded to the survey (defined as those who filled in their demographic details and answered the first question – there were 541 responses which consented to taking part but filled in no further information; we do not have data for the number of clicks on the survey link). Due to the low number of participating sonographers, their response data was not included in any formal comparisons (Table 21). 271 people (70.0%) completed all questions in the survey. The majority of participants (62.5%) worked full time and almost all participants (97.4%) worked for the NHS. Experience of respondents varied, with 40.0% having practised for ten years or fewer, 37.5% having practised for 11 to 20 years, 17.0% for 21 to 31 years and 5.4% for 31 years or more.

In general, there was a lot of agreement between obstetricians and midwives in their responses. In addition, a significant percentage of people who responded to the survey were uncertain about the role of fetal movement counting (11.4% to 33.6% answered 'unsure' for questions in this section) and about definitions of RFM (2.6% to 43.0% answered 'unsure' for questions in this section).

Table 21 – Demographic details of participants

	Midwives (n=293)	Obstetricians (n=91)	Sonographers (n=3)	All participants (n=387)
Hours				
Full time	166 (56.6%)	75 (82.4%)	1 (33.3%)	242 (62.5%)
Part time	96 (32.8%)	14 (15.4%)	2 (66.6%)	112 (28.9%)
Not currently practising	31 (10.6%)	2 (2.2%)	0	33 (8.5%)
Years of practice				
≤ 10 years	137 (46.8%)	17 (18.7%)	1 (33.3%)	155 (40.1%)
11-20 years	95 (32.4%)	49 (53.8%)	1 (33.3%)	145 (37.5%)
21-30 years	48 (16.4%)	17 (18.7%)	1 (33.3%)	66 (17.1%)
>31 years	13 (4.4%)	8 (8.8%)	0	21 (5.4%)
Type of practice				
NHS	286 (97.6%)	89 (97.8%)	2 (66.6%)	377 (97.4%)
Private practice only	1 (0.3%)	1 (1.1%)	0	2 (0.5%)
NHS and private practice	6 (2.0%)	1 (1.1%)	1 (33.3%)	8 (2.1%)

5.4.2 Questions relating to encouraging awareness of RFM and RFM definitions

The majority of obstetricians and midwives thought that asking about fetal movements should be part of routine antenatal care from all gestations after 24 weeks, with the percentage of midwives indicating that this should be the case in all pregnancies ranging from 93.4% at 24+0 to 27+6 weeks to 99.3% above 34+0 weeks and the percentage of obstetricians ranging from 78.0% to 95.6% at the same gestations. The distribution of responses between groups was statistically significantly different at all gestations (Table 22).

Table 22 – Responses to the question "Please indicate at which gestations, if any, you think asking about fetal movement should be part of routine antenatal care"

	Midwives (n=293)			Obstetricians (n=91)			
	All pregnancies	High risk pregnancies only	Never	All pregnancies	High risk pregnancies only	Never	P value
24+0 to 27+6 weeks' gestation	275 (93.4%)	9 (3.1%)	9 (3.1%)	71 (78.0%)	13 (14.3%)	7 (7.7%)	**<0.001**
28+0 to 30+6 weeks' gestation	286 (97.6%)	3 (1.0%)	4 (1.4%)	81 (89.0%)	5 (14.3%)	5 (5.5%)	**0.002**
31+0 to 33+6 weeks' gestation	287 (97.6%)	2 (0.7%)	4 (1.4%)	83 (91.2%)	4 (4.4%)	4 (4.4%)	**0.002**
34+0 to 36+6 weeks' gestation	291 (99.3%)	1 (0.3%)	1 (0.3%)	87 (95.6%)	1 (1.1%)	3 (3.3%)	**0.035**
37+0 to 40+6 weeks' gestation	291 (99.3%)	2 (0.7%)	0	87 (95.6%)	1 (1.1%)	3 (3.3%)	**0.007**
Above 41+0 weeks' gestation*	290 (99.3%)	2 (0.7%)	0	87 (95.6%)	1 (1.1%)	3 (3.3%)	**0.007**

*includes one incomplete response for midwives

Written responses from midwives indicated that fetal movements are "a key indicator of fetal wellbeing", are "important at all gestations", "should be discussed throughout pregnancy" and are "a key part of practice". Midwives who did not think that asking about fetal movements as part of routine care before 31 weeks' gestation stated that fetal movements should be asked about "once a normal pattern is established" and that "fetal development is not yet completed". Obstetricians who responded that they thought asking about fetal movement should never be part of routine care at any gestation said that this was because it "does not prevent stillbirth and causes significant anxiety" and stated that there is a lack of evidence. Other obstetricians said that asking about fetal movements is "important at all gestations" and "relevant to all pregnancies, regardless of risk".

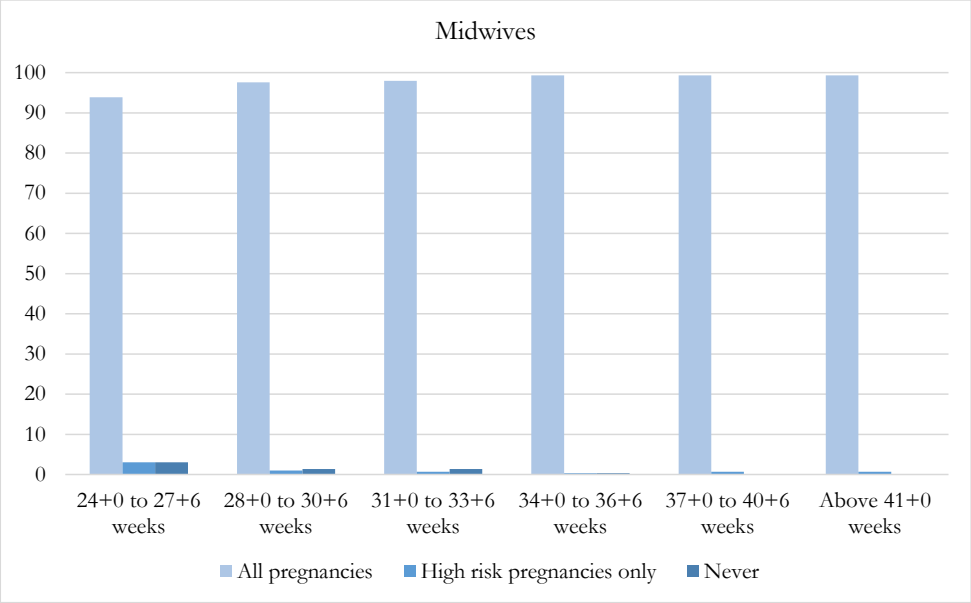
In line with current UK guidelines, the majority of respondents do not use kick charts as part of routine antenatal care, with 1% of midwives and obstetricians using them for high-risk pregnancies and 3.4% of midwives and 1% of obstetricians using them in all pregnancies (Table 23). The distribution of responses did not differ between groups (Chi-squared 1.35, p=0.51).

Table 23 – Responses to the question "Do you use a kick chart as part of routine antenatal care?"

	Midwives (n=292)	Obstetricians (n=91)
Yes, for all pregnancies	10 (3.4%)	1 (1.1%)
Yes, for high risk pregnancies	3 (1.0%)	1 (1.1%)
No	279 (95.5%)	89 (97.8%)

However, some participants who do not use kick charts thought that they should be used, "I think we should use kick charts, patients found them easy" but others stated that changes in the normal pattern of movement is more important. One participant stated, "a lot of women second guess themselves and think 'it's probably nothing' so having a chart will give women the confidence to phone a health care professional".

When asked the question "Do you routinely provide any other information about RFM as part of routine antenatal care, such as leaflets or other guidance?", 251 out of 377 participants (66.6%; 199 midwives and 52 obstetricians) stated that a leaflet is provided, with 102 (86 midwives and 16 obstetricians) of these specifically mentioning the Tommy's leaflet and 24 (22 midwives and 2 obstetricians) mentioning the Kicks Count leaflet. 26 responses (16 midwives and 10 obstetricians) stated that there was no other information about RFM routinely provided.



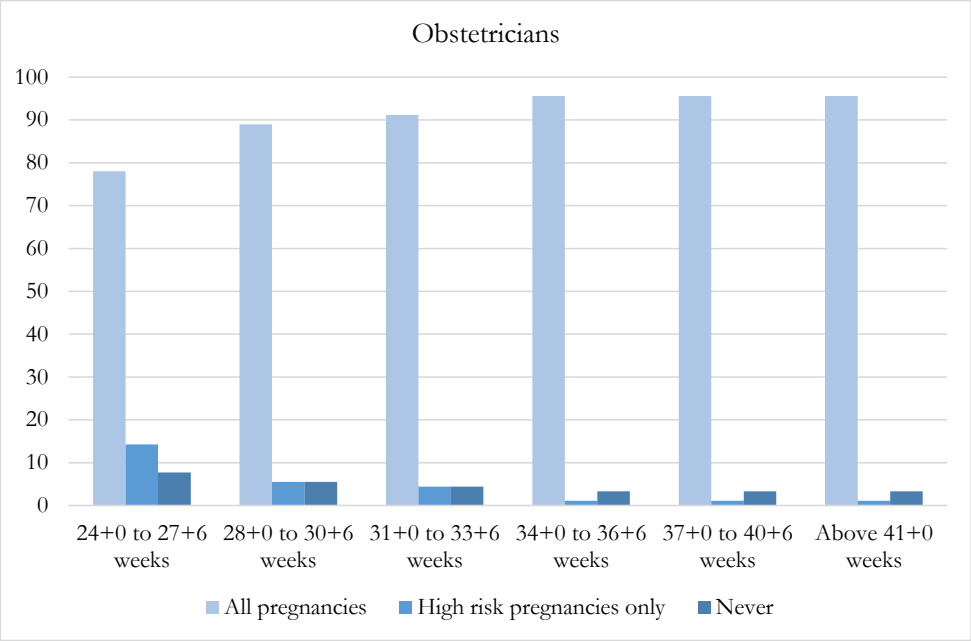


Figure 12 - Responses to the question "Please indicate at which gestations, if any, you think asking about fetal movement should be part of routine antenatal care"

There was more variation in the responses that were received when participants were asked for their level of agreement with statements about the potential advantages and disadvantages of kick charts (Table 24). For example, 48.3% of midwives either agreed or strongly agreed with the statement "asking pregnant women to formally count fetal movements using a kick chart is of no benefit" while 22.3% either disagreed or strongly disagreed. 54.7% of midwives and 87.3% of obstetricians did not agree with the statement "asking pregnant women to formally count fetal movements using a kick chart is proven to prevent stillbirth". Distribution of responses was significantly different between

obstetricians and midwives when asked whether fetal movement counting leads to unnecessary interventions and whether it is helpful in antenatal care for all pregnancies, but not for any other questions.

Table 24 - Whether midwives and obstetricians agree with the following statement: "Asking pregnant women to formally count fetal movements using a kick chart…"

	Midwives (n=256)						Obstetricians (n=79)						
	Strongly agree	Agree	Unsure	Disagree	Strongly disagree	Total	Strongly agree	Agree	Unsure	Disagree	Strongly disagree	Total	p
…helps women to remember to notice movements every day	20 (7.8%)	59 (23.0%)	59 (23.0%)	85 (33.2%)	33 (12.9%)	256	2 (2.5%)	16 (20.3%)	23 (29.1%)	30 (38.0%)	8 (10.1%)	79	0.347
…increases maternal-fetal attachment	16 (6.3%)	43 (16.8%)	64 (25%)	96 (37.5%)	37 (14.5%)	256	1 (1.3%)	6 (7.6%)	23 (29.1%)	37 (46.8%)	12 (15.2%)	79	0.085
…increases maternal anxiety	83 (32.4%)	111 (43.4%)	42 (16.4%)	17 (6.6%)	3 (1.2%)	256	19 (24.1%)	45 (57.0%)	9 (11.4%)	6 (7.6%)	0	79	0.244
…assists in detecting fetal growth restriction	6 (2.3%)	17 (6.6%)	69 (27.0%)	113 (44.1%)	51 (19.9%)	256	1 (1.3%)	3 (3.8%)	18 (22.8%)	43 (54.4%)	14 (17.7%)	79	0.544
…avoids unnecessary consultations for RFM	5 (2.0%)	14 (5.5%)	63 (24.6%)	125 (48.8%)	49 (19.1%)	256	0	2 (2.5%)	16 (20.3%)	44 (55.7%)	17 (21.5%)	79	0.426

…results in unnecessary interventions	20 (7.8%)	56 (21.9%)	86 (33.6%)	69 (27.0%)	25 (9.8%)	256	8 (10.1%)	28 (35.4%)	28 (35.4%)	13 (16.5%)	2 (2.5%)	79	**0.021**
…is helpful in routine antenatal care for all women	16 (6.25%)	37 (14.5%)	59 (23.0%)	100 (39.1%)	44 (17.2%)	256	2 (2.5%)	3 (3.8%)	16 (20.3%)	41 (51.9%)	17 (21.5%)	79	**0.033**
…is only useful for women considered to be at high risk of pregnancy complications	0	7 (2.7%)	70 (27.3%)	121 (47.3%)	58 (22.7%)	256	1 (1.3%)	2 (2.5%)	23 (29.1%)	39 (49.4%)	14 (17.7%)	79	0.398
…is of no benefit	48 (18.8%)	78 (30.5%)	73 (28.5%)	35 (13.7%)	22 (8.6%)	256	19 (24.1%)	31 (39.2%)	20 (25.3%)	6 (7.6%)	3 (3.8%)	79	0.186
…is proven to prevent stillbirth	10 (3.9%)	20 (7.8%)	86 (33.6%)	89 (34.8%)	51 (19.9%)	256	1 (1.3%)	1 (1.3%)	8 (10.1%)	50 (63.3%)	19 (24.1%)	79	**<0.001**

Table 25 Whether midwives and obstetricians consider the following to be reduced fetal movements in the third trimester of pregnancy

Definition	Midwives (n=231)				Obstetricians (n=76)				
	Yes (RFM)	No (not RFM)	Unsure	Total	Yes (RFM)	No (not RFM)	Unsure	Total	p
<3 fetal movements per hour over 12 hours	64 (26.4%)	74 (32.0%)	93 (40.3%)	231	34 (44.7%)	22 (28.9%)	20 (15.2%)	76	**0.015**
<10 movements total in 2 hours	25 (10.8%)	108 (46.8%)	98 (42.4%)	231	8 (10.5%)	45 (59.2%)	23 (30.3%)	76	0.140
<10 movements total in 12 hours	77 (33.5%)	54 (23.5%)	99 (43.0%)	230*	34 (44.7%)	12 (15.8%)	30 (39.5%)	76	0.155
<10 movements total in 2 days	140 (60.6%)	32 (13.9%)	58 (25.2%)	230*	50 (65.8%)	11 (14.5%)	15 (19.7%)	76	0.620
Maternal perception of RFM lasting 12 hours	222 (96.1%)	3 (1.3%)	6 (2.6%)	231	72 (94.7%)	2 (2.6%)	2 (2.6%)	76	0.728

*Includes 1 incomplete response

Views on definitions of RFM based around the number of movements in a given time period varied, with many participants (up to 43%) stating that they were unsure whether these definitions should be considered as RFM or not (Table 25). Many of these respondents stated that the pattern of fetal movements and/or maternal perception are more important, and how they quantify RFM clinically, and so these definitions are not used. Despite this, there was almost universal agreement that maternal perception of RFM lasting 12 hours should be considered as RFM (96.1% of midwives and 94.7% of obstetricians).

The importance of normal patterns of fetal movement was also apparent in the responses to when pregnant women in the third trimester of pregnancy should report a complete absence of fetal movements, with 57.8% of midwives and 46.9% of obstetricians selecting the 'other' option (rather than <12 hours, <24 hours, or <48 hours) (Figure 13). Some respondents suggested other timeframes ("1-2 hours", "less than 6 hours") but the majority again cited that time is less important; "any deviation from the normal pattern", "any length of time that concerns them", "as soon as they notice", "any length of time", "what is unusual for them". The distribution of responses between midwives and obstetricians did not differ significantly (chi-squared 5.76, p=0.056).

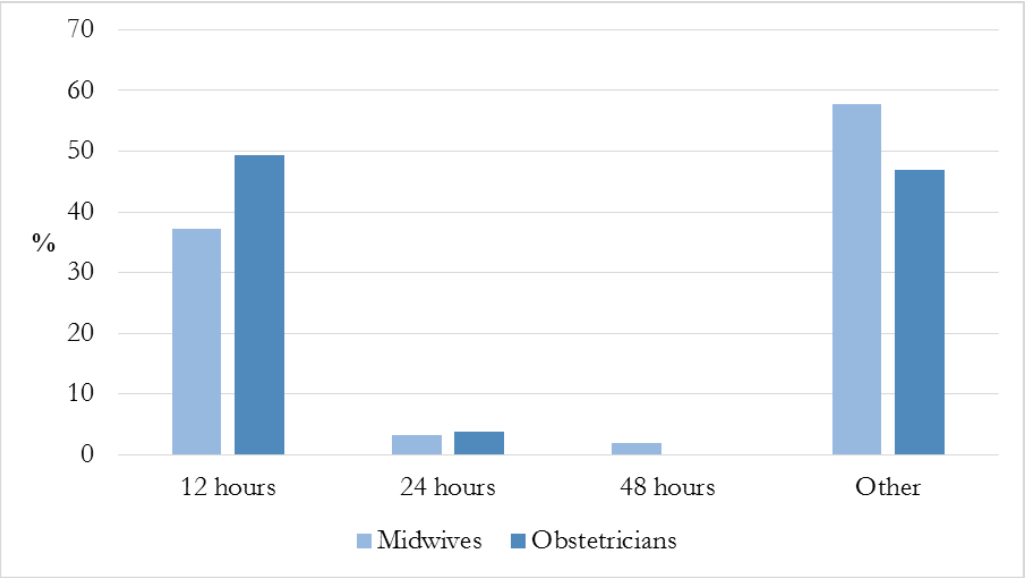


Figure 13 - Pregnant women in the third trimester of pregnancy should report a complete absence of fetal movements lasting for a period of at least…

5.4.3 Questions relating to the subsequent clinical management of RFM

When asked, "Are you aware of any clinical practice guidelines within your institution for the management of RFM?" 98.3% of midwives and 98.7% obstetricians said yes (0.9% of midwives and 1.3% of obstetricians were unsure, 0.9% of midwives and no obstetricians said they were not aware of any). RCOG guidelines were followed by 12% of midwives and 17.8 % of obstetricians, the NHS England Saving Babies' Lives Bundle by 73.2% of midwives and 64.4% of obstetricians. Other guidelines that were followed, when this was elaborated upon, were trust or local guidelines (including adapted or mixed versions of the RCOG and NHS guidelines).

When asked about which clinical interventions they would perform for presentations with RFM from 28+0 to 37+6 weeks of gestation, over 95% of both midwives and obstetricians said that they would perform a CTG. The distribution of responses between obstetricians and midwives differed only when asked about performing Kleihaur-Betke's test and requesting an ultrasound for biophysical profile (Table 26). Both midwives and obstetricians stated that it was difficult to respond to this question definitively without knowing the full clinical picture — interventions would depend on what the risk factors were, how many times someone had presented with RFM, and the results of other testing such as CTG testing. Some midwives stated that these interventions would not be at their discretion and they would refer the patient for an obstetric review. Similarly, when asked about the same clinical interventions after 37 weeks' gestation, participants stated that they would still need to know more information and the results of other testing (Table 27).

Table 28 shows responses to when participants would consider induction or expedited birth for maternal perception of RFM; responses varied based on gestation. The distribution of midwives' and obstetricians' responses differed significantly when asked when they would consider induction or expedited birth for maternal perception of RFM ($p=0.010$) and for objective evidence of absent fetal movements ($p=0.034$).

Table 26 – Responses to the question "which of these interventions, if any, would you perform on women presenting with reduced fetal movements from 28+0 to 37+6 weeks of gestation?"

	Midwives (n=223)				Obstetricians (n=73)				
	Always	Sometimes	Never	Total	Always	Sometimes	Never	Total	p
Give a kick chart	11 (5.0%)	112 (5.5%)	199 (89.6%)	222*	0	5 (6.9%)	67 (93.1%)	72*	0.144
Measure symphysis-fundal height	141 (63.2%)	73 (32.7%)	9 (4.04%)	223	47 (64.4%)	21 (28.8%)	5 (6.8%)	73	0.451
CTG	212 (95.1%)	11 (4.9%)	0	223	70 (95.9%)	2 (2.7%)	1 (1.4%)	73	0.162
Vibro-acoustic stimulation	8 (3.6%)	27 (12.2%)	187 (84.2%)	222*	2 (2.7%)	4 (5.5%)	67 (91.8%)	73	0.128
Ultrasound scan for growth	38 (17.1%)	183 (82.4%)	1 (0.5%)	222*	18 (24.7%)	55 (75.3%)	0	73	0.255
Ultrasound biophysical profile	24 (10.8%)	139 (62.6%)	59 (26.6%)	222*	6 (8.2%)	29 (39.7%)	38 (52.1%)	73	**<0.001**
Kleihaur-Betke's test	2 (1.0%)	46 (20.7%)	174 (78.4%)	222*	0	25 (34.7%)	47 (65.3%)	72*	**0.04**
Umbilical artery Doppler	34 (15.2%)	184 (82.5%)	5 (2.2%)	223	15 (20.5%)	56 (76.7%)	2 (2.7%)	73	0.455
Admit to hospital	6 (2.7%)	198 (89.2%)	18 (8.1%)	222*	1 (1.4%)	64 (87.7%)	8 (11.0%)	73	0.227
Consider expedited birth	7 (3.2%)	206 (92.8%)	9 (4.1%)	222*	3 (4.1%)	63 (86.3%)	7 (9.6%)	73	0.197

Note: 'sometimes' was 'sometimes (dependent on risk status)' in the questionnaire. * denotes that one incomplete response is included

Table 27 – Responses to "Which of these interventions, if any, would you perform on women presenting with RFM after 37 weeks of gestation?"

	Midwives (n=214)				Obstetricians (n=71)				
	Always	Sometimes	Never	Total	Always	Sometimes	Never	Total	p
Give a kick chart	11 (5.1%)	10 (4.7%)	193 (90.2%)	214	0	6 (8.6%)	64 (91.4%)	70*	0.08
Measure symphysis-fundal height	128 (59.8%)	72 (33.6%)	14 (6.5%)	214	44 (62.9%)	19 (27.1%)	7 (10.0%)	70*	0.192
CTG	206 (96.3%)	8 (3.7%)	0	214	68 (95.8%)	3 (4.2%)	0	71	0.887
Vibro-acoustic stimulation	9 (4.2%)	33 (15.4%)	172 (80.4%)	214	2 (2.8%)	8 (11.3%)	61 (85.9%)	71	0.297
Ultrasound scan for growth	56 (26.2%)	156 (72.9%)	2 (0.9%)	214	16 (22.5%)	54 (76.1%)	1 (1.4%)	71	0.852
Ultrasound biophysical profile	31 (14.5%)	128 (59.8%)	55 (25.7%)	214	7 (9.9%)	32 (45.1%)	32 (45.1%)	71	**0.001**
Kleihaur-Betke's test	2 (0.9%)	51 (23.8%)	161 (75.2%)	214	0	27 (38.6%)	43 (61.4%)	70*	0.072
Umbilical artery Doppler	47 (22.0%)	160 (74.8%)	7 (3.3%)	214	13 (18.3%)	51 (71.8%)	7 (9.9%)	71	0.093
Admit to hospital	19 (8.9%)	184 (86.0%)	11 (5.1%)	214	2 (2.8%)	59 (83.1%)	10 (14.1%)	71	**0.003**
Consider expedited birth	33 (15.4%)	177 (82.7%)	4 (1.9%)	214	14 (19.7%)	56 (78.9%)	1 (1.4%)	71	0.584

Note: 'sometimes' was 'sometimes (dependent on risk status)' in the questionnaire

Table 28 – Responses to "At which gestation(s), if any, would you consider induction or expedited birth for reduced fetal movement in the absence of any other complications?"

	Midwives (n=205)						Obstetricians (n=71)						
	<34 weeks	34 to 36+6 weeks	37 to 40 weeks	Over 40 weeks	Never	Total	<34 weeks	34 to 36+6 weeks	37 to 40 weeks	Over 40 weeks	Never	Total	p
Maternal perception of RFM	4 (2.0%)	2 (1.0%)	118 (57.6%)	70 (34.1%)	11 (5.4%)	205	0	0	33 (47.9%)	37 (52.1%)	0	71	**0.010**
Maternal perception of absent fetal movements	9 (4.4%)	13 (6.34%)	146 (71.2%)	30 (14.6%)	7 (3.4%)	205	0	4 (5.7%)	57 (81.4%)	9 (12.9%)	0	70*	0.193
Objective evidence of RFM	17 (8.3%)	32 (15.6%)	126 (61.5%)	23 (11.2%)	7 (3.4%)	205	3 (4.3%)	7 (10.0%)	55 (78.6%)	5 (7.1%)	0	70*	0.095
Objective evidence of absent fetal movements	36 (17.6%)	43 (21.1%)	106 (52.0%)	11 (5.4%)	8 (3.9%)	204*	5 (7.1%)	19 (27.1%)	44 (62.9%)	1 (1.4%)	1 (1.4%)	70*	**0.034**

*includes one incomplete response

Table 29 – Responses to the question "In general, do you feel that any of the following are significantly increased in women presenting with RFM?"

	Midwives (n=199)				Obstetricians (n=68)				
	Yes	No	Unsure	Total	Yes	No	Unsure	Total	P
Maternal wish for additional scan	136 (68.3%)	36 (18.1%)	27 (13.6%)	199	49 (72.1%)	11 (16.2%)	8 (11.8%)	68	0.879
Maternal anxiety levels	189 (95.0%)	2 (1.0%)	8 (4.0%)	199	66 (97.1%)	3 (2.9%)	0	68	0.055
Maternal depression	92 (46.2%)	42 (21.1%)	65 (32.7%)	199	31 (46.3%)	16 (23.9%)	20 (29.9%)	67*	0.858
Maternal obesity (BMI >30)	109 (54.8%)	57 (28.6%)	33 (16.6%)	199	37 (54.4%)	20 (29.4%)	11 (16.2%)	68	0.994
Anterior placental site	153 (76.9%)	28 (14.1%)	18 (9.0%)	199	40 (59.7%)	15 (22.4%)	12 (17.9%)	67*	**0.002**
Primigravida	105 (52.8%)	62 (31.2%)	32 (16.1%)	199	42 (61.8%)	17 (25.0%)	9 (13.2%)	68	0.379
Male fetal sex	0	124 (62.3%)	75 (37.7%)	199	0	46 (67.6%)	22 (32.4%)	68	0.886
Female fetal sex	0	124 (62.3%)	75 (37.7%)	199	0	47 (69.1%)	21 (30.9%)	68	0.667
Fetal hypoxia/fetal distress	135 (67.8%)	34 (17.1%)	30 (15.1%)	199	44 (65.7%)	14 (20.9%)	9 (13.4%)	67*	0.690
Fetal growth restriction	150 (75.4%)	26 (13.1%)	23 (11.6%)	199	49 (73.1%)	10 (14.9%)	8 (11.9%)	67*	0.667
Pre-term labour	73 (36.7%)	74 (37.2%)	52 (26.1%)	199	20 (29.4%)	32 (47.1%)	16 (23.5%)	68	0.158
Preeclampsia	107 (53.8%)	49 (24.6%)	43 (21.6%)	199	31 (45.6%)	21 (30.9%)	16 (23.5%)	68	0.286
Umbilical cord pathology	117 (58.8%)	36 (18.1%)	46 (23.1%)	199	35 (52.2%)	16 (23.9%	16 (23.9%)	67*	0.394

In general, midwives and obstetricians agreed about which factors were increased in women presenting with RFM (Table 29). The only statistically significant difference in the distribution of responses between groups was for anterior placental site. Factors that over 50% of midwives and obstetricians thought are significantly increased in women with RFM are: maternal wish for additional scan, maternal anxiety levels, maternal obesity, anterior placental site, primigravida, fetal hypoxia/fetal distress, FGR, and umbilical cord pathology.

5.5 Discussion

5.5.1 Main findings

This study describes midwives and obstetricians' current knowledge and practice relating to RFM in the UK. Fetal movement is viewed as an important indicator of fetal wellbeing throughout pregnancy (once a normal pattern has been established) and 95% of clinicians consider maternal perception of reduced movement lasting 12 hours an acceptable definition of RFM. This differs from the uncertainty seen in the responses to other definitions based on given numbers of fetal movements.

Almost all respondents (over 98%) were aware of guidelines for the management of RFM, with the Saving Babies' Lives Care Bundle followed by over 65% of participants and RCOG guidelines by 13.5%, with modified or combined versions of these also frequently mentioned by those who stated that other guidelines were followed in their unit.

5.5.2 Current evidence and guidelines

In line with SBLCBv2[270] and the underpinning guidelines that this relates to,[11] over 95% of all respondents would commence CTG testing for all presentations with RFM, and responses to the question of which interventions are appropriate for presentations for RFM indicate that subsequent management would be tailored based on this result. Universal ultrasound for RFM is largely not supported, in line with guidelines and perhaps due to increased levels of interventions seen in the AFFIRM study. SBLCBv2 also recommends that induction of labour after 38+6 weeks should be an individualised decision, based upon evidence of fetal compromise or other risk factors; this was reflected by the majority of participants (82.7% of midwives and 78.9% of obstetricians) who responded that they would consider induction or expedited birth after 37 weeks' gestation based on other risk factors.

Kick charts are now rarely used in routine antenatal care, with clinicians choosing to favour definitions of RFM based on maternal perception. Practice may be influenced by recent studies such as Mindfetalness[9] and My Baby's Movements[77] in which the focus was on the normal pattern, strength, and frequency of fetal movements, and presenting to hospital in

cases of deviations from this, rather than kick counting using pre-specified 'alarm limits.' However, this result may also be based on a perceived association with maternal anxiety (believed to exist by 75% of midwives and 81% of obstetricians), which is not supported by the current literature; Chapter 3 found evidence from three studies suggesting that maternal anxiety may be lower when comparing fetal movement counting with standard care.

Variation in practice still exists, although it is unsure how much of this is due to variation in guidelines (the most referenced guidelines share recommendations, and we did not gather information about how guidelines are combined or adapted by people who made this response) and how much this could be improved if guidelines were more evidence-based.

5.5.3 Comparisons with the 2008 UK survey

One of the most striking differences between this survey and the survey by Heazell et al.[2] relates to midwives and obstetricians' attitudes towards maternal perception of RFM. In the 2008 survey, the percentages of midwives and obstetricians who agreed that "mother's perception of RFM for 12h" should be regarded as RFM were 73.4% and 69.0% respectively, now it is 96.1% and 94.7%.

Another important finding is that guidelines for RFM are now far more commonplace; 98.3% of midwives and 98.7% of obstetricians reported that guidelines were in place in their hospital compared to 74% and 70% respectively in 2008. Meanwhile, kick chart usage has fallen further among obstetricians: the 2008 survey found that 3% of midwives and 5% of obstetricians used kick charts in routine care; these numbers are now 3.4% and 1% respectively.

Clinicians still associate RFM with maternal anxiety and maternal wish for an extra ultrasound scan, with slightly more support for these associations than previously. The percentages of midwives and obstetricians who associate RFM with maternal obesity has also risen from 45% and 40% to 54.8% and 54.4%; interestingly, systematic reviews published recently have found limited evidence for this association.[197,273]

5.5.4 Comparison with other surveys

5.5.4.1 Presence of policies for the management of RFM

In addition to the survey by Heazell et al., surveys by Unterscheider et al. (2010)[268] and Smith et al.[103] (2014) in Ireland, and Flenady et al. (2009) [274] in Australia have asked participants whether their hospital has a policy for the management of RFM. Tables

comparing the responses can be seen in Appendix 7.11; it should be noted that not all data were available and there were differences in question wording between studies.

The number of clinicians reporting that guidelines are available was highest in the UK-based surveys, and has increased over time. Over 50% of participants in each of the other surveys stated that no guidelines were available; data that are more recent would reveal whether this is an effect of time or if this prevails.

5.5.4.2 Management of RFM — CTG testing

Again, surveys differed in the question that was asked, yet it can be seen from the responses to all surveys that CTG testing is usually offered (at least 80.3% of participants in all surveys would always offer a CTG) — whether this is universal or based on other factors.

5.5.4.3 Definitions of RFM and their acceptability

Data are shown in Appendix 7.11 for definitions that are directly comparable. The survey by Unterscheider et al. did not ask this. There is wide variation across surveys, though this may be down to the specific questions that were asked as well as study year and setting. Smith et al. found the least support for maternal perception of RFM, although respondents could only pick one definition. This survey also found that kick charts were recommended at a higher rate and were seen to have more benefits than in other studies; it should be noted that this survey was carried out over ten years ago with a comparatively smaller sample, so practice may have changed, but a follow up survey would be needed to investigate this. Similarly, Flenady et al. found that usage of kick charts in routine antenatal care was common at 38.8%, but again, this survey was carried out in 2005 and so may not reflect current practice.

5.5.5 Surveys of practice in other areas of maternity care

Surveys have been carried out to describe practice around umbilical cord clamping, as described in Chapter 2. These surveys, in Canada and Ireland, found that practice was largely influenced by clinicians' own preferences and hospital routines despite the presence of systematic reviews and guidelines.[100,101] A more recent survey of midwives in France, published in 2022, again found of variation in practice and identified a need for guidelines.[275] Similarly, a survey of obstetricians in Ireland about the definition and management of FGR showed that there was not one approach that was consistently used over others; respondents stated that a national guideline was desired.[102] Follow-up surveys in both these areas, in the same countries, would allow the influence of guidelines, evidence syntheses, and trials to be seen.

However, it is possible that these surveys, and the other RFM surveys discussed previously, demonstrate the difficulties with ensuring that clinical practice is evidence-based and the importance of implementing guidelines (so long as guidelines themselves are based on high quality studies, which is often not the case).[276] Latibeaudiere et al. suggest that the presence of guidelines alone is not enough, and that they need to be accompanied by implementation tools such as targeted training.[277] Introducing guidelines as part of care bundles may also be an effective way of changing practice; responses to our survey show that the SBLCBv2 has been widely adopted, though there is still a way to go before it is followed by all hospitals.

5.5.6 Strengths and limitations

This survey is strengthened by its sample size (387 participants, 271 of which completed all questions) and its diversity in terms of years of experience. More midwives than obstetricians completed the survey, 46.8% of which have been practising for under ten years — this may be a reflection of a younger demographic who saw the survey promoted via social media.

As personal data were not collected during the survey, we were unable to send reminders (but people did have the option to save their responses and return later), meaning that 30% of responses were incomplete. Due to this, people could potentially take the survey multiple times; to combat this, all responses have been checked for duplication but we were unable to employ more stringent methods such as IP checking.[186] Another limitation of this study is that self-reported practice may differ from what happens in the real world, and that people who are not as interested in practice relating to RFM, or do not believe in the usefulness of RFM as an indicator of adverse outcome, may be less likely to participate. We could not look at the effect of country of residence due to the number of participants who stated that their country of practice was the UK — to permit this, the survey design should have allowed participants to select their country from a list.

It may have been useful to ask a question regarding the management of recurrent RFM, as recommended management in SBLCBv2 (offer induction for RFM alone, if recurrent, after 38+6 weeks) differs slightly, and whether other definitions of RFM based on maternal perception, with different or no associated timeframes, are supported, to facilitate comparisons with other surveys.

Although not planned as part of this study, it may have also been beneficial to survey service users (people with first-hand experience of care related to RFM in pregnancy) to see if their experiences align with clinicians' views on the care that is provided.

5.5.7 Conclusions

This survey has described current knowledge and practice related to RFM in the UK and has compared results with other surveys. Almost all hospitals have guidelines in place and most clinicians would offer a CTG to all presentations with RFM despite heterogeneity in these guidelines. Future surveys may be useful after national guidelines have been updated and implemented.

Discussion

6.1 Summary of main findings

The objectives of this thesis were to conduct a systematic review of studies of interventions for encouraging awareness and/or improving the subsequent clinical management of RFM, to create COS for future studies of these interventions, and to describe current knowledge and clinical practice related to RFM in the UK. This thesis presents original research that advances knowledge in this field and has the potential to improve clinical practice by strengthening the evidence base for recommendations in guidelines.

This work identified ongoing uncertainties about the effectiveness of interventions for RFM. The reported systematic review is the most contemporary and comprehensive available and uses robust methods that have not been applied in this area until now. Despite this, meta-analyses were restricted by heterogeneity of published studies in terms of the interventions evaluated and the outcomes that they measured. Flaws in existing studies such as low fidelity of the intervention also hindered synthesis and introduced bias, for example in the My Baby's Movements trial only 9.4% of participants in the intervention group downloaded the app designed to help them understand their baby's movements and to encourage contacting hospital in the event of any concerns. Additionally, many published NRS could not be considered due to their design (mainly uncontrolled before-after studies where any observed differences in outcomes cannot be directly attributed to the intervention), limiting the information derived from this body of literature.

Based on the synthesis of current evidence it is not possible to conclude that interventions aimed at encouraging awareness and/or improving the clinical management of RFM reduce stillbirths or perinatal deaths. Nevertheless, analyses that were possible demonstrated that there may be benefits of encouraging maternal and/or clinician awareness of RFM, such as reduced NICU admissions, and encouraging kick counting, such as decreased maternal anxiety and increased maternal-fetal attachment. We did not find high-certainty evidence that encouraging awareness of RFM is harmful and leads to higher caesarean section rates, as advocated by some commentators.[20] Ultimately, there is still a lot of uncertainty around the effects of interventions for RFM on adverse pregnancy outcomes, which this thesis has highlighted. As well as more robust evidence, data from a wider range of settings may enhance decision making, as it was notable that most studies included in the review were from a high-income, low-burden setting. Studies from lower income settings suggest that the association between RFM and stillbirth may be comparatively higher,[278] meaning that

studies of interventions could potentially show greater effects on stillbirth reduction, and may more easily demonstrate these effects due to the higher incidences of stillbirth and other adverse outcomes.

The systematic review and meta-analysis identified gaps in the literature which could be addressed by a COS for studies of RFM, as well as a survey of clinicians' knowledge and practice related to RFM to understand the impact of this uncertainty. Using an international Delphi survey with 128 participants (clinicians, researchers, and parents from 16 countries), two COS for studies i) aiming to encourage awareness of RFM and/or ii) improve the subsequent clinical management of RFM were subsequently created, comprised of eight outcomes (four maternal and four neonatal) and ten outcomes (two maternal and eight neonatal) respectively. These COS will provide researchers with minimum sets of outcomes that should be measured and reported in future studies of interventions for RFM and, if successfully adopted, will reduce the likelihood that evidence syntheses are limited by outcome reporting. The next steps for this project are to operationalise the measurement outcomes (by consulting the definitions extracted from included studies), to establish how outcomes such as acceptability of information about RFM and maternal knowledge of RFM should be measured, and to successfully publish and promote awareness of these COS.

An online survey of UK clinicians was conducted to see if the observed variation in research translates into variation in knowledge and practice related to RFM, and whether this has changed in relation to the results of a similar 2008 survey. This survey of 293 midwives and 91 obstetricians, with various levels of experience, showed that:

- over 98% of participants stated that their hospital had guidelines in place for the management of RFM (as opposed to just over 70% in 2008),
- maternal perception is the preferred way of defining RFM (maternal perception lasting 12 hours was considered as RFM by 96.4% of participants, up from 70.1%),
- over 95% of clinicians will perform CTG testing for maternal presentations with RFM after 37 weeks' gestation (in accordance with national guidelines),
- subsequent clinical management depends on the individual patient.

The majority of participants said that their institution followed the NHS SBLCB (71.1%) or RCOG (13.5%) guidelines, or adapted/mixed versions of these. This means that there is still variation in the guidelines that are followed, although this may not translate into variation in practice in all areas — many recommendations are shared by guidelines and we

do not have all the information on how and why these guidelines are adapted by individual units.

It is unclear how much the current literature affects variation in clinical practice, although evidence syntheses and guidelines can only make strong recommendations if they are based on high certainty evidence, which may also affect their implementation. Evidence synthesis is primarily being held back by a lack of robust adequately powered studies; therefore, the next step for future research should be to design and conduct these trials.

6.2 Implications for future research

6.2.1 Trials of interventions for RFM

Sample size and study design

To attain adequate sample sizes, trials should recruit from multiple sites, and ideally from both high- and low-income settings. Chapter 3 estimated that an adequately powered trial (for the primary outcome of stillbirth) in a high-income country would require at least 460,000 participants, assuming 50% effectiveness in the 25% of RFM pregnancies with suboptimal management. In low-income countries, this sample size may be lower due to higher stillbirth rates; but the percentage of pregnancies with suboptimal management may be higher too, and so may amplify this.

The CEPRA trial,[217] which is in progress, will allow the feasibility of running an international multicentre trial of an intervention for RFM to be seen (in high income countries) and will hopefully achieve a sample size with enough statistical power to detect differences in its primary outcome — a composite outcome including stillbirth. It may also be beneficial for studies to model the financial impact of interventions for RFM; this has been performed for the AFFIRM trial, though such analyses are unable to account for differences in fidelity between sites or any longer-term benefits of interventions.[279]

Alternatively, it could be argued that the most useful next step for research into interventions for RFM would not take the form of randomised trials, and instead large-scale retrospective and non-randomised designs would be more appropriate; as discussed in Chapter 4 these study designs may allow the effects of guidelines to be evaluated in a real-world situation (although population stillbirth rates then need to also be considered). Consideration of the interventions to be employed — their effectiveness, how to implement them, and potential to lead to unnecessary harms — is also crucial.

Interventions

As touched upon previously, it needs to be ensured that interventions are wide reaching, i.e. have good uptake by service users and clinicians — this is worth reiterating as it is only useful to study interventions that will reach everyone who needs them and that are acceptable to parents as well as clinicians, which is often overlooked by trials and is an area in which more work is needed. This is particularly pertinent in high-income countries such as the UK and USA, where the stillbirth rate is significantly higher in Black and minority ethnic groups.[280,281] It is hoped that the precedent set by the My Baby's Movements trial and the outcomes listed in the COS will make measuring (and ensuring) the acceptability of interventions far more commonplace.

A 2021 qualitative study of data from nine studies in four high-income countries (Sweden, Australia, UK, New Zealand) showed that even though multiple sources of information about RFM are accessed during pregnancy, participants in these studies preferred that information was given as handouts or leaflets rather than verbally.[282] Preferences were also found for specific information about monitoring fetal movement and when to seek advice, although it was stated that information that too specific to fetal movement, rather than general health and wellbeing, could cause (or increase) anxiety. Factors that could prevent people from contacting healthcare professionals were also identified, such as worries that their concerns would not be taken seriously (often based on experience), or fear that they would have to be induced;[282] this reinforces the importance of public and community involvement when designing research studies.

Appendix 7.1 describes other factors that need to be considered and how they interlink, such as the baseline rate of adverse outcomes in the study population (and, linked to this, demographics and risk factors of the study population), and what the intervention is being compared to, i.e. what was clinical practice and awareness of RFM like before the intervention. Interventions are more likely to have an effect where there is more 'room for improvement', whether this is in clinical practice and adherence to guidelines, or whether this is in a population with higher rates of adverse outcomes.

The COS also revealed that maternal knowledge of RFM, acceptability of information provided about RFM, and maternal anxiety are seen as important outcomes, and so studies should design interventions that consider these variables and allow them to be measured.

Outcomes

From the results of Chapters 3 and 4, it can be seen that many of the most important outcomes for interventions for RFM, as included in the COS, are not routinely measured in trials. In particular, outcomes relating to interventions for encouraging awareness of RFM,

such as acceptability of information related to RFM and maternal knowledge of RFM, as well as hypoxic ischaemic encephalopathy, are rarely measured by existing studies.

Future studies should ensure that all outcomes specified by the COS are measured, so that the full effect of interventions for RFM is more likely to be seen; not measuring all the most important outcomes may mean that there are effects of interventions that trials to this point have failed to show.

Care bundles

The effects of interventions for encouraging awareness of and/or improving the clinical management of RFM as part of care bundles could also be studied; the NHS England SBLCB has been shown to be effective in reducing stillbirths[244] and was mentioned by respondents to the survey in Chapter 5. Studying the effect of care bundles may more accurately reflect clinical practice in the real world (outside of trial conditions) and reflects how managing RFM is just one part of a multifaceted process when aiming to reduce stillbirths; however, when studying care bundles it is difficult to know which part of the bundle is having any (or the greatest) effect, and data from randomised trials may still be preferred when studying interventions.[283] The costs of implementing care bundles should also be considered when evaluating their impact.[244]

6.2.2 Evidence synthesis

Future systematic reviews will only be able to draw further conclusions once trials that meet the parameters above have been conducted. As mentioned, successful implementation of the COS is crucial to improve future evidence synthesis in this area, though it will take time for trials to be designed and conducted after the COS is published.

As the COS was created as a response to the RFM review in Chapter 3, we do not have full data on when these outcomes have and have not been measured. With the creation of the RFM COS, systematic reviews can now use this as a template for which outcomes should be included, and collecting data on these outcomes (as well as whether data are available), will enable researchers to measure uptake of the COS and to see if collecting data for outcomes that were not previously measured is more commonplace.

IPD analysis of studies of interventions for RFM is yet to be explored, and was originally going to be a part of this thesis until it was decided, from speaking to study authors, that the available data would not be sufficient. Another issue is that IPD analysis would not solve existing problems such as intervention comparability and heterogeneity in outcome measures. Without adequately powered trials, results of IPD analyses are unlikely to differ

from conventional meta-analysis, but there may be some use (in the future, if and when more data are available) in determining whether interventions are more effective for RFM in different groups at different gestations. This may reflect when RFM is a useful indicator of adverse outcome, and may vary as the association between RFM and stillbirth is not consistent in terms of effect size across pregnancy.[12] IPD analysis could also show whether other risk factors for adverse outcome interact with interventions for RFM.

6.3 Implications for guidelines and clinical practice

6.3.1 Guideline quality in maternity care

Currently, guidelines in maternity care are of variable quality. Lau et al. rated 75 maternity guidelines from 19 hospitals using the AGREE II tool, four of these guidelines were recommended for use in clinical practice without modifications (5.3%) and 54 were recommended for use dependent on modifications (72%).[271] Notably, six out of the 12 guidelines that were not recommended for use in clinical practice were related to the management of RFM. Guidelines were also compared with recommendations in the SBLCB, and recommendations for providing information relating to RFM at 24 weeks of gestation were omitted by guidelines from 12 out of 18 units (one did not submit a guideline for RFM).

Jokhan et al. proposed that the generally low quality evidence used to create national guidelines could lead to variation in local guidelines. However, they did not find a direct relationship between the strength of evidence behind individual recommendations in national guidelines for RFM, and whether these recommendations were included in local guidelines.[74]

Despite this, maternity care in general is lacking in high quality evidence upon which to base recommendations in clinical practice guidelines,[276] and so improvement in the underlying evidence base is needed where possible. Future work could aim to look at specific recommendations made by guidelines for the clinical management for RFM and the evidence behind them, to see whether this explains any of the variation in management demonstrated both by this work and by other studies.[74,271]

6.3.2 Updating the RCOG guideline for the management of RFM

The results of the systematic review described in Chapter 3 have the potential to inform future guidelines. For example, incorporating the results of the review could lead to some recommendations in the RCOG guideline for management of RFM changing. Specifically, the guideline currently states that instructing pregnant women to monitor fetal movements is associated with anxiety — this is a Grade B recommendation, is not based on any

evidence from systematic reviews, and contrasts the review findings.[11] This was also reflected by the findings of the survey in Chapter 5, where over 50% of respondents thought that RFM was associated with maternal anxiety, which may be in part due to a guideline that is not fully informed by the current evidence.

The RCOG guideline also recommends that women should be advised to be aware of the normal pattern of fetal movements — this is a Grade C recommendation.[11] Incorporating the results of the review here, which showed that awareness of RFM may lead to reduced NICU admission and is unlikely to lead to any harms, may increase the strength of this recommendation and lead to more support for encouraging awareness of fetal movements. The results of the survey show that although asking about the normal pattern of fetal movements is largely a routine part of clinical practice, the numbers of obstetricians who always do this (in comparison to midwives) could be improved; as this is supported by the evidence then guidelines should be updated to reflect this and aim to make this practice even more widespread.

6.3.3 Improving guideline implementation

Clinical practice could also be improved by greater implementation of guidelines. Clinicians' knowledge and attitudes have been identified as general barriers to guideline implementation,[284] and these may be particularly relevant to guidelines for the management of RFM. The survey of knowledge and practice related to RFM showed that some clinicians hold views that are not supported by the current evidence, suggesting that there is scope to improve the implementation of guidelines. Specific education and training for clinicians may help to ensure that guidelines are followed outside of trial settings, though the costs in time and money should be considered.[277,284] This is particularly relevant to ensuring that clinicians provide information about RFM and encourage maternal awareness, as subsequent clinical management and improving pregnancy outcomes depends on this.

It is also possible that trust in guidelines (and research) may have been lowered by previous events such as when the findings from the Term Breech Trial were incorporated into guidelines and then subsequently overturned;[276] education and training may help to overcome this (as well as guidelines based on high quality evidence).

6.3.4 Other considerations for clinical practice

Following on from above, it is vital that all maternity units provide information about RFM during pregnancy to ensure that people with RFM contact maternity services (which is also more likely if patient values and preferences are incorporated into the guideline

development process). It needs to be ensured that concerns of people who present with RFM are taken seriously, which has been identified by investigations into maternity services.[285] Media promotion may also help to raise awareness; analysis of the Count the Kicks campaign in Iowa, which aims to improve awareness of fetal movement by encouraging the use of an app during pregnancy as well as information leaflets, showed increased uptake over time (2,375 app users from 37,935 births in 2018, also higher than in neighbouring states).[286]

6.4 Strengths and limitations of this thesis

Strengths of this thesis include that established, reproducible, and transparent methods were followed (PRISMA and COS-STAR statements, GRADE, and RoB 2 and ROBINS-I for risk of bias assessment) and the synthesis of evidence that had not been included in systematic reviews until now. Novel research has been carried out: the most up to date systematic review of studies of interventions for RFM, the first COS for future studies of encouraging awareness and/or improving the clinical management of RFM, and a survey allowing current knowledge and practice related to RFM in the UK to be described. This work has also involved collaborations with researchers from different countries and with varied areas of expertise.

The main limitation of this thesis is the strength of the current evidence, which affects the number of conclusions related to the effects of interventions on adverse outcome that could be drawn by the systematic review. The COS and the survey of practice are limited by recruitment and sampling, as this cannot ever be truly representative without unlimited time and resources. Both surveys and the systematic review would benefit from data from a wider range of settings, specifically lower resource countries. Inequality and socioeconomic factors are both major drivers of adverse outcome in pregnancy[287,288] and more work on how this may interlink with RFM and interventions for RFM is needed.

Alternative avenues for this thesis could have involved looking at other factors affecting uptake and acceptability of interventions in more detail, potentially using numerical data to expand upon the created logic model in terms of what the greatest limiting factors are and theorising more about what the best interventions for future studies would look like; however, creation of a COS and researching the state of current practice were prioritised over this.

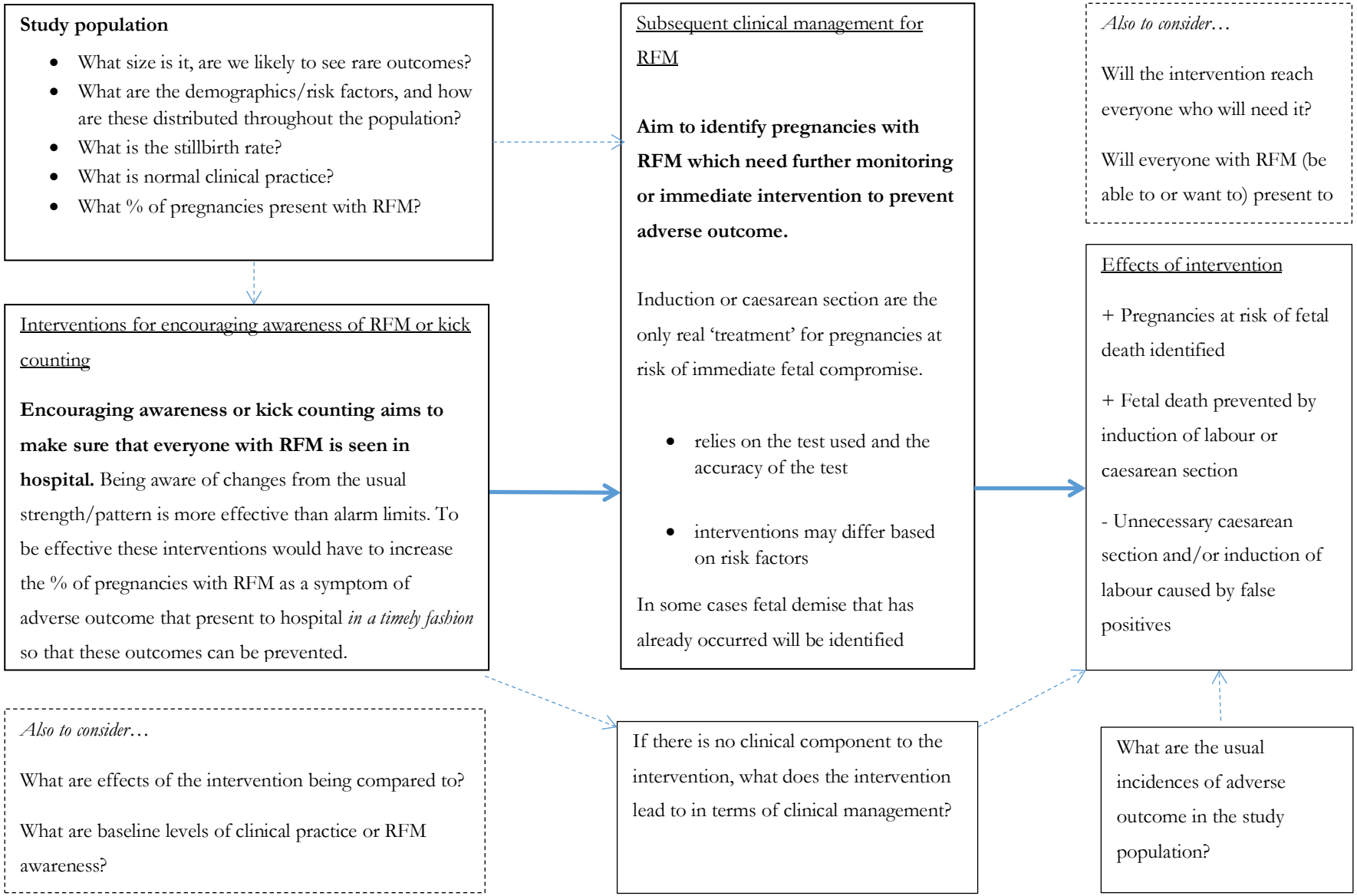
6.5 Conclusions

This thesis has added an up to date, robust, systematic review of interventions for RFM to the current literature, which has the potential to inform future guidelines and improve

clinical practice, and a COS to improve future studies and evidence syntheses. Studies of interventions for RFM with appropriate design, sample size, and outcome measurement are now needed.

Appendices

7.1 Logic model for the effects of RFM interventions



7.2 Effect of management of RFM on pregnancy outcome: protocol for a systematic review and meta-analysis

7.2.1 Background

7.2.1.1 Description of the condition

RFM are defined as a decrease or change in a baby's normal pattern of movements *in utero;*[1] current NHS guidance is to contact a midwife or maternity unit if your baby is moving less than usual or not at all.[205] Most people who are pregnant become aware of fetal movements by 18-20 weeks of gestation and usually become aware of the pattern of their baby's movements and the time of day that the baby moves the most.[187]

Maternal concern leads to presentation hospital with concerns regarding RFM in 5-15% of pregnancies.[2] Around 70% of these pregnancies have a pregnancy outcome[191] but RFM are associated with adverse outcomes such as stillbirth and FGR.[2] Case control studies have consistently demonstrated an association between RFM and stillbirth after 28 weeks' gestation.[13,193,194] It is important to recognise that these study designs may suffer from recall bias due to asking about perceived RFM after a stillbirth has occurred; although these studies do show similar effects across different populations, supporting the potential for a common aetiology. It is thought that there is a reduction of fetal movements in cases of insufficient nutrient transfer and hypoxia, which may be caused by placental insufficiency (where the placenta cannot meet the metabolic demands of the fetus) or other fetal stressors, in an attempt to conserve energy and oxygen consumption.[8,196]

A systematic review of 27 observational studies[197] identified that anterior placenta, ethnicity, oligohydramnios, polyhydramnios, and smoking may be predictive of RFM. The association between RFM and other factors such as body mass index (BMI) and parity is also still unclear.[198]

7.2.1.2 Description of the intervention

This review is focused on interventions for improving awareness of RFM as well as interventions for its clinical management.

Interventions for improving awareness of RFM

The first type of intervention aims to increase awareness of the importance of RFM in people who are pregnant and/or clinicians. This may be as part of clinical training, information campaigns, or instructions to parents to be aware of or to count fetal

movements. Information be may be given in the form of leaflets, videos, training sessions, or other material.

Being aware of RFM may involve counting or being more mindful of fetal movements. Current Royal College of Obstetricians and Gynaecologists (RCOG) guidance states that there is 'insufficient evidence to recommend formal fetal movement counting'.[11] It is thought that fetal movement counting may not always be beneficial as the frequency of individual fetal movement varies greatly within a normal range. Specified 'alarm limits' may also not be useful due to the subjective nature of RFM; the most commonly used alarm limit (fewer than 10 movements in 12 hours) is based on a study of 61 high risk women[11,289] and so is unlikely universally applicable. It is stated in the guideline, however, that women should be advised to be aware of their baby's movement patterns.

Interventions for the clinical management of RFM

Clinical management strategies for people presenting with RFM usually aim to identify underlying issues such as fetal compromise or placental dysfunction, which may lead to adverse pregnancy outcomes such as a small for gestational age fetus and stillbirth. Management may take the form of several clinical interventions, described below.

In the UK, current RCOG guidance[11] for women reporting RFM recommends auscultation of the fetal heart to exclude fetal death. After fetal viability has been confirmed, recommended clinical assessment for pregnancies over 28 weeks' gestation is to monitor the fetal heart rate by CTG for at least 20 minutes in order to detect fetal compromise. The fetal heart rate tracing obtained using CTG should be interpreted using NICE's categorisations for baseline fetal heart rate.[290] For women presenting to hospital with RFM between 24 and 28 weeks of gestation then fetal viability should be confirmed by the presence of a fetal heartbeat using a handheld Doppler device. It is also recommended that ultrasound scan assessment should be undertaken when women have additional risk factor for adverse pregnancy outcomes or if maternal perception of RFM persists after 28 weeks' gestation, even in the case of normal CTG. Ultrasound assessment should include measurement of fetal abdominal circumference, and/or estimated fetal weight, and measurement of amniotic fluid volume (by AFI or maximal pool depth). Fetal morphology should also be measured if this has previously not been performed;[11] fetal assessment may take the form of biophysical profile assessment, which combines CTG, AFI, and ultrasound assessment of fetal movement and measurement. Additional testing may include umbilical artery Doppler to assess blood flow to the fetus. If these assessments identify

abnormalities, alone or in combination, this may lead to expedition of birth via induction of labour or caesarean section.

It is important to consider that caesarean section and induction of labour are also likely to take place for reasons other than suspected RFM: caesarean section may be elective or may take place during labour for other indications such as breech presentation or previous caesarean section; induction of labour may be recommended in prolonged pregnancies; in cases such as these, such procedures will not be considered part of the intervention for RFM.

7.2.1.3 How the intervention might work

Interventions for improving awareness of RFM

Interventions for improving awareness of RFM may target people who are pregnant and their families, and/or clinicians. RFM may provide early warning of developing fetal compromise. By providing information regarding what RFM is and why it is important, women with a compromised fetus may then be more likely to present to hospital if they perceive reduced movements. Clinicians may be more likely to ask about babies' movements or to prescribe clinical testing to perceive RFM. Timely presentation at hospital and appropriate management may prevent adverse outcomes.

Kick counting may be used to define RFM, where advice to parents is to seek care if a baby's movements drop below a specified 'alarm limit'. Some studies have shown that kick charts may be linked to an associated decrease in perinatal death,[220,291] however, the largest RCT in this area (n=68,654) did not show any associated effect.[200]

Alternatively, interventions may encourage awareness of or to be more mindful of babies' movements and for parents to seek care if anything seems unusual. In an RCT of 49,865 women, published since the guideline was last updated, providing pregnant women and midwives with information about fetal movements was associated with a lower incidence of caesarean section and babies born small-for gestational age but the number of babies born with low Apgar scores and the number of stillbirths were unaffected.[9]

Interventions for the clinical management of RFM

The current RCOG guideline states that the aim of antenatal monitoring in cases of RFM is to identify pregnancies in which the fetus is compromised or at risk of adverse outcome but also to avoid unnecessary intervention that may cause harm.[11] Initial fetal heart rate monitoring is performed with the aim of determining whether there is any fetal

compromise and to detect cases in which fetal death has occurred in utero; the fetal heart accelerates with most maternally perceived fetal movements and so fetal heart rate accelerations coupled with maternally perceived fetal movements are an indicator that the fetus is healthy and moving normally.[11] Following this, a reassuring, or normal, CTG result may be interpreted as indicating that reduced movements were unrelated to acute fetal compromise so no further testing is needed. A reassuring CTG may lead to discharge from hospital or additional testing may be performed as well, such as ultrasound scanning. Conversely, a non-reassuring or abnormal CTG (classified as suspicious, pathological, or requiring intervention) indicates that RFM may be due to acute fetal compromise, which may be confirmed using further clinical testing or may prompt action if sufficiently concerning.

Ultrasound scan assessment may be performed to identify additional risk factors for stillbirth such as SGA fetuses or to assess amniotic fluid volume, or to detect fetal movements that are not being perceived, as women may not perceive all movements detected by ultrasound.[292] The presence of an SGA fetus or reduced amniotic fluid volume may be indicative of placental dysfunction as mentioned previously. If it is determined that the fetus shows evidence of significant compromise then birth may be expedited as this is the only available treatment for concerns about fetal wellbeing or placental insufficiency.[293] The decision to expedite birth is considered against the risk of iatrogenic prematurity as earlier gestations at birth adversely affect the likelihood of survival.[294]

Concerns related to these current management strategies are that including additional testing such as ultrasound scanning may lead to unnecessary intervention such as caesarean section or induction of labour, as the sensitivity of ultrasound EFW to detect SGA fetuses is generally poor.[240] There are also concerns with CTG testing, a Cochrane review of continuous compared to intermittent CTG showed no significant reduction in the rate of perinatal death.[295]

We anticipate that studies may employ combinations of these two types of interventions.

7.2.1.4 Why it is important to do this review

Two Confidential Enquiries into Antepartum Stillbirth conducted almost 20 years apart both highlighted the importance of information about fetal movements and a clear plan of management for RFM.[188] However, there is no general consensus on the best clinical management for RFM.[2] The most recent Cochrane review on the assessment of fetal wellbeing, published in 2015,[296] highlighted the paucity of high-quality data from RCTs to

inform the management of RFM (data from five RCTs with 71,548 women were included; no studies were judged at low risk of bias for all criteria), although results from several randomised trials have been published since.

Despite the presence of RCOG guidance described above, there is currently wide variation in both knowledge and practice when it comes to the management of RFM; a UK survey found that 89.9% of 129 obstetricians and 95.7% of 94 midwives would always commence CTG testing in women who presented with RFM. Yet, just 20.2% and 14.9% respectively would always perform an ultrasound scan for growth.[2] Variation has also been found in the quality of clinical guidelines in individual maternity units.[74] Surveys in Norway,[201] Australia, and New Zealand[104] have also shown inconsistencies in both the management of RFM and the information given to women.

Variation in practice may result from the lack of evidence; many recommendations in the RCOG Green-top guideline are rated as low certainty of evidence due to a lack of data from RCTs, though there are many relevant observational studies which have not been reviewed in detail. Consequently, the management of RFM is not informed by all the available evidence, limiting the conclusions that can be drawn and hence clinical recommendations derived. The second version of the guideline is currently in development.

7.2.1.5 Objectives

The primary objective of this review is to assess whether different interventions for encouraging awareness of RFM, and management of presentations for RFM, affect adverse maternal or perinatal outcomes when compared with each other or to no prescribed management strategy.

The secondary objectives of the review are:

- to summarise current evidence for strategies to increase awareness of RFM and management of presentations for RFM, highlighting gaps in the literature
- to determine if randomised and non-randomised studies of interventions for RFM produce significantly different effect estimates
- to determine if individual study design aspects within these study types significantly affect the estimates produced by these study types (to determine which characteristics, if any, are associated with bias)

7.2.2 Methods

7.2.2.1 Study inclusion criteria

Types of studies

Randomised studies (RCTs, quasi-randomised trials, cluster RCTs) as well as non-randomised controlled studies with clearly reported mechanism of group formation, clearly defined inclusion criteria, and described methods of ascertainment of eligible patients and their recruitment will be included. NRS designs that fit these criteria may include cohort studies with prospective or retrospective controls, quasi-randomised controlled trials, controlled before-after studies, or interrupted time series studies (ITS). These study designs will allow the inclusion of interventions at both the individual and organisational level.

Uncontrolled before-after studies, cross-sectional studies, case control studies, and cohort studies without clearly defined comparator groups will not be included as these study designs mean that it would not be possible to attribute any differences in outcomes to the intervention. We will include studies irrespective of their publication status and language of publication.

Participants

Studies of singleton pregnancies presenting at least once in a hospital setting after 24 weeks' gestation will be included. For studies in which interventions are targeted at pregnancies with RFM rather than all pregnancies, we will accept definitions of RFM based on maternal perception, kick counting, and/or confirmed by clinical assessment of fetal activity.

Interventions

Interventions for improving awareness of RFM

Interventions targeted at parents or clinicians with the aim of raising their awareness of RFM will be included, as well as those that encourage fetal movement counting or increased recording, monitoring, or mindfulness of fetal movements.

Interventions for the clinical management of RFM

Interventions, management strategies, and policies composed of the following tests, alone or in combination, will be included: CTG for fetal heart rate (FHR); ultrasound for estimated fetal weight (EFW), biophysical profile, or assessment of liquor volume (by amniotic fluid index, AFI); umbilical artery Doppler (or other fetal Doppler measurements such as middle cerebral artery); instructions to keep a kick chart or count fetal movements;

and admissions for observation. Other blood tests may also be conducted if testing for placental insufficiency.[196,297] We also intend to include interventions that determine the mode of birth, i.e. caesarean section or induction of labour when this is performed as a result of the other investigations (for example, induction of labour may be recommended in the presence of non-reassuring CTG and/or ultrasound when a pregnancy is near term) or when it is part of the hospital or trial management policy.

Data extraction and intervention mapping will be used to classify interventions, categories will be created based on whether components were used universally or whether they were performed due to other indicators. Interventions will be broadly grouped into the following:

1. Awareness of RFM	2. Management Strategies for RFM
No intervention to increase awareness	No specified management protocol
Educating parents about RFM	CTG alone
Educating clinicians about RFM	CTG + selective USS
Structured counting e.g. kick charts	CTG + USS for all
	Other tests
	Offer expedited birth for RFM

These categories are based on what we anticipate from current literature and will allow gaps in the current RCOG guideline to be addressed, such as whether ultrasound scanning is beneficial compared to no scanning, as well as comparisons to existing recommendations. However, we anticipate that some of these categories may have to be expanded or adapted due to methodological heterogeneity of the included studies.

Studies will be included if the intervention for management of RFM is clearly described, whether this takes the form of a trial intervention, the introduction of a policy, or details of tests that were received by study participants in response to clinical indications. Studies in which management of RFM is one component of a larger more complex intervention, e.g. as part of a package or care bundle to reduce stillbirth rates, will not be included.

We will include trials comparing interventions for RFM with no intervention, or with any other intervention (including usual care or practice in accordance with local guidelines or protocols).

7.2.2.2 Outcomes

Primary outcomes

The primary outcome for this review is stillbirth, defined in the UK as death of a baby before birth and after 24 weeks' gestation.[298] If other definitions are used by studies, for example the WHO defines stillbirth for international comparison as a baby born with no signs of life after 28 weeks' gestation, then these will be recorded. Timing of stillbirth, whether antepartum or intrapartum, will also be recorded if data are available. Stillbirth has been chosen as the primary outcome as it is the most serious consequence of RFM and the one that management strategies are trying to prevent.

Secondary outcomes

Secondary outcomes are: neonatal death (death of a baby during the first 28 days of life), perinatal death (stillbirth or death within 7 days of birth), small-for-gestational-age infant (birthweight <10th percentile), Apgar score (<7 at 5 minutes of age), preterm birth (<37 weeks of pregnancy), NICU admission, umbilical artery pH <7.05 or BE >-12; and maternal outcomes (postpartum haemorrhage (PPH), mode of birth, proportion of labours induced). We will also record measures of maternal-fetal attachment and maternal anxiety using any standardised scale. For interventions aimed at raising awareness we will record the number of presentations at hospital where appropriate/possible and will define delayed presentation as >24h with absent fetal movements and >48h with RFM.

In some cases these outcomes, such as caesarean section, may be a part of the management strategy and this will be considered separately. We will consider study authors' definitions of outcomes where appropriate, such as for outcomes for which several reasonable definitions exist (for example small-for-gestational-age infant).

Studies that only report secondary outcomes will be included in the review. If a study is otherwise eligible but does not report any of these pre-specified outcomes then study authors will be contacted to attempt to establish whether any relevant outcomes were measured but not reported. Our outcomes of interest are unlikely to be measured more than once in each participant; small-for-gestational age infant may be measured antenatally using ultrasound rather than calculated using the birthweight centile but we are only interested in this condition at birth. If several definitions for the same outcome are presented by one study then best judgement determined by consensus amongst the authors and comparisons to existing definitions will be used to determine which, if any, should be used.

There may be other long term outcomes that could result from RFM and associated pathologies and that may be clinically relevant (e.g. congenital abnormalities, neurodevelopmental delay), however, those are beyond the scope of this review.

7.2.2.3 Search methods for identification of studies

We will search the following databases: Medline, Medline (In-Process and Other Non-Indexed Citations), Embase, EBSCO CINAHL Plus, the Cochrane Central Register of Controlled Trials (CENTRAL), the Cochrane Pregnancy and Childbirth's Trials Register. Other trial registries such as clinicaltrials.gov, WHO ICTRP, and the EU clinical trials register will also be searched.

As trials with significant results are more likely to be published and unpublished trials are more likely to report on adverse effects of interventions,[299] we will also conduct a grey literature search to identify studies not indexed in the databases listed above, including databases such as OpenGrey (www.opengrey.eu), Joanna Briggs Institute (www.joannabriggs.edu.au), and the National Institute for Health and Clinical Excellence website (NICE; www.nice.org.uk).

We will also review reference lists of all included studies and relevant systematic reviews for additional potentially eligible primary studies. We will contact authors of included studies to clarify published data where necessary, for example where outcome data are missing, and to seek unpublished results. We will provide appendices for all strategies used, including a list of sources screened and relevant reviews/primary studies reviewed.

7.2.2.4 Data collection and analysis

Selection of studies

We will download all titles and abstracts retrieved by electronic literature searches to a reference management database and remove duplicates. Titles and abstracts will be screened independently by two review authors using Covidence. We will retrieve the full-text of studies selected for inclusion and two review authors will independently screen these and identify reasons for inclusion or exclusion. Disagreements will be resolved though discussion or consultations with other review authors when this is not possible.

If data from a single study is presented in multiple publications then such a study will be included once with data taken from as many sources as necessary. We will record the selection process in sufficient detail to produce a PRISMA flow diagram.[24]

Data extraction and management

We will produce an adapted data extraction form for study characteristics and outcome data which will be piloted on three studies before use. Two review authors will independently extract information on study design, participant characteristics (with particular attention paid to the key confounders below), intervention detail (using the TIDieR checklist, a template for describing interventions to improve the completeness of reporting[135]), recorded outcomes and their definitions, and notes on trial funding and author conflicts of interest where appropriate. Data will be extracted as 2x2 tables when possible. We will note in the 'Characteristics of included studies' table if outcome data were reported in a way that means they cannot be included in analyses.

Assessment of risk of bias in included studies

Two review authors will independently assess risk of bias for each study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* Section 8.5.[23] Randomised trials (including cluster RCTs) will be assessed using the Risk of Bias 2 (RoB 2) tool[128,211] and non-randomised studies will be assessed using the ROBINS-I tool.[131] Assessment of confounding will be particularly important in non-randomised studies, we consider key confounders to be: estimated birthweight centile, maternal body mass index (BMI), deprivation index,[300] maternal ethnicity, fetal sex, gestation at birth, maternal age, gravidity and/or parity, stillbirth rate in the study population, and smoking status.

Measures of treatment effect

For binary outcomes we will calculate RRs and their corresponding 95% CIs from each included study. The RR is the ratio of the risk of an event between the intervention and control groups and describes the multiplication of the risk that occurs with implementation of the intervention; therefore a value of 1 indicates that the effect is the same in both groups.

For NRS, if available we will include adjusted and unadjusted treatment effects, using ROBINS-I to indicate which confounding factors have been controlled for. If analyses are adjusted for several confounders then we will choose the one that is judged to best account for our pre-specified confounders (see above); this will be justified for each relevant study.

Data synthesis

Included data will be synthesised narratively and also using meta-analysis where possible, using random-effects models to account for underlying variation between studies.

Random-effects meta-analysis assumes that all studies are estimating slightly different intervention effects due to variation in trial populations and study design; this involves adjusting the standard errors from each study estimate to incorporate a measure of the heterogeneity seen in the effect sizes across studies.[139,148] RRs will be combined by meta-analysis using the random effects method (DerSimonian and Laird inverse variance[148]).

Data from RCTs and NRS will be presented separately. Only adjusted treatment effects will be included in our primary synthesis due to the inherent high risk of bias in unadjusted effects. Meta-analysis will be performed using Review Manager 5.3[301] and Stata version 15.[272] Forest plots will be generated where possible.

To determine the relative effectiveness of management strategies for preventing adverse outcomes, RRs will be compared across interventions for our primary outcome of stillbirth and our secondary outcomes.

When meta-analysis is not possible we will provide a narrative synthesis of the findings of included studies in relation to the relevant outcomes.

Assessment of heterogeneity and sensitivity analyses

We will investigate statistical heterogeneity using methods outlined in Chapter 10 of the Cochrane Handbook.[139] Heterogeneity is a measure of the variability in results between studies, which can arise as a result of differences in study design or differences in study populations; significant heterogeneity suggests that not all studies are measuring the same thing but does not necessarily mean that the true effect varies.[139] The Chi-squared statistic, χ^2,[as] as well as I-squared, will be calculated to assess whether any differences in effect sizes between studies are likely due to chance; a low *p* value indicates that there is significant heterogeneity and variation is unlikely to be due to chance.[150]

We anticipate that sources of heterogeneity in this study may be: study design (including whether interventions are at the individual or organisational level), adherence to the intervention, maternal demographics, and study location.

We will perform sensitivity analyses to determine whether effect sizes are influenced by risk of bias (for example, including studies at high risk of bias in meta-analysis to see if effect sizes differ significantly) and to determine whether studies that did not exclude multiple pregnancies and congenital anomalies have a significant effect on the overall estimates. Analyses will be performed to look at the effects of including unadjusted as well as adjusted effect size estimates.

Assessing the certainty of evidence and "Summary of findings" tables

GRADE[160] will be used to determine an overall certainty of the body of evidence associated with our primary outcome of stillbirth, as well as for our secondary outcomes of perinatal death and neonatal death for each comparison of interest. We will present a separate summary of findings table for each comparison made between interventions to evaluate the effects on our primary outcome of stillbirth listing effect estimates and GRADE judgements.

7.3 Search strategies for the systematic review of interventions for RFM

Medline

Two searches were performed in Medline, the first a wider search for RFM and pregnancy outcome and then a more specific search using named pregnancy outcomes after it became apparent that some studies were left out of the initial search.

First search:

1. Fetal movement (6995)
2. Fetal motility (6969)
3. 2 or 3 (10 759)
4. Pregnancy outcome (141 557)
5. Pregnancy outcome [MeSH Major Topic] (32 432)
6. Pregnancy outcome [MeSH Terms) (74 519)
7. 4 or 5 or 6 (141 557)
8. Perinatal outcome.ti,ab (4286)
9. Adverse outcome.ti,ab (8705)
10. Poor pregnancy outcome.ti,ab (399)
11. 9 or 10 or 11 (13 167)
12. 7 or 11 (148 943)
13. 3 and 12 (706)

Second search:

14. (stillbirth or infant, small for gestational age or fetal growth retardation or perinatal death or caesarean section).me (66 037)
15. 6 or 7 (125 203)
16. 5 and 8 (11 347)
17. (neonatal death or stillbirth or perinatal death or preterm delivery or preterm birth or intrauterine death or growth restrict* or Apgar score or c?esarean section or induction of labo?r or labo?r induc*) (156 787)
18. 7 or 10 (171 313)
19. 5 and 11 (810)
20. Limit 12 to humans (698)

A combination of these strategies was used to search Embase and Cinahl.

Embase

1. F?etal movement (1272)
2. F?etus or f?etal (359 149)
3. 2 and (move* and motil*) (16 381)
4. 1 or 3 (17 610)
5. Adverse pregnancy outcome (2 295)
6. neonatal death or stillbirth or perinatal death or preterm delivery or preterm birth or intrauterine death or growth restrict* or Apgar score or c?esarean section or induction of labo?r or labo?r induc* (138 410)
7. 5 or 6 (139 578)
8. 4 and 7 (404)
9. Limit 8 to humans (359)

Cinahl

1. F?etal movement (674)
2. F?etus or f?etal (42 644)
3. 2 and (move* or motil*) (907)
4. 1 or 3 (907)
5. Adverse pregnancy outcome (6 507)
6. neonatal death or stillbirth or perinatal death or preterm delivery or preterm birth or intrauterine death or growth restrict* or Apgar score or c?esarean section or induction of labo?r or labo?r induc* (41 980)
7. 5 or 6 (45 551)
8. 4 and 7 (236)

Other databases

Search strings were not conducted for The Cochrane Library, Web of Science, or Google Scholar; instead, combinations of keywords such as 'fetal movement', 'reduced fetal movement', and 'pregnancy outcome' were searched for along with specific pregnancy outcomes such as stillbirth or fetal death. Numbers of results were not recorded due to this approach. OpenGrey was also searched in this manner, no relevant results were found.

The date of the last search was the 20th of January 2022.

7.4 Classification of interventions used in Chapter 3

Interventions were broadly grouped into the following, using the categories drawn up in the study protocol, based on what was already known about studies in this area and to allow gaps in the current RCOG guideline to be addressed, such as whether ultrasound scanning is beneficial compared to no scanning, as well as comparisons to existing recommendations.

Interventions were first separated based on whether they were aimed at all pregnancies (group one) or all presentations with RFM (group two).

1. Encouraging awareness of RFM	2. Subsequent clinical management of RFM
No intervention to encourage awareness	No specified management protocol
Educating parents about RFM	CTG alone
Educating clinicians about RFM	CTG + selective USS
Structured counting e.g. kick charts	CTG + USS for all
	Other tests
	Offer expedited birth for RFM

The TIDieR checklist was used as well as data extraction of included studies to gain a clearer picture of each study's intervention and to determine which studies were similar enough to be grouped for meta-analysis.

This resulted in the following classifications:

1. Interventions for encouraging awareness of fetal movement

1a Interventions aimed at encouraging awareness of RFM in pregnancy and/or increasing clinicians' knowledge/awareness

Two randomised studies of encouraging awareness of RFM in pregnancy were found; these also incorporated components to increase clinicians' awareness so these groups from the table above were combined. Both these studies compared the intervention to standard care (judged as similar).

Another study compared encouraging awareness at 28 weeks with 24 weeks, this study was considered to be in its own category for meta-analyses due to the different comparator group.

1b Fetal movement counting

Interventions based on encouraging structured fetal movement counting (FMC) and the use of 'alarm limits'. This was judged to differ significantly from interventions to encourage awareness, where the emphasis is on being mindful of changes in fetal movements rather than if they fall below a certain threshold.

Within this group there were eight randomised studies that compared FMC to standard care.

There was also one randomised study that compared two different FMC charts, and one randomised study that compared FMC to a blood test; these studies were considered to be in their own groups as the comparators are significantly different in a clinical context.

2. Interventions for the subsequent clinical management of RFM

2a Universal CTG and ultrasound screening for all RFM presentations

One non-randomised study compared universal CTG and ultrasound screening to universal CTG and targeted ultrasound when indicated. This study reported outcomes in women who self-reported RFM.

2b Universal CTG and ultrasound plus blood tests (and expedited birth)

Two randomised studies combined universal ultrasound screening with blood tests in women who presented to hospital with RFM, both studies compared the intervention to standard care (CTG and ultrasound if indicated). Blood tests were used as indicators for expedited birth. These studies were considered not similar enough clinically to pool data as different blood tests were employed by each study.

3. Combined interventions

One randomised study combined an intervention to encourage awareness of RFM among both clinicians and pregnant women, with a protocol for the subsequent clinical management of RFM, and compared this to standard care. As this study implemented an intervention that combined encouraging awareness of RFM with its subsequent clinical management, it was considered to be in its own category.

7.5 Excluded studies for the RFM review

The following studies were excluded after full text screening:

Study	Reason	Notes
Ahn 1987	No control group	Study of outcomes in a group of RFM women who received CTG
Akkaya 2018	Study of outcomes in RFM	Study of relationship between RFM gestation and outcomes
Akselsson 2017	Not relevant	Test of effectiveness and adherence to mindfetalness
Akselsson 2019	Study of outcomes in RFM	Population-based cohort study
Anandakumar 1993	Not relevant	Evaluation of AFI in high risk pregnancies
Anjanappa 2017	Not relevant	Results of a quality improvement pathway to reduce stillbirth rate
Armstrong-Buisseret 2020	Not relevant	Verification of testing for included 2020 study
Armstrong-Buisseret 2018	Study protocol	Protocol for included 2020 study
Arulkuraman 1989	Not relevant	Study of outcomes in sound provoked fetal movement and correlation to CTG and other testing
Aviram 2015	Study of outcomes in RFM	Study comparing outcomes in pregnancies with and without RFM
Awad 2017	Study design not included	Retrospective observational study without controls
Bainton 2015a	No control group	Audit of RFM management
Bainton 2015b	Not relevant	Audit of inductions
Balasandrum 2015	No control group	Audit of RFM management
Bartfai 1982	Not relevant	Study of CTG in high risk pregnancies

Berbey 2001	No control group	Study of outcomes in FMC cohort
Bernatavicius 2013	Not relevant	Feasibility study for Heazell 2013
Bhatia 2019	Study of outcomes in RFM	Retrospective study of outcomes in an RFM cohort
Binder 2018	Not relevant	Study of CPR in women with and without RFM
Birger 1980	Not relevant	Study of normal fetal movement patterns
Boog 2005	Letter	Comment on Sergent 2005 study
Bradford 2019	Study of outcomes in RFM	Case control study for stillbirth
Chaku et al 2018	Study design not included	Before and after study
Chan 2018	Not relevant	Qualitative study of RFM knowledge and experience of maternity services
Chauveau et al 2016	Study design not included	Retrospective cohort study
Chew 1992	No control group	Study of outcomes in women with RFM who had CTG
Church 2016	No control group	Audit of one unit included in Norman 2018
Christensen 2003	No control group	Cross over study, all women received both charts
Coates 2020	Not relevant	Evaluation of guidelines for induction of labour
Czapla et al 1987	Study design not included	Before and after study
Daly 2011	No control group	Study of outcomes in RFM pregnancies with CTG evaluation
Daly 2018	Not relevant	Update of an RFM guideline
Daniels 2017	Not relevant	Evaluation of Saving Babies' Lives Care Bundle
De Muylder 1988	No control group	Study of outcomes in women who were given kick charts

Debdas 1984	Could not be found	
Del Mar 2004	Letter	
Dillon 2013a	Not relevant	Study of knowledge and practice in midwives
Dillon 2013b	No control group	Study of adherence to RFM guidelines
Draper 186	Letter	
Dubiel 1997	No control group	Outcomes in one group of women with RFM who were all given CTG and UA Doppler
Dutton 2012a	Not relevant	Retrospective study of placentally-derived factors in women with RFM
Dutton 2012b	No control group	Study of blood tests for predicting adverse outcome in a cohort of women with RFM
Eggertsen 1987	No control group	Study of acceptability and use of kick charts
Ehrstrom 1984	Not relevant	Study of fetal movement monitoring
Elbourne 1990	Letter	
Farrell 1998	Not relevant	Study quantifying fetal movements
Flenady 2009	Not relevant	Survey of practice
Foord 2019	Letter	Abstract for a presentation
Franks 2014	Review	
Freda 1993	Not relevant	Study of acceptability of two FMC methods
Froen 2005	Not relevant	Study of outcomes in RFM, part of FEMINA study
Froen 2008	Not relevant	Proposed RFM guideline and outcomes in RFM pregnancies
Gardener 2019	Letter	
Ghidini 2018	No control group	Study of compliance in FMC
Gnirs 1989	Not relevant	
Gnirs 1998	Not relevant	
Gordon 2011 560-S	Not relevant	Case control study of RFM in women with SB
Gordon 2014	Abstract	Abstract for included Chaku study

Gordon 2011 559-S	Not relevant	Case control study for stillbirth - published as Sydney stillbirth study
Grant 1982	Letter	
Hannah 2000	Not relevant	RCT for IoL v monitoring in post term pregnancy
Hantoushzadeh 2015	Not relevant	Study of RFM perception
Harrington 1998	No control group	Study of outcomes in an RFM cohort
Haws 200	Review	Review of various screening techniques in high risk pregnancies
Hayi 2012	No control group	Study of outcomes in RFM
Heazell 2005	No control group	Retrospective study of outcomes in RFM in a single centre
Heazell 2017	Not relevant	Protocol for AFFIRM
Heazell 2018	Not relevant	Case control for perception of RFM in stillbirths
Heazell 2008	Not relevant	Study of midwives and obstetricians' knowledge of RFM
Higgins 2018	No control group	Study of placental assessment for predicting outcomes in RFM
Ho 2018	Not relevant	Case control study for cardiac function in RFM
Hor 2014	Not relevant	Retrospective review of stillbirth case notes
Jha 2011	Not relevant	Audit of information given to pregnant women
Jansa 2019	Review	
Jokhan 2015	Not relevant	Evaluation of RFM guidelines
Jovic 2015	No control group	Audit of inductions for RFM
Kantrowitz-Gordon 2019	Not relevant	Validation study for an RFM awareness scale
Kapaya et al 2020	Study design not included	Before and after study
Kellison 2013	No control group	RFM audit of practice
Kelly 2016	Not relevant	Audit of stillbirths

King 2018	Not relevant	Audit of third trimester ultrasound
Kinsella 2018	Not relevant	Audit of inductions
Korszun 2002	No control group	Evaluation of Doppler in RFM pregnancies
Koshida 2019	No control group	Study of FMC charts given to all pregnant women
Koshida 2017	Not relevant	Study of time to present with RFM
Koshida 2020	Letter	
Krishna 2012	Not relevant	Audit of RFM management
Kuwata 2008	Not relevant	Study to establish reference value for kick charts
Laband 1985	Could not be found	
Leader 1981	No control group	Study of outcomes in relation to FMC
Lema 1988	No control group	Study of outcomes in RFM
Levy 2020	No control group	Study of outcomes in RFM
Lindner	Could not be found	Abstract – unable to find full study
Lobb 1985	Not relevant	Comparison of low risk v high risk pregnancies
Maksym	No control group	Study looking at use of ultrasound in RFM
Malm 2014	Not relevant	Quantitative knowledge study
Manning 1986	Not relevant	Study of biophysical profile in all pregnancies
Manning 1987	Not relevant	Study of biophysical profile
Manning 1985	Not relevant	Study of biophysical profile
Maputle 2006	No control group	Study of maternal awareness in relation to outcomes
Marden 1997	Not relevant	Study of fetal acoustic stimulation
Mbanzulu 1986	No control group	Study of prognostic relevance of fetal movements and blood tests

McCarthy 2016	No control group	Study of outcomes in RFM vs in women without
Michaan 2016	Not relevant	RCT for effects of glucose on FM
Moore 1989	Study design not included	Uncontrolled before and after study
Moran 2019	No control group	Audit of RFM management
Morgan 2017	Not relevant	Comparison of outcomes in different IoL groups
Mor-Yosef 1983	Not relevant	Study of fetal movements in FGR
Narain 2013	No control group	Audit of RFM treatment at a single site
Neville 2018	Not relevant	Audit of Saving Babies' Lives Care Bundle
Nor Azlin 2015	No control group	Study of outcomes in RFM
Noreen 2010	Not relevant	Study of outcomes in pregnancies with abnormal CTG results
Olagbuji 2014	No control group	Cohort study of RFM awareness
Olagbuji 2011	Not relevant	Case control study for outcomes for induction in RFM vs post term pregnancy
Olowu 2012a	Review	review of ultrasound for fetal outcomes
Olowu 2012b	No control group	Study of outcomes in RFM
Oniah 2013	Not relevant	Audit of inductions
O'Sullivan 2009	No control group	Study of outcomes in RFM
Pagani 2014a	No control group	Study of association between rfm and first trimester biomarkers
Pagani 2014b	No control group	Study of association between Doppler with RFM and adverse outcome
Pal 1981	Could not be found	
Parveen 2016	Not relevant	Audit of stillbirths
Patrelli 2011	Not relevant	study of outcomes in relation to fetal movements via actography during labour

Platt 1985	Not relevant	Trial for biophysical profile v non-stress test in high risk pregnancies
Radestad 2016	Not relevant	Methodology for Akselsson 2020
Rayburn 1995	Review	
Redford 2018	No control group	Study of outcomes in RFM
Ross 2015	No control group	Study of outcomes in RFM
Rudra 2019	No control group	
Saastad 2008	Not relevant	Study of RFM knowledge, part of FEMINA study
Saastad 2011	Not relevant	Erratum for included study
Saastad 2012	Not relevant	Outcomes from this study combined with included Saastad study
Sadovsky 1986	No control group	Study of outcomes in FMC
Sadovsky 1983	No control group	Study of outcomes in RFM
Sadovsky 1981	No control group	
Sadovsky 1974	Not relevant	Study of FMC in normal and pathologic pregnancy
Sage 2012	No control group	Study of outcomes in RFM
Saunders 2019	Letter	Letter re: Daly study
Scala 2015	Not relevant	Study of association between RFM and adverse outcome
Sergent 2005	No control group	Screening RFM pregnancies in a cohort
Shafi 1989	Not relevant	
Shamsudin 2013	No control group	Comparison of outcomes in an RFM cohort between women who did or did not have IoL
Sheikh 2014	Not relevant	Study of RFM perception in a cohort of pregnant women
Singh & Sidhu 2008	Study design not included	Uncontrolled before and after study
Sinha 2007	Not relevant	Case control study of outcomes in RFM v normal FM

Skornick-Rapaport 2011	No control group	Study comparing outcomes in RFM in a retrospective cohort in a single unit between women who were admitted and discharged after testing
Skorupskaite 2013	No control group	Study of outcomes in RFM
Smith 2013	Not relevant	Survey of practice
Smith 1992	Not relevant	Study of acceptability of different FMC
Sorensen 1980	Not relevant	
Stacey 2011	Not relevant	Findings from Auckland stillbirth study
Sterpu 2020	No control group	Study of outcomes in RFM pregnancies
Sterpu 2018	Not relevant	
Taylor-Hannan 2014	No control group	Audit of management and outcomes in RFM pregnancies
Toh 2018	No control group	Audit of RFM management
Torkestani 2011	No control group	Study of outcomes in RFM
Turner et al. 2021	Study design not included	Before and after study
Tveit 2009a	Study design not included	Uncontrolled before and after study
Tveit 2009b	No control group	Study of outcomes in RFM
Tveit 2010	No control group	Study of outcomes in RFM
Tyrrell 1990	Not relevant	RCT of assessment of high risk pregnancies
Unterscheider 2010	Not relevant	Online survey of obstetricians' RFM practice
Valentin 1987	No control group	Study of outcomes in women instructed to count fetal movements
Valentin 1986	No control group	Comparing outcomes in women with and without alarm signals who were told to count fetal movements

Wackers 2018	Study design not included	Prospective cohort study, no control group
Weller 2018	Not relevant	Preliminary study for Flenady 2020
Westgate & Jamieson 1986	Study design not included	Uncontrolled before and after study
Whittaker 2017	Not relevant	Audit of SBLCBv2
Whitty 1991	No control group	Single centre study of screening for RFM
Williams 2014	No control group	Study of outcomes in RFM
Winje 2011	Not relevant	Study of mean time to perceive ten fetal movements at various gestations
Yong 2018	No control group	Study of outcomes in RFM

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7.6 Data used for analyses in the RFM review

Group one – encouraging awareness of RFM compared with standard care

Study	Outcome	Intervention		Comparator	
		Events	Non events	Events	Non events
Akselsson	Stillbirth	33	19606	29	20197
	Neonatal death	2	19637	5	20221
	Perinatal death	35	19604	34	20192
	5 min Apgar score <7	207	19432	213	20013
	NICU admission	1242	18397	1377	18849
	SGA	1994	17609	2166	18012
	Caesarean section	3741	15898	4048	16178
	Induction of labour	3747	15892	4010	16216
	Preterm birth	700	18939	716	19510
Flenady	Stillbirth	312	139828	367	149712
	Neonatal death	133	140007	183	149896
	Perinatal death	445	139695	550	149529
	Caesarean section	44549	95591	47856	102223
	5 min Apgar score <7	2822	137318	3199	146880
	NICU admission	7598	132542	9808	140271
	SGA	1074	139066	1235	148844
	Induction of labour	48915	91225	49422	100657
	Preterm birth	11118	129022	12139	137940

Group one – encouraging awareness of RFM at different gestational ages

Study	Outcome	Intervention		Comparator	
		Events	Non events	Events	Non events
Wackers	Time to present >24h	32	28	43	37

Group one – encouraging fetal movement counting compared with standard care

Study	Outcome	Intervention		Comparator	
		Events	Non events	Events	Non events
Delaram	Stillbirth	0	100	0	108
	IUGR	0	100	0	108
	Preterm birth	0	100	0	108
Grant	Stillbirth	99	31549	100	36221
Liston	Stillbirth	2	176	2	185
	SGA	0	178	0	187
	Preterm birth	0	178	0	187
Neldam	Stillbirth	0	1125	8	1117
Saastad	Stillbirth	0	544	0	532
	Caesarean section	36	508	38	494
	Perinatal death	0	544	0	532
	5 min Apgar score <7	0	544	2	530
	SGA	46	498	46	486
	Preterm birth	20	524	24	508
	NICU admission	33	511	30	502

Group one – encouraging fetal movement counting compared with hormone analysis

Study	Outcome	Intervention		Comparator	
		Events	Non events	Events	Non events
Thomsen	Stillbirth	1	500	0	611
	5 min Apgar score <7	4	497	2	609
	Caesarean section	59	518	53	561
	IUGR	20	481	22	589
	uA pH <7.15	48	453	73	538

Group two – universal ultrasound compared with ultrasound when indicated

Study	Outcome	Intervention		Comparator	
		Events	Non events	Events	Non events
Awad	Stillbirth	1	280	2	296

Group two – universal ultrasound compared with standard care

Study	Outcome	Intervention		Comparator	
		Events	Non events	Events	Non events
Armstrong-Buisseret	Stillbirth	0	109	0	107
	Neonatal death	0	109	0	107
	5 min Apgar <7	1	108	1	106
	NICU admission	4	105	4	103
	UA pH <7.05	4	105	0	107
	SGA (INTERGROWTH)	9	100	2	105
	SGA (GROW)	15	94	7	100
	Emergency caesarean section	11	98	13	94
	Caesarean section for RFM	1	108	0	107
	IoL for RFM	25	84	29	78
Heazell	CS	4	56	8	50
	SB	0	60	0	58
	NICU admission	1	59	3	53
	BW <10th	5	55	11	47
	Metabolic acidosis	1	59	3	55
	IoL for RFM	30	30	15	43

Group three – awareness and clinical management v standard care

Study	Outcome	Intervention		Comparator	
		Events	Non events	Events	Non events
Norman	Stillbirth	550	140930	1084	251293
	Perinatal death	753	224859	1454	115262
	5 min Apgar <7	2356	139124	3740	249237
	Caesarean section (all)	40050	101430	66848	185529
	Caesarean section (emergency)	21444	120036	35532	216845
	BW <10th centile	6391	135089	13429	247911
	NICU admission	10733	130747	22392	238948
	IoL	44726	96754	92715	159662
	Preterm birth	10330	131150	21516	230861

7.7 Development of a COS for studies of RFM: study protocol

7.7.1 Background

RFM and adverse pregnancy outcome

RFM are usually defined as a subjective decrease or change in a baby's normal pattern of movements *in utero;* [1] current guidance in the UK and Australia is for people who are pregnant to contact a midwife or maternity unit if their baby is moving less than usual or not at all.[11,250] Most people who are pregnant become aware of fetal movements by 18-20 weeks of pregnancy and of the pattern of their baby's movements and the time of day that the baby moves the most by 28 weeks' gestation.[187] Awareness of fetal activity is recognised as one component of maternal-fetal attachment.[251]

Concerns regarding RFM leads to maternal presentation at hospital in 5-15% of pregnancies.[2] Around 70% of these pregnancies have a normal outcome, [191,252,253] but observational studies have recurrently demonstrated that RFM are associated with adverse pregnancy outcomes including FGR and stillbirth, supporting the potential for a common aetiology. [254,255] Case-control studies have consistently demonstrated an association between reduced frequency and strength of fetal movements and stillbirth after 28 weeks' gestation;[13,193,194] this effect has also been seen in low income settings.[18] It is thought that RFM may be an attempt by the fetus to conserve energy and oxygen consumption in cases of insufficient nutrient transfer and hypoxia, which in turn may be caused by placental insufficiency or other fetal stressors.[8,196,256]

Studies of awareness of or interventions for RFM

Studies have aimed to improve pregnancy outcomes by evaluating interventions that raise maternal and/or clinical awareness of RFM, such as mindfulness or kick counting, [76,200] and/or by evaluating clinical management interventions, for example, interventions for further monitoring and/or clinical testing such as CTG or US to identify whether RFM is an indicator of an underlying condition that may warrant further clinical intervention or even expedited birth. [201,202]

Despite the association between RFM, stillbirth and FGR, a COS for studies aiming to improve pregnancy outcomes via better identification (and subsequent clinical management) of RFM does not currently exist. This means that studies often measure and report different outcomes, and employ different definitions for these outcomes, which hinders meta-analysis of studies. A COS describes a standardised set of outcomes that should be measured and reported in all studies in a specific area as a minimum;[82] COS are

currently in use across several healthcare fields including maternity care.[92,257,258] It is anticipated that developing a COS will ensure that the most important and relevant outcomes, as agreed by stakeholder consensus, are measured, thus optimising synthesis of individual studies. This will further facilitate interpretation of the evidence based on prioritised outcomes.

7.7.2 Methods

Aim

This protocol describes the development of a COS for measurement and reporting in studies that aim to raise awareness of RFM and/or evaluate the clinical management of RFM. Development and adoption of this COS will ensure consistent and relevant outcome measurement and reporting in studies for raising awareness and/or evaluating the clinical management of RFM, which may lead to more robust results, improved wellbeing in pregnancy, and may also be applicable in clinical practice.

This COS will apply to controlled randomised and non-randomised study designs.

Objectives

1. To systematically review the outcomes included in intervention studies for raising awareness of RFM and/or evaluating its clinical management;
2. To develop a consensus on a preliminary COS using these outcomes via the Delphi survey;
3. To develop a final COS for use in all future intervention studies aimed at raising awareness of RFM and/or evaluating the clinical management of RFM, via an international consensus meeting with key stakeholders;
4. To disseminate and promote the use of the COS.

Design

The COS development project was registered with the Core Outcome Measures in Effectiveness Trials (COMET) initiative (http://comet-initiative.org/Studies/Details/928) on the 24th of September 2020.

This protocol was developed in accordance with the COMET handbook.[82] A study steering committee will be established, comprising at least one representative from the following stakeholder groups: researchers, clinicians, and patient representatives (described in more detail later). We will include at least one professional and patient representative from low or middle-income countries on the steering committee.

Scope

The purpose of developing this COS is for use in future research studies (randomised or non-randomised controlled studies) that measure the effectiveness of interventions for identification of RFM and/or awareness of fetal movements, as well as systematic reviews of these studies.

This COS may also be applicable to intervention studies for the clinical management of RFM only, however, these studies are less common[225,235] and answer slightly different research questions from the studies we are interested in (see below) – for example they are less likely to focus on maternal outcomes. A COS for these studies may be another avenue for future research but will not be developed by us at this time.

The target population is people with non-anomalous singleton pregnancies after 28 weeks' gestation; this threshold has been chosen over other definitions of stillbirth to facilitate international comparisons.[260] We will not include studies of multiple pregnancies because observational data about the association between RFM and adverse outcome in this group is less clear.

Stage 1: systematic review

A systematic review of the literature will be conducted to identify outcomes measured in studies of interventions where any part of the intervention is designed to encourage maternal awareness or detection of RFM and/or improve the subsequent clinical management of RFM.

We will include controlled randomised and non-randomised studies with clearly reported mechanisms of group formation, clearly defined inclusion criteria, and clearly described methods of ascertainment of eligible patients and their recruitment. Studies will be included regardless of their publication status and language of publication.

Pregnancy, labour, and birth outcomes will be extracted with their corresponding definitions where possible. Outcomes will be grouped as maternal or neonatal and different definitions of the same outcome will be grouped into single outcome measures. This will be facilitated by discussions between members of the study team. This final list of outcomes will be used in stage two.

We will search the following databases: Medline, Medline (In-Process and Other Non-Indexed Citations), Embase, EBSCO CINAHL Plus, the Cochrane Central Register of Controlled Trials (CENTRAL), the Cochrane Pregnancy and Childbirth's Trials Register,

and the Cochrane Database of Systematic Reviews. Other trial registries such as clinicaltrials.gov, WHO ICTRP, and the EU clinical trials register will also be searched, as well as databases such as OpenGrey (www.opengrey.eu), Joanna Briggs Institute (www.joannabriggs.edu.au), and the National Institute for Health and Clinical Excellence website (NICE; www.nice.org.uk) with the aim of finding unpublished studies. References lists of included papers will be reviewed for additional studies.

Studies identified by the literature searches will be independently screened for inclusion by two study authors using our study inclusion criteria. Disagreements will be resolved by consulting a third author. The following data will be extracted from included studies: study aim, location, population, setting, description of the intervention and comparator, and outcomes reported in the study.

Study inclusion criteria for the systematic review	
Population	Singleton pregnancies presenting at least once in a maternity care setting after 28 weeks' gestation
Intervention	Any intervention aiming to encourage awareness of RFM and/or evaluating the clinical management of RFM
Comparator	Any other intervention described above or no intervention
Outcome	Any maternal or fetal outcomes
Study design	Controlled randomised and non-randomised studies with clearly reported mechanism of group formation, clearly defined inclusion criteria, and described methods of ascertainment of eligible patients and their recruitment

Stage 2: online international Delphi survey

A sequential three round electronic international Delphi study will be conducted including key stakeholders to produce a preliminary COS. Each round will remain open for 14 days and a reminder email will be sent out three working days before closure. Data from each round will be analysed and presented to participants in the next round (described in more detail below). Attrition rates for each round will also be assessed. All participants' contact information will remain confidential.

The Delphi survey and following consensus meeting will allow the possibility of producing either one COS (for all studies relating to raising awareness and/or evaluating the clinical management of RFM) or two COS (one for studies raising awareness of RFM and another

for studies evaluating the clinical management of RFM). This will be dependent on whether there is significant overlap or similarity in the final outcomes in the two lists. This follows the precedent set by other COS in maternity care that have started by running two surveys simultaneously and then voted on whether one COS should be produced[92,262]

Participants

We will invite people from all stakeholder groups, aiming for at least 15 people from each of the following three groups to ensure adequate representation. Eligible participants will be: 1. Researchers, research funders, and policy makers who are actively involved in work related to RFM; 2. Clinicians (midwives, obstetricians, neonatologists, GPs/family physicians) with experience of caring for people with RFM; 3. Anyone who is or who has been pregnant and their partners if applicable. We will recruit participants through professional organisations, electronic discussion lists, and patient organisations or charities. As with formation of the steering group, we will ensure that participants from low income countries are adequately represented. Authors of all included studies will be invited to participate; we will also use snowball sampling, whereby we will request participants to forward the survey to other that they consider eligible to participate.

Participants of the Delphi survey will receive all information regarding the study as part of the invitation email. Consent to take part in the survey will be ensured by requiring participants to click an 'I agree to take part' box before gaining access to the survey. All personal data of participants will only be accessible to members of the research team and any response to the survey will be confidential. Participants will have the right to withdraw at any point.

Round 1

Round one will collect demographic data including nationality, age, stakeholder group, and role. Participants will be presented with a list of all outcomes identified from the systematic review and will be asked to rate the importance of each using a nine point Likert scale. On this scale, a score of 1-3 indicates limited importance, 4-6 signifies importance, and 7-9 is used for critically important outcomes. Participants will also be prompted to add additional outcomes that they feel are important but are not included in the preliminary list. Suggested outcomes will be included in round two if they are mentioned by at least two participants. All outcomes from round one will be forwarded to round two.

Feedback will be provided to all who participated in round one in the form of descriptive statistics and graphical representations for ease of interpretation. For each outcome,

participants will receive their scores from the first round and a graphical representation of the percentages of each group who voted for each score for each outcome. All feedback provided to participants will be anonymised.

Standardised consensus criteria will be applied to the results from this round, which will be used through all three rounds to reach the preliminary list of outcomes to be included. Outcomes that are not scored by participants will not be included in analyses or consensus definitions.

Consensus criteria for outcomes	
Definition	Criteria
Consensus in	Scored as 7-9 by 70% or more of all participants, including at least one from each stakeholder group, and as 1-3 by less than 15% of participants
Consensus out	Scored as 1-3 by over 70% of participants and as 7-9 by less than 15%
No consensus	Any other combination of scores

Round 2

Participants will be presented with their scores from the previous round as well as feedback given in the same way as described in round one. All participants who completed the first round will be asked to re-score all outcomes using the same nine-point Likert scale, including any additional suggested outcomes from round one, in light of their and others' ratings.

In round two, outcomes will be presented in two lists. Participants will be asked to rate the outcomes in each list according to how important they think each outcome is for measuring and reporting in studies of i) interventions for raising awareness of RFM and in studies of ii) interventions for the clinical management of RFM. The ratings for the two separate lists will be reviewed and analysed separately.

Outcomes will be included in round three if they are rated as 'consensus in' or 'no consensus' using the consensus criteria in Table 2; those rated as 'consensus out' will be removed. Outcomes will be removed from lists (i) and (ii) of the survey individually based on their ratings in each list. We will also assess the rates of attrition from each round and whether participants change their scores based on the feedback they receive.

Round 3

Round three will only include participants who completed round two. Participants will again be provided with feedback and asked to re-rate the outcomes retained from round 2 in the same way as in round 2, in two separate lists for i) RFM awareness studies and ii) RFM clinical management studies using the 9-point Likert scale. The consensus criteria will again be used to determine which outcomes are retained in each distinct outcome list following this round and forwarded to the consensus meeting. Those defined as 'consensus out' and 'no consensus' will be removed. Round three will include a question asking if participants are willing to take part in the final consensus meeting, and if they consent to being contacted.

Stage 3: consensus meeting

A consensus meeting with an international panel representing views of all key stakeholders will be held to discuss, vote and agree on the final RFM COS. This meeting will include a presentation of the findings of the Round 3 Delphi, including the final list of outcomes by category (i.e. awareness and clinical management) and how they were voted for by each stakeholder group. This will be followed by a timed discussion and a vote on each outcome for each list. Outcomes will be included if voted for by at least 70% of participants, including at least one from each stakeholder group.

The final COS for (i) interventions for raising awareness of RFM and (ii) interventions for the clinical management of RFM will then be compared. If the outcomes included in these two COS lists are largely the same, then a majority vote will be held on whether to combine the lists to produce one COS for studies of both the awareness and clinical management of RFM. If the outcomes in the lists are different, then two separate COS will be created.

The consensus panel will be comprised of at least three representatives from each stakeholder group described earlier. The meeting will be held in English and group facilitators will be used for discussions. Due to the COVID-19 pandemic and to facilitate international attendance we are planning that this meeting will be online.

Stage 4: dissemination

The final COS will be published in an open access journal. After publication, it will be made available through the COMET and CoRe Outcomes in Women's and Newborn health (CROWN) databases. In addition, we plan to disseminate the COS at national and international conferences and through relevant professional and patient organisations. We will share the COS with clinical trial registries, relevant consumer groups such as maternity service users, and will ask all participants to share as they see appropriate.

Discussion

Research into the management of RFM was identified by the Stillbirth Priority Setting Partnership (PSP) which prioritised the question "Which investigations identify a fetus which is at risk of stillbirth after a mother believes she has experienced reduced fetal movements?" [266]. The PSP had extensive input from researchers, clinicians, stakeholder groups and bereaved parents. There is currently no published COS for studies that evaluate interventions to raise awareness of RFM and/or for the clinical management of RFM. A well-developed COS for research studies that aim to quantify the effects of these interventions will provide researchers with a minimum set of outcomes that should be recorded, facilitating comparisons of interventions. We have taken steps to ensure that pregnant women and their views are adequately represented in this study and the final COS.

7.8 Scores for the RFM COS by stakeholder group

Median scores for all outcomes in round three

	Awareness studies			Management studies		
Maternal outcomes	Parents	Researchers	Clinicians	Parents	Researchers	Clinicians
Acceptability of information about RFM	9	9	8	9	8	8
Maternal admission to hospital	8	7	7	8	8	8
Maternal admission to intensive care	7	5	5	8	7	7
Antepartum haemorrhage	8	6	7	8	7	8
Caesarean section	7.5	7	8	8	8	8
Maternal concern about RFM	9	9	9	9	9	8
Duration of RFM before presenting to hospital	9	9	8	9	9	8
Maternal health status postpartum	7	6	6	7	6	6
Maternal health status six months postpartum	6.5	5	5	7	5	6
Induction of labour	8	8	8	8	8	9
Instrumental birth	6	7	7	7	7	7
Intrapartum infection	8	7	7	8	7	7
Maternal knowledge of RFM	9	9	9	9	8	8
Length of hospital stay	6	5	5	6	6	6
Maternal anxiety	8	8	8	8	7	7
Maternal-fetal attachment	7	7	7	6.5	6	6
Maternal hypertension	8	6	7	8	7	7
Number of presentations with RFM	9	9	8	9	9	8
Obstetric cholestasis	7	5	6	7	6	6
Postnatal depression	7	6	7	7.5	5	7
Postpartum haemorrhage	7	5	5	7	5	6
Postpartum infection	6.5	5	6	7	5	6
Prelabour rupture of membranes	8	5	6	8	5	7
Vaginal birth	7	7	7	7	8	8
Maternal wellbeing	8	8	8	8	7	8
	Awareness studies			**Management studies**		
Neonatal outcomes	Parents	Researchers	Clinicians	Parents	Researchers	Clinicians
Abnormal fetal heart rate in labour	9	8	8	9	9	8
Apgar score <7 at 1 minute	8.5	6	6	9	6	6
Apgar score <7 at 5 minutes	9	8	7	9	9	8
Birthweight	7	7	7	8	8	7
Dysmaturity score	8.5	7	6	8.5	7	6

Gestation at birth	8	8	8	9	9	8
Hypoxic ischemic encephalopathy	9	8	9	9	9	9
Meconium aspiration syndrome	8	7	8	8	8	8
Need for intubation	8	7	8	8	8	8
Neonatal acidaemia	7.5	7	8	8	8	8
Neonatal death	9	9	9	9	9	9
NICU admission	8.5	8	8	9	8	8
NICU admission after 37 weeks	8	8	8	9	8	8
Need for resuscitation	9	8	8	9	8	8
Neonatal seizures	8	8	8	8	8	8
Oligohydramnios	8	6	7	8	7	7
Perinatal death	9	9	9	9	9	9
Postterm birth	8	8	7	8	8	7
Preterm birth	8	8	7	8	8	8
Respiratory distress	8	7	7	8	8	8
Severe neonatal depression	8.5	8	7	8.5	8	8
Small-for-gestational-age	8	8	7	8	8	8
Spontaneous birth	7	7	7	7	7	7
Stillbirth	9	9	9	9	9	9
Use of therapeutic cooling for babies admitted to NICU	7.5	7	8	8	7	8
Use of mechanical ventilation	8	7	7	8	7	8
Healthcare costs	7	7	7	7	8	8

Median scores for all outcomes in round two

	Awareness studies			Management studies		
Maternal outcomes	Parents	Researchers	Clinicians	Parents	Researchers	Clinicians
Acceptability of information about RFM	9	8	8	8	7	7
Maternal admission to hospital	8	7	8	9	8	8
Maternal admission to intensive care	7	5	6	8	7	6
Antepartum haemorrhage	7	6	7	7.5	6.5	7
Caesarean section	7	7	8	7.5	8	8
Maternal concern about RFM	9	9	9	9	8	8
Duration of RFM before presenting to hospital	9	9	8	9	8.5	7
Maternal health status postpartum	6	5	6	6.5	6	6
Maternal health status six months postpartum	6	5	5	6	5	5
Induction of labour	7	8	8	8	9	9
Instrumental birth	6.5	6.5	7	7	7	8
Intrapartum infection	7	6	7	8	7	7
Maternal knowledge of RFM	9	9	9	9	7.5	8
Length of hospital stay	6	5	6	6	6	7
Maternal anxiety	8.5	8.5	8	8	7	7
Maternal-fetal attachment	7	7	7	7	6	7
Maternal hypertension	7	6.5	6	8	7	7
Number of presentations with RFM	9	9	8	9	8	8
Obstetric cholestasis	6	5.5	7	7	5.5	7
Postnatal depression	8	7.5	7	7	6	7
Postpartum haemorrhage	6.5	4.5	6	8	5	6
Postpartum infection	6.5	4.5	6	7	5	6
Prelabour rupture of membranes	8	5	6	8	6	6
Vaginal birth	7	6	8	7.5	7.5	8
Maternal wellbeing	9	8	8	8	7.5	8
	Awareness studies			**Management studies**		
Neonatal outcomes	Parents	Researchers	Clinicians	Parents	Researchers	Clinicians
Abnormal fetal heart rate in labour	9	8	8	9	8	8
Apgar score <7 at 1 minute	8	5	7	9	6	8
Apgar score <7 at 5 minutes	8	7	8	9	8.5	8
Birthweight	7	7.5	8	8	8	8
Dysmaturity score	8	5.5	7	9	7	8

Gestation at birth	9	8	8	9	8.5	8
Hypoxic ischemic encephalopathy	9	8	9	9	9	9
Meconium aspiration syndrome	8	7	7	8	8	8
Need for intubation	8	6.5	7	8	7.5	8
Neonatal acidaemia	7	7	8	8	8	8
Neonatal death	9	9	9	9	9	9
NICU admission	8	8	8	9	8	8
NICU admission after 37 weeks	8	8	8	8	8	8
Need for resuscitation	9	7.5	8	9	8	8
Neonatal seizures	8	8	8	9	8	8
Oligohydramnios	8	6	8	8	7	8
Perinatal death	9	9	9	9	9	9
Postterm birth	8	7	7	8	7	7
Preterm birth	8	7.5	8	8	8	8
Respiratory distress	8	7	7	8	7	8
Severe neonatal depression	8	8	7	8	8	8
Small-for-gestational-age	8	8	8	8	8	8
Spontaneous birth	7	6	8	7	6	8
Stillbirth	9	9	9	9	9	9
Use of therapeutic cooling for babies admitted to NICU	7	8	7	8	8	8
Use of mechanical ventilation	8	7	8	8	7	7
Healthcare costs	7	7	8	6.5	7	8

7.9 Definitions from included studies for COS outcomes

Outcomes selected to the final COS for studies aiming to encourage awareness of RFM

Outcome	Measured by	Defined as	Measured as
1. Acceptability of information about RFM	Flenady et al. (2022)	Acceptability of information on RFM	Survey at 35 weeks' gestation
2. Duration of RFM before presenting to hospital	Chauveau et al. (2016)	Time to present with RFM	<12 hours >12 hours
	Flenady et al. (2022)	Delay in maternal reporting of DFM >24h	N
	Tveit et al. (2009)	Time to contact in absence of fetal movement	<24h >48h
3. Maternal knowledge of RFM	Flenady et al. (2022)	Women and clinicians' knowledge of RFM	Survey at 35 weeks' gestation
4. Number of presentations with RFM	Akselsson et al. (2022)	No of unscheduled visits due to RFM	From 0 to 9 and % of each
	Chauveau et al. (2016)	Number of consultations for RFM in each group	N, %
	Moore & Piacquadio (1989)	Complaint of RFM	N, %
	Singh & Sidhu (2007)	No. of mothers with live fetuses with loss of movements	N, %
	Tveit et al. (2009)	Consultation rate for RFM	N, %
5. Gestation at birth	Flenady et al. (2022)	Gestation at birth in weeks	28 to 32 33 to 36 37 to 39 40 to 41 42+
	Kapaya et al. 2020	Gestational age at birth	Mean, SD
	Saastad et al. (2011)	Gestational age at birth in days	Mean, SD
6. Neonatal death	Akselsson et al. (2020)	Death within 27 days after birth	N, %
	Chaku et al.	Neonatal death	N
	Czapla et al. (1987)	Early neonatal death Late neonatal death	N

	Flenady et al. (2022)	Neonatal death 28+ weeks Neonatal death 20+ weeks gestation	N
	Gomez et al. (2007)	Neonatal death	N
	Moore & Piacquadio (1989)	Neonatal mortality	N, %
7. Perinatal death	Czapla et al. (1987)	Perinatal death Intrapartum death	N
	Delaram & Jafarzadeh (2016)	Fetal death	N
	Moore & Piacquadio (1989)	Fetal mortality	N, %
	Norman et al. (2018)	Stillbirth at 24 weeks' gestation and above or death in the first 7 days of life	N, %
	Saastad et al. (2011)	Perinatal death	N, %
	Westgate & Jamieson (1986)	Perinatal death	N, %
8. Stillbirth	Akselsson et al. (2020)	Apgar score=0	N, %
	Armstrong-Buisseret et al. (2020)	Stillbirth or death before discharge	N, %
	Awad et al. (2018)	IUFD within 2 weeks post discharge IUFD after 2 weeks post discharge	N
	Chaku et al.	Stillbirth	N
	Czapla et al. (1987)	Stillbirth	N
	Flenady et al. 2022	Stillbirths 28+ weeks Also 20+, 24+, 37+ weeks as post hoc	N, %
	Grant et al. (1989)	Antepartum late fetal death	N, %
	Gomez et al. (2007)	IUFD	N
	Heazell et al. (2013)	Stillbirth	N, %
	Kapaya et al. 2020	Stillbirth	N
	Lobb, Beazley & Haddad (1985)	Stillbirth (all weights) Stillbirth <1500g Stillbirth <1500g	N
	Neldam (1980)	Stillbirth (gestation and weight given for each)	N
	Norman et al. (2018)	Stillbirth (after 24 weeks or >500g) Stillbirth at 37 weeks or more	N, %

		Stillbirth at 28 weeks or more (WHO definition) Stillbirth at 22 weeks or more (ISA definition) Stillbirth at 24 weeks or more	
	Singh & Sidhu (2007)	Intrauterine death	N, %
	Tveit et al. (2009)	Stillbirth in RFM Normally formed stillbirth in RFM Stillbirth	N, %
	Westgate & Jamieson (1986)	Stillbirth Unexplained stillbirth	N, %

Outcomes selected to the final COS for studies aiming to improve clinical management of RFM			
Outcome	Measured by	Defined as	Measured as
1. Caesarean section	Akselsson et al. (2020)	Caesarean section (total) Pre-labour In labour	N, %
	Armstrong-Buisseret et al. (2020)	Caesarean section, grade 1 (emergency) Caesarean section, grade 4 (elective) Caesarean section recommended by test result	N, %
	Awad et al. (2018)	Caesarean section on admission	N
	Chaku et al.	Caesarean section	N, %
	Flenady et al. (2022)	Caesarean section Caesarean section 28+ weeks	N, %
	Heazell et al. (2013)	Caesarean section	N, %
	Kapaya et al. 2020	Caesarean section	N
	Moore & Piacquadio (1989)	Caesarean section for fetal distress	N, %

	Norman et al. (2018)	Elective caesarean section Emergency caesarean section	N, %
	Saastad et al. (2011)	Elective caesarean section Emergency caesarean section	N, %
2. Induction of labour	Akselsson et al. (2020)	Induction of labour	N, %
	Armstrong-Buisseret et al. (2020)	Induction Induction recommended by test result Induction for reduced fetal movement	
	Chaku et al.	Induction of labour	N, %
	Chauveau et al. (2016)	Induction of labour Induction for reduced fetal movements	N, %
	Flenady et al. (2022)	Induction of labour	N, %
	Heazell et al. (2013)	IOL IOL for RFM IOL for other indications	N, %
	Moore & Piacquadio (1989)	Induction of labour	N, %
	Norman et al. (2018)	Induction of labour (none, ARM or ARM and OXY, oxytocics, any prostaglandin, other or unknown) Induction of labour Induction of labour >39 weeks' gestation	N, %
	Saastad et al. (2011)	Induced vaginal delivery Inductions and interventions on fetal indication	N, %
3. Birthweight	Chaku et al.	Birthweight (g)	Mean, SD
	Delaram & Jafarzadeh (2016)	Birth weight	Mean, SD

	Flenady et al. 2022	Birthweight (g) <2500g 2500 to 3499g, 3500g to 3999g >4000g	N, %
	Kapaya et al. 2020	Birth weight (g)	Mean, SD
	Norman et al. (2018)	Birthweight <2500g 2500g to <3500g 3500g to <4000g >4000g	N, %
	Saastad et al. (2011)	Birth weight (g)	Mean, SD
4. Gestation at birth	Flenady et al. (2022)	Gestation at birth in weeks 28 to 32 33 to 36 37 to 39 40 to 41 42+	N, %
	Kapaya et al. 2020	Gestational age at birth	Mean, SD
	Norman et al. (2018)	Estimated gestation, weeks Estimated gestation for inductions only, weeks	Mean, SD
	Saastad et al. (2011)	Gestational age at birth in days	Mean, SD
5. HIE	Flenady et al. (2022)	Hypoxic ischemic encephalopathy, measured as part of a composite measure of adverse neonatal outcome	N, %
6. Neonatal death	Akselsson et al. (2020)	Death within 27 days after birth	N, %
	Chaku et al.	Neonatal death	N
	Czapla et al. (1987)	Early neonatal death Late neonatal death	N

	Flenady et al. (2022)	Neonatal death 28+ weeks Neonatal death 20+ weeks gestation	N
	Gomez et al. (2007)	Neonatal death	N
	Moore & Piacquadio (1989)	Neonatal mortality	N, %
7. NICU admission	Akselsson et al. (2020)	Admission to NICU	N, %
	Chaku et al.	Admission to NICU (at term)	N, %
	Heazell et al. (2013)	Unexpected admission to NICU	N, %
	Norman et al. (2018)	Admitted to neonatal unit Admitted to neonatal unit for >48h Admitted to neonatal unit at >37 weeks' gestation	
	Saastad et al. (2011)	Transferred to neonatal care unit	N, %
	Tveit et al. (2009)	Admitted to neonatal care (in RFM)	N, %
8. Perinatal death	Czapla et al. (1987)	Perinatal death Intrapartum death	N
	Delaram & Jafarzadeh (2016)	Fetal death	N
	Moore & Piacquadio (1989)	Fetal mortality	N, %
	Norman et al. (2018)	Stillbirth at 24 weeks' gestation and above or death in the first 7 days of life	N, %
	Saastad et al. (2011)	Perinatal death	N, %
	Westgate & Jamieson (1986)	Perinatal death	N, %
9. Preterm birth	Akselsson et al. (2020)	Preterm birth (<37+0)	N, %

	Norman et al. (2018)	Pretem baby	N, %
	Saastad et al. (2011)	Preterm birth	N, %
	Tveit et al. (2009)	Preterm births 28+0 to 36+6 weeks (in RFM)	N, %
10. Stillbirth	Akselsson et al. (2020)	Apgar score=0	N, %
	Armstrong-Buisseret et al. (2020)	Stillbirth or death before discharge	N, %
	Awad et al. (2018)	IUFD within 2 weeks post discharge IUFD after 2 weeks post discharge	N
	Chaku et al.	Stillbirth	N
	Czapla et al. (1987)	Stillbirth	N
	Flenady et al. 2022	Stillbirths 28+ weeks Also 20+, 24+, 37+ weeks as post hoc	N, %
	Grant et al. (1989)	Antepartum late fetal death	N, %
	Gomez et al. (2007)	IUFD	N
	Heazell et al. (2013)	Stillbirth	N, %
	Kapaya et al. 2020	Stillbirth	N
	Lobb, Beazley & Haddad (1985)	Stillbirth (all weights) Stillbirth <1500g Stillbirth <1500g	N
	Neldam (1980)	Stillbirth (gestation and weight given for each)	N
	Norman et al. (2018)	Stillbirth (after 24 weeks or >500g) Stillbirth at 37 weeks or more Stillbirth at 28 weeks or more (WHO definition)	N, %

		Stillbirth at 22 weeks or more (ISA definition) Stillbirth at 24 weeks or more	
	Singh & Sidhu (2007)	Intrauterine death	N, %
	Tveit et al. (2009)	Stillbirth in RFM Normally formed stillbirth in RFM Stillbirth	N, %
	Westgate & Jamieson (1986)	Stillbirth Unexplained stillbirth	N, %

7.10 A UK based survey of midwives and obstetricians' knowledge and practice regarding RFM: study protocol

7.10.1 Introduction

Concerns about RFM, defined as a decrease or (more latterly) change in a baby's normal movements *in utero*,[1] lead to presentation at hospital in up to 15% of pregnancies[267] and maternal perception of RFM is associated with adverse pregnancy outcomes such as stillbirth and FGR.[192–194]

Current UK guidance from the NHS regarding RFM is to contact a midwife or maternity unit if your baby is moving less than usual or not at all,[205] however, there is a lack of consensus on how RFM pregnancies should be managed clinically. NICE guidelines state that anyone who is pregnant should be advised to contact maternity services with any concerns about fetal movement or in the case of RFM after 24+0 weeks, but that the use of structured fetal movement awareness packages (with the AFFIRM trial as an example[202]) has not been shown to reduce stillbirth rates.[269] This guideline states that current practice is to follow recommendations in the NHS SBLCBv2,[270] which states that pregnant women should be made aware of the importance of RFM.

Recommendations within the RCOG Green-top guideline[11] are generally based on evidence rated as 'B' or 'C', meaning that data are from high quality cohort studies or systematic reviews of these studies, rather than high quality randomised trials or meta-analyses of trials. The strongest recommendation in this guideline is that ultrasound should be carried out to assess fetal morphology in presentations with RFM, this is given an 'A' rating. The wide variation in the strength of recommendations may lead to uncertainty in clinical practice; hospitals often have their own protocols and national guidelines are not always adhered to.[74]

A survey of UK midwives and obstetricians published in 2008 found significant variation in both knowledge of RFM and its clinical management.[2] Between 4.7 and 12.4% of respondents were unsure of how RFM should be defined and 7.8 to 24.8% were unsure of the role of formal fetal movement counting in clinical practice. This survey also found that the definition of RFM as <10 movements in 12 hours was not supported; subjective definitions were more likely to be defined as adequate (especially by midwives).

At the time of the 2008 survey, NICE guidelines stated that formal fetal movement counting should not be a part of routine antenatal care, this was reflected in the responses as the majority of respondents held negative views about their use; only 5% of obstetricians

and 3% of midwives used kick charts in routine antenatal care. The majority of respondents, 70% of obstetricians and 74% of midwives, said that their institution had guidelines for the clinical management of RFM in pregnancy. Knowledge of reported associations with RFM and adverse pregnancy outcomes, such as FGR and fetal hypoxia, was variable.

The RCOG guideline has been updated and reviewed in this time but there is still recognised to be a lack of evidence rated as high quality on which to base recommendations. Several large trials of interventions to prevent adverse outcomes in RFM pregnancies have been published,[76,202] which may have influenced practice. Recent studies in this area such as those by Akselsson et al.[9] and Flenady et al[77] focus on being mindful of fetal movements and presenting to hospital in cases of deviations from normal movement, rather than kick counting using pre-specified 'alarm limits'. Notably, neither of these studies recommended management for women presenting with RFM.

A systematic review and meta-analysis of intervention studies for RFM, which included 18 studies, showed wide variation in terms of what was considered standard care at different study sites.[302] This suggests that national guidelines are still not followed at all hospitals; a finding that is corroborated by two reviews of clinical practice guidelines regarding RFM.[74,271] Hayes et al. found that it is uncertain whether fetal movement counting, compared with standard care, leads to a difference in the rate of stillbirth and found a lack of evidence for effects of other forms of clinical management on stillbirth; meta-analysis of data from studies of fetal movement counting suggested that fetal movement counting may lead to an increase in maternal-fetal attachment with no associated change in maternal anxiety.[302]

A survey of UK midwives and obstetricians will explore whether knowledge of RFM and clinical practice concerning RFM pregnancies has changed over the past decade and will highlight areas of practice to improve.

7.10.2 Methods

Aim

This study aims to survey UK-based clinicians to describe knowledge and practice around RFM, to determine whether this has changed since the 2008 survey, and if this relates to guidelines or studies that have been published during this time. We are interested in whether opinions regarding definitions of RFM have changed in the past decade, and whether opinions of kick charts and their usage reflects this.

Objectives

1. To survey UK-based clinicians about their RFM knowledge and practice;

2. To see if responses by midwives and obstetricians differ;

3. To investigate whether any other factors, such as country of residence and the presence of guidelines, are linked to certain responses;

4. To compare responses with a previous survey to determine if there have been changes over time;

5. To disseminate the results of the survey.

Design

This will be a cross sectional UK-based survey of midwives and obstetricians, and will be structured in the same way to facilitate comparison with UK guidelines and with the survey by Heazell et al. (2008). This survey will be online rather than postal; this is to easily maximise its reach and a reflection of how research is now conducted. We do acknowledge that some potential participants (those without internet access or who do not feel comfortable using the internet) may be excluded by this approach.

The survey will be comprised of five sections: 1. Demographics of participants, including whether they work part or full time, their area of practice, years of experience, and whether they work for the NHS or privately; 2. Asking women about RFM, knowledge of and attitudes towards fetal movement counting; 3. Definitions of RFM and their acceptability; 4. Clinical management of RFM pregnancies, and; 5. Knowledge of associations of RFM with adverse outcomes and other characteristics.

Participants will be asked to elaborate on their answers, providing reasoning and justifications where appropriate. A five point scale (strongly agree, agree, unsure, disagree, strongly disagree) will be used for questions that ask about the acceptability of definitions of RFM or its management.

Scope

The purpose of this survey is to describe knowledge and practice relating to RFM in the UK; this will identify areas in which knowledge is lacking or in which practice could be improved, but will also give an overview of these areas and how much they are influenced by the current guidelines.

Responses may not be applicable to other countries or income settings, however, this may be an avenue for future research.

Participants and sampling

Anyone who is currently practising, or has practised, as a midwife or obstetrician in the UK is eligible to take part. There are no inclusion or exclusion criteria based on other demographic criteria.

Participants will be recruited by contacting relevant organisations (such as the Royal College of Midwives and the British Maternal Fetal Medicine Society) and asking them to disseminate the survey to their members. We will also contact authors of studies about RFM who are based in the UK. The survey will be advertised using social media.

We will aim for a sample size of 200 to facilitate comparisons with the previous survey, however, as the response rate for the previous survey was fairly low (30% for clinicians and 34% for midwives), we will not put an upper limit on the number of potential participants that we will approach.

We will aim to collect responses from all countries in the UK and for as many areas as possible within these countries. Participants will be encouraged to forward the survey to other people who are eligible and may be interested.

Participants will be provided with an information sheet describing the study and its aims and what participation would entail. Consent to take part in the survey will be ensured by requiring participants to click an 'I agree to take part' box before gaining access to the survey.

Analysis

Data will be collected using REDCap software and exported to Microsoft Excel for analysis. Descriptive statistical analysis will be performed and the Chi-squared test or Fisher's exact test will be used to assess statistical differences in responses, and a p value of <0.05 will be considered as statistically significant.

Dissemination

The results of the survey will be published in an open access journal and findings will be publicised using social media. In addition, we plan to present the results of the survey at national and international conference and through relevant professional organisations.

7.11 Survey of practice questionnaire

Survey questions

Thank you for choosing to take part in this survey. This questionnaire contains 16 questions for you to answer about your knowledge and practice in relation to reduced fetal movement in pregnancy. Please elaborate on your answers and give reasoning where possible/applicable.

1. Are you completing this survey as someone who practises, or has practised as a midwife, obstetrician, sonographer or another role?

Midwife ☐ Obstetrician ☐ Sonographer ☐ Other (please describe) ☐

2. Do you currently practise clinically?

Full time ☐ Part time ☐ Not currently ☐

3. How long have (or had) you been in practice (including training)?

≤ 10 years ☐ 11-20 years ☐ 21-30 years ☐ >31 years ☐

4. What best describes your practice?

NHS only ☐ Private only ☐ Both NHS & private ☐

5. In which country do you or did you most recently practise?

6. Please indicate at which gestations, if any, you think asking about fetal movement should be part of routine antenatal care?

Gestational age (weeks)	All pregnancies	High risk pregnancies only	Never
$24^{+0} – 27^{+6}$	☐	☐	☐
$28^{+0} – 30^{+6}$	☐	☐	☐
31^{+0} - 33^{+6}	☐	☐	☐
$34^{+0} – 36^{+6}$	☐	☐	☐
$37^{+0} – 40^{+6}$	☐	☐	☐
$> 41^{+0}$	☐	☐	☐

Please give reasons for your response:

7. Do you use a kick chart as part of antenatal care?

Yes for all pregnancies ☐ Yes, for high risk pregnancies ☐ No ☐

If yes, please provide reasons why:

If yes, please provide details of the chart you use:

Name or author of chart	
Instructions for using this chart	
Procedure for counting (e.g. all day, for 2 hours)	
When to report reduced fetal movements (e.g. less than *x* movements in *y* hours)	

8. Do you routinely provide any other information about RFM as part of antenatal care, such as leaflets or other guidance? If so, what is recommended in your unit?

9. Please indicate your level of agreement with the following statements: "Asking women to formally count fetal movements using a kick chart…

	Strongly agree	Agree	Unsure	Disagree	Strongly disagree
… is helpful in routine antenatal care for all women	☐	☐	☐	☐	☐
… helps women to remember to notice movements every day	☐	☐	☐	☐	☐
… increases maternal-fetal attachment	☐	☐	☐	☐	☐
... increases maternal anxiety	☐	☐	☐	☐	☐
… assists in detecting fetal growth restriction	☐	☐	☐	☐	☐
… avoids unnecessary consultations for reduced fetal movements	☐	☐	☐	☐	☐
… is proven to prevent stillbirth	☐	☐	☐	☐	☐
… is only useful for women considered to be at high risk of pregnancy complications	☐	☐	☐	☐	☐
… results in unnecessary intervention	☐	☐	☐	☐	☐
… is of no benefit	☐	☐	☐	☐	☐

10. Please indicate what you consider to be reduced fetal movements in the **third trimester** of pregnancy.

Fetal movements	**Duration**	**Reduced fetal movements**		
		Yes	**No**	**Unsure**
<3 movements per hour	Over 12 hours	☐	☐	☐
< 10 movements total	Over 2 hours	☐	☐	☐
< 10 movements total	Over 12 hours	☐	☐	☐
<10 movements per 12 hours	Over 2 days	☐	☐	☐
Maternal perception of reduced fetal movement	Over 12 hours	☐	☐	☐
Maternal perception of reduced fetal movement	Over 24 hours	☐	☐	☐
Any maternal perception of reduced fetal movements	Any	☐	☐	☐
Maternal perception of reduced fetal movements with recorded data (e.g. kick chart)	-	☐	☐	☐

Please give reasons for your response:

11. Women in the **third trimester** of pregnancy should report **complete absence** of fetal movements lasting for a period of …

12 hours ☐ 24 hours ☐ 48 hours ☐ Other ☐

If other, please state:

12. Are you aware of any clinical practice guidelines within your institution for the management of women with reduced fetal movements?

Yes ☐ No ☐ n/a ☐

If yes, which guidelines are followed:

RCOG ☐ NHS England Saving Babies Lives Care Bundle ☐ Other ☐

13. Which of these interventions, if any, would you perform on women presenting with reduced fetal movements **from 28+0 to 37+6 weeks of gestation**:

Management	**Always**	**Sometimes (dependent on risk status of patient)**	**Never**
Give a kick chart	☐	☐	☐
Measure symphysis-fundal height	☐	☐	☐
CTG	☐	☐	☐
Vibro-acoustic stimulation	☐	☐	☐
Ultrasound scan for growth	☐	☐	☐
Ultrasound biophysical profile	☐	☐	☐
Kleihaur-Betke's test	☐	☐	☐
Umbilical artery Doppler	☐	☐	☐
Admit to hospital	☐	☐	☐
Consider expedited birth	☐	☐	☐

Please give reasons for your responses:

14. Which of these interventions, if any, would you perform on women presenting with reduced fetal movements **after 37 weeks of gestation**:

Management	**Always**	**Sometimes (dependent on risk status of patient)**	**Never**
Give a kick chart	☐	☐	☐
Measure symphysis-fundal height	☐	☐	☐
CTG	☐	☐	☐
Vibro-acoustic stimulation	☐	☐	☐
Ultrasound scan for growth	☐	☐	☐
Ultrasound biophysical profile	☐	☐	☐
Kleihaur-Betke's test	☐	☐	☐
Umbilical artery Doppler	☐	☐	☐
Admit to hospital	☐	☐	☐
Consider expedited birth	☐	☐	☐

Please give reasons for your responses:

15. At which gestation(s), if any, would you consider induction or expedited birth for reduced fetal movements in the absence of any other complications?

RFM definition	**<34 weeks**	**34-36^{+6} weeks**	**37-40 weeks**	**Over 40 weeks**	**Never**
Maternal perception of reduced fetal movements	☐	☐	☐	☐	☐
Maternal perception of absent fetal movements	☐	☐	☐	☐	☐
Objective evidence of reduced fetal movements	☐	☐	☐	☐	☐
Objective evidence of absent fetal movements	☐	☐	☐	☐	☐

16. In general, do you feel that any of the following are significantly increased in women presenting with reduced fetal movements?

Condition	**Yes**	**No**	**Unsure**
Maternal anxiety levels	☐	☐	☐
Pre-term labour	☐	☐	☐
Pre-eclampsia	☐	☐	☐
Primigravida	☐	☐	☐
Male or female fetal sex	☐	☐	☐
Anterior placental site	☐	☐	☐
Fetal hypoxia/fetal distress	☐	☐	☐
Fetal growth restriction	☐	☐	☐
Maternal obesity (BMI >30)	☐	☐	☐
Umbilical cord pathology	☐	☐	☐
Maternal depression	☐	☐	☐
Maternal wish for additional scan	☐	☐	☐

7.12 Comparisons between surveys of practice

Clinicians' responses to whether written guidelines or policies for the management of RFM are available

	Heazell et al. (2008)	Flenady et al. (2009)	Unterscheider et al. (2010)	Smith et al. (2014)	Hayes et al.
Yes	71.7%	n/a	31.3%	n/a	98.4%
No	n/a	51.0%	55.2%	53.1%	1.0%
Unsure	n/a	n/a	13.5%	n/a	0.6%

n/a = data not available

When clinicians would perform a CTG for presentations with RFM

	Heazell et al. (2008)	Flenady et al. (2009)	Unterscheider et al. (2010)	Smith et al. (2014)		Hayes et al.	
	All presentations	Third trimester	Low risk after 39+3w	Low risk	High risk	28+0w to 37+6 w	After 37w
Always	92.4%	80.3%	93.8%	88.5%	96.2%	91.2%	96.1%
Sometimes	n/a	18.5%	n/a	n/a	n/a	4.4%	3.9%

n/a = data not available

Clinicians' views on definitions of RFM

	Heazell et al. 2008	Flenady et al. 2009	Smith et al. 2014*	Hayes et al.
<10 movements in 12h	62.3%	74.0%	67.0%	36.0%
<10 movements in 24h	48.9%	n/a	16.9%	n/a
Any maternal perception of RFM	71.3%	n/a	11.5%	n/a
Maternal perception of RFM lasting 12h	70.1%	60.0%	n/a	96.4%
Maternal perception of RFM lasting 24h	76.7%	76.0%	n/a	n/a

*participants could choose one response that best defined RFM

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