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Review Article

Pregnancy, birth and neonatal outcomes associated with reduced fetal movements: A systematic review and meta-analysis of non-randomised studies

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ABSTRACT

Problem: Maternal perception of reduced fetal movements (RFM) is identified as an important alarm signal for possible risk of impending adverse perinatal outcomes.
Background: Perinatal outcomes associated with RFM are increasingly being investigated in non-randomised studies with several associated outcomes, including stillbirth, preterm birth, fetal growth restriction and neonatal death being reported. Findings from studies, however, are conflicting.
Aim: To synthesise the findings of published studies regarding pregnancy, birth and neonatal outcomes in women who presented with RFM.
Methods: PubMed, EMBASE, CINAHL complete, Maternity and Infant Care, PsycINFO, and Science Citation Index databases were searched up to 8th July 2021 and updated again on 8th September 2022. Non-randomised studies involving pregnant women ≥24 weeks' gestation, who presented with a primary complaint of RFM compared to women who did not present with RFM were included. Data were meta-analysed using a random-effects model and presented as Odds Ratios (OR) or Standard Mean Differences (SMD) with 95% Confidence Intervals (CI).
Findings: Thirty-nine studies were included. Women with RFM had increased odds of stillbirth (OR 3.44, 95% CI 2.02-5.88) and small for gestational age (OR 1.37, 95% CI 1.16-1.61) when compared with women who did not have RFM. Associations were also found for induction of labor, instrumental birth and caesarean section but not for preterm birth (OR 0.92, 95% CI 0.71-1.19) or neonatal death (OR 0.99; 95% CI 0.52-1.90).
Conclusion: This review revealed that RFM is associated with increased odds of stillbirth, small for gestational age, induction of labor, instrumental birth and caesarean section but not preterm birth or neonatal death.

Introduction

Over the past three decades there has been renewed interest in the assessment of fetal well-being using fetal movements as a screening tool to prevent adverse outcomes. Maternal perception of reduced fetal movements (RFM) has been identified as an important alarm signal for possible risk of impending adverse perinatal outcomes. Outcomes associated with RFM are increasingly being investigated in non-randomised studies with several associated outcomes, including stillbirth, preterm birth, fetal growth restriction and neonatal death being reported. Findings from studies, however, are conflicting, especially those of more recent versus earlier studies (Stacey et al., 2011; Turner, Flenady, Ellwood, Coory, & Kumar, 2021), and large-scale versus smaller scale studies (Levy, Kovo, Barda, et al., 2020; Norman et al., 2019; Zamstein, Wainstock, & Sheiner, 2019).

The inconsistency in findings between studies warrants a comprehensive systematic review to provide robust evidence of the overall association for pregnant women, clinicians, and policy makers. Systematic reviews conducted to date on RFM in pregnancy are centred on methods of fetal movement counting to assess fetal well-being, management of reported RFM during pregnancy and interventions to enhance maternal awareness of RFM

Abbreviations: RFM, reduced fetal movements; SGA, small for gestational age.

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(Hofmeyr & Novikova, 2012; Mangesi, Hofmeyr, Smith, & Smyth, 2015; Winje et al., 2016). There are no published systematic reviews and meta-analyses that synthesis the evidence from non-randomised studies on the potential adverse pregnancy, labour and neonatal outcomes associated with RFM. Meta-analysis of data from published studies may provide a more precise estimate of adverse pregnancy risk associated with RFM and provide higher level evidence to inform policy and practice. Collating the empirical evidence in a systematic way, minimises bias and thus can provide more reliable findings and conclusions.

For this reason, we undertook a systematic review and meta-analysis to investigate and quantify the association between RFM and pregnancy, birth and neonatal outcomes. The protocol for the review is registered with the international prospective register of systematic reviews (PROSPERO) (ID: CRD42017082685). We reported our review using the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines (Page et al., 2021).

Methods

Search strategy

To retrieve relevant studies, PubMed, EMBASE, CINAHL complete, Maternity and Infant Care, PsycINFO, and Science Citation Index databases were searched from their inception dates to 8th July 2021. This search was subsequently updated on 8th September 2022. Language restrictions were not applied to the searches. The inclusion criteria were nonrandomised, observational studies, reporting maternal or perinatal outcomes in pregnant women with at least one episode of RFM $\geq$ 24 weeks' gestation. For comparator analyses, reported data for non-exposed participants (women without RFM) was also required. As definitions for RFM are inconsistent in the literature, the definition described by the included studies' authors were accepted. Search terms used to guide the search strategy centred on fetal movement terms, combined with the Boolean operands 'OR' and 'AND' as appropriate, and adapted across databases. We used Medical Subject Headings (MeSH), free-text and expanded synonyms (fetal OR foetal). The full search strategy is available in Supplementary File 1. We supplemented the results with a manual search of the reference lists of all articles selected for full text review.

Study selection

Retrieved citations were imported from reference manager Endnote X9 to Covidence. Two review authors independently screened the title and abstracts of all imported citations, forwarding potentially eligible papers for full text review. Two review authors independently assessed full text articles against the review's pre-specified inclusion criteria. Any discrepancies were resolved following discussion amongst the reviewers. Single studies reported across two or more papers were counted as one study. Where an abstract and paper reported on the same study, the abstract was only included if there were additional data reported. Where different papers reported different outcomes on the same cohort these were amalgamated and reported as one study. Due to translation constraints only studies published in English or Spanish were included.

Outcomes

A core outcome set (COS) for studies on RFM is currently unavailable. For the purposes of the systematic review, the research team pre-specified important outcomes based on knowledge of the topic, outcomes commonly reported in recent studies, and outcomes that are likely to be meaningful to clinicians and the public.

The primary outcomes of the review were stillbirth (defined by intrauterine death at or after 24 weeks' gestation) or as defined by the study, preterm birth (birth before 37 weeks' gestation), small for gestational age (SGA) (birthweight less than the 10^{th} centile for gestational age) or as defined by the study and neonatal death (death in the first 28 days of birth). Secondary outcomes were induction of labour, caesarean section (emergency and planned), assisted vaginal birth, birthweight (kgs), Apgar score $<$ 7 at 5 minutes following birth, incidence of meconium-stained liquor, metabolic acidosis and neonatal intensive care units (NICU) admission rates.

Quality assessment

The Quality in Prognosis Studies (QUIPS) tool was used by at least two reviewers to assess the quality of the included studies. The QUIPS tool evaluates six domains of research validity and bias: study participation, study attrition, prognostic/risk factor measurement, confounding measurement and account, outcome measurement and analysis and reporting (Hayden, van der Windt, Cartwright, Cote, & Bombardier, 2013). Studies were evaluated as either low, moderate or high risk of bias for each domain.

Data extraction and analysis

Two reviewers (LC & VS; LC & LG) independently extracted data from each included study and checked for accuracy using a pre-specified data extraction excel spreadsheet. The following data were extracted: aim of study, author, year of publication, country of study, time of study, study design, inclusion/exclusion criteria, characteristics of cohort, description of RFM exposure, reported maternal and perinatal outcomes including definitions and methods of assessment, number of participants with and without RFM who did and did not develop the review's pre-specified outcome(s), unadjusted and adjusted effect measures, including details of the variables/confounders that were adjusted for, and other statistical results as presented in the included paper (e.g. sensitivity, specificity, and positive and negative predictive values).

Meta-analyses were conducted where feasible using Review Manager 5.4 software. Dichotomous data were summarized using odds ratio (OR) and 95% confidence intervals (CI). Continuous data were summarized using mean difference (MD) and 95% CI for outcomes measured in the same way and the standard mean difference (SMD) was used where outcomes were measured using different methods. Outcomes measures from individual studies were combined using a random effect model. Statistical heterogeneity was assessed using I^2. Publication bias and the effect of small studies were visually assessed for similar outcomes reported by at least ten studies using funnel plots. To enable synthesis of all available evidence, all studies' data irrespective of study quality were included in the meta-analyses. We conducted sensitivity analyses to investigate potential sources of heterogeneity by restricting analyses by study design (prospective versus retrospective) and to studies of low risk of bias in all domains for primary outcomes.

Results

The search identified 5416 citations. Forty-two duplicate records were found. Following title and abstract screening, 225 records were forwarded for full-text screening. Of these, 170 were excluded (Supplementary File 2). A review of the reference lists of retrieved papers did not identify any additional papers. One additional study (Smith et al., 2014), published in abstract format

only by one of the review authors (VS) was also included and additional data provided as appropriate. This resulted in 55 records reporting on 51 studies for inclusion. The abstract and full report of one study were included because they reported additional data to each other (McCarthy, Meaney, & O'Donoghue, 2016). Two studies were reported across two papers each (Levy, Kovo, Barda, et al., 2020; Levy, Kovo, Izaik, et al., 2020; Pagani, D'Antonio, Khalil, Akolekar, et al., 2014; Pagani, D'Antonio, Khalil, Papageorghiou, et al., 2014) and two abstracts of the same study (Sage & Fretts, 2012; Sage & Fretts, 2012a) were also included. On further review of these 51 studies, 12 studies did not report on specified outcomes following RFM and were subsequently excluded. This resulted in a final inclusion of 39 non-randomised studies (Akselsson, Lindgren, Georgsson, Pettersson, & Rådestad, 2019; Aviram et al., 2016; Binder, Monaghan, Thilaganathan, Morales-Roselló, & Khalil, 2018; Bradford et al., 2019; Christou et al., 2019; Daly, Brennan, Foley, & O'Herlihy, 2011; Eng, Karki, & Trivedi, 2016; Eshraghi, Jamal, Eshraghi, Kashanian, & Sheikhansari, 2020; Harrington et al., 1998; Heazell et al., 2018; Heazell et al., 2017; Ho et al., 2018; Holm Tveit, Saastad, Stray-Pedersen, Bordahl, & Froen, 2009; Inukollu, Sulthana, Solipuram, Kunamneni, & Kothagadi, 2021; Levy, Kovo, Barda, et al., 2020; Levy, Kovo, Izaik, et al., 2020; Linde, Pettersson, & Radestad, 2017; McCarthy et al., 2016; O'Sullivan, Stephen, Martindale, & Heazell, 2009; Olagbuji, Ezeanochie, Kubeyinje, Dunsin, & Ande, 2011; Pagani, D'Antonio, Khalil, Akolekar, et al., 2014; Sadovsky, Yaffe, & Polishuk, 1974; Y. H. Sage & R. Fretts, 2012b; Saglam et al., 2022; Sheikh, Hantoushzadeh, & Shariat, 2014; Sinha, Sharma, Nallaswamy, Jayagopal, & Bhatti, 2007; Skornick-Rapaport et al., 2004; Stacey et al., 2011; Sterpu et al., 2020; Turner et al., 2021; Valencia-Rincon et al., 2017; Valentin & Marsal, 1987; Warrander et al., 2012; Williams, Southam, Malik, & Gardosi, 2014; Winje, Roald, Kristensen, & Froen, 2012; Zamstein et al., 2019) from 14 countries and 724,826 women that reported on maternal and perinatal outcomes following RFM in pregnancy (Fig. 1).

Characteristics of the included studies

Characteristics of the included studies, including inclusion and exclusion criteria, exposure, and outcomes, are provided in Table 1. The thirty-nine studies were published between 1974 and 2022, with most (n=28) published in the last ten years, highlighting renewed interest in the topic of fetal movements. The majority of the studies were from Europe (17 studies), followed by the Middle East (10 studies), Australia (3 studies), New Zealand (2 studies), Asia (1 studies), North America (2 studies), South America (1 study), West Africa (1 study) and South Africa (1 study). An international study was also included, involving participants from, among others, the UK, US, Canada. Of the 39 studies, 14 were retrospective cohort or case-control studies, 13 were prospective population based cohort or case-control studies, 5 case-control studies and in 7 studies the research design was not clearly specified. Various definitions of RFM exposure were used. The majority of studies reported maternal perception of RFM or self-reported RFM or altered movements (n=24), while other studies (n=6) used arbitrary time limits for RFM such as <3 FM per hour, < 4 FM per hour, <5 FM per day for 2 consecutive days. In nine studies definition of RFM was not explicit. There was a variation in the gestation beyond which pregnancies with RFM were included in each study. Nine studies explicitly examined one or more of our pre-specified outcomes in women with RFM at ≥36 weeks' gestation while the remaining studies examined one or more pre-specified outcomes in women with RFM ≥24 weeks gestation. The method of data collection in studies also varied. In the majority of studies (n=27), data was collated from either medical records or hospital electronic databases, however, in some studies it was also collected via a questionnaire (n=6) or interviews (n=2). The data collection method was not specified or unclear for seven studies.

Outcome definitions

Studies varied with regard to criteria for defining stillbirth, and some had no specific gestational age or birth weight criteria for stillbirth. Preterm birth was defined as birth prior to 37 weeks gestation however most did not differentiate between spontaneous and iatrogenic preterm birth. SGA was either defined as birthweight below the 10th percentile for gestational age or birth >37 weeks gestation with a birthweight of >2500g. The measurement of gestational age used was either reliable last menstrual period or ultrasound measurements of crown rump length in the first trimester or biparietal diameter in the second trimester. Metabolic acidosis was defined as either umbilical arterial cord pH <7.0, <7.05 or ≤7.10 or a pH base excess >12mmols/L.

Quality of the studies

Only studies reported in full-text format (n=34) were assessed using the QUIPS tool. The proportion of studies considered to have low, moderate, or high risk of bias in each domain is illustrated in Fig. 2. Table 2 provides an overview of the results of the risk of bias assessments. Twenty-one studies were rated low risk of bias for study participation (domain 1). Thirteen studies were rated either moderate or high risk of bias as the description of the sampling frame, recruitment and inclusion or exclusion criteria were not explicit or evident. All except five studies were rated low risk of bias for study attrition (domain 2). Five studies were rated either moderate or high risk of bias due to study participation rate or they did not report reason for attrition or loss of participants to follow up. Six studies were rated either moderate or high risk of bias for risk factor measurement because the definition or description of reduced fetal movements was unclear or not reported. Seven studies were rated as moderate or high risk of bias for domain four, due to either unreported or unclear definitions for outcome measurement used in the studies. Eleven studies in total were rated either moderate or high risk of bias for domain five (study confounding), due to either no reporting of confounding or no description of multivariate regression within the paper. Studies were rated low risk of bias if the studies reported methods of case-controlling, matching or control groups (n=23). Thirty-two studies were rated low risk of bias for domain six (statistical analysis and presentation). One study was rated moderate risk of bias and one study was rated high risk of bias due to either no documentation of analytical strategy or insufficient presentation of data to assess the analytical strategy.

Outcomes in women with RFM during pregnancy

Primary outcomes

RFM was associated with a more than 3-fold increase in stillbirth (OR 3.44 95% CI 2.02 to 5.88, 23 studies, 513124 participants I^2=84%,). Five studies reported on stillbirth ≥36 weeks' gestation. The effect of RFM remained significant for stillbirth at gestational age ≥36 weeks gestation although less so than overall; (OR 2.38, 95% CI 1.22-4.68, 5 studies; 318552 participants, I^2=31%). RFM was also associated with, although to a lesser extent, an increase in SGA (OR 1.37, 95% CI 1.16 to 1.61, 19 studies, 456207 participants, I^2=78%,). No differences between the groups in preterm birth (OR 0.92, 95% CI 0.71 to 1.19, 13 studies, 423944 participants, I^2=84%) or neonatal death (OR 0.98, 95% CI 0.51 to 1.91, 8 studies, 168988 participants, I^2=0%) were observed (Fig. 3; Table 3). A sensitivity analysis was conducted on all primary outcomes for study design

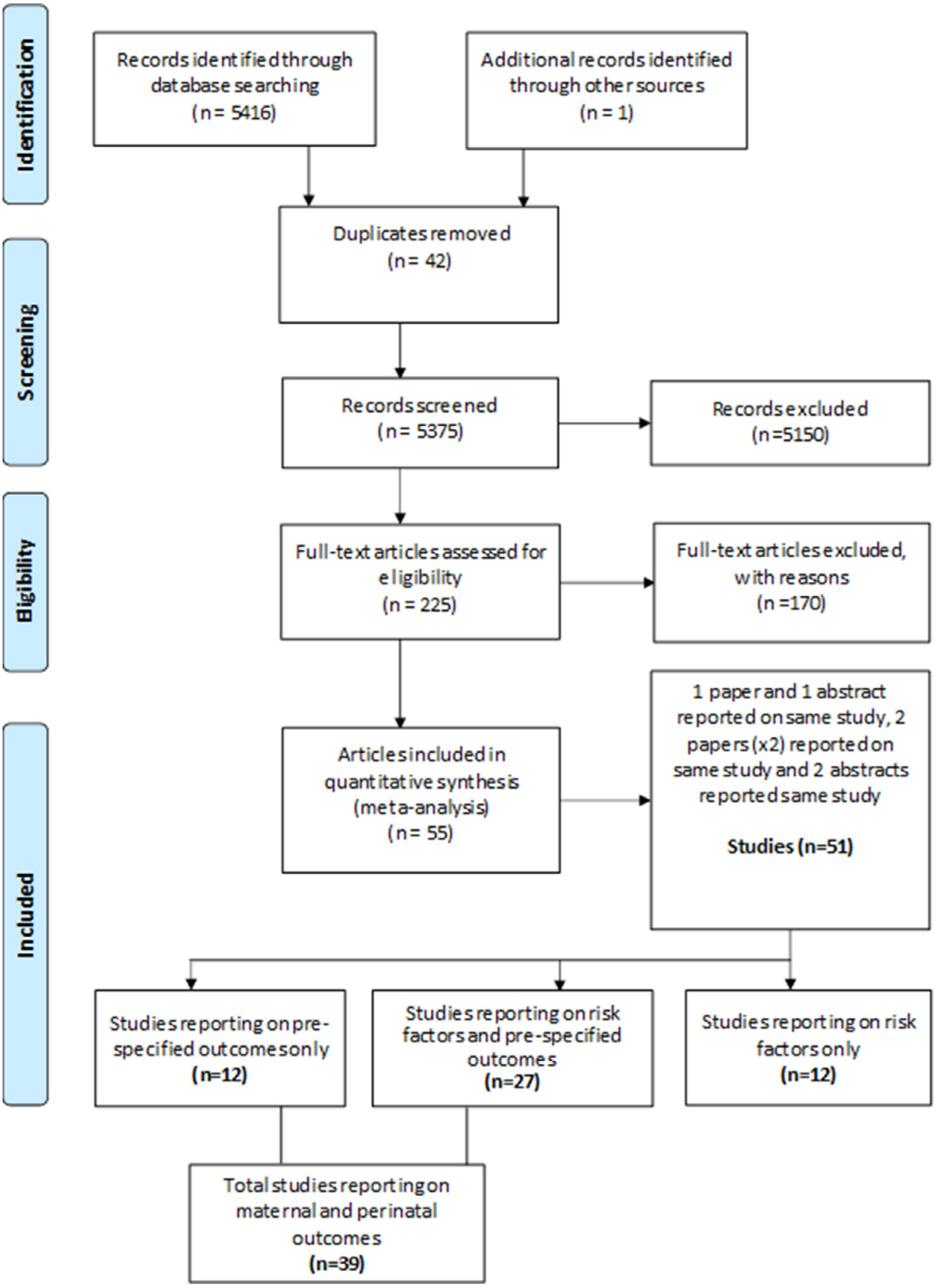

Fig. 1. PRISMA flow chart of study selection and inclusion.

and removing studies at moderate or high risk of bias further supported these findings and lowered heterogeneity (Fig. 3A, Fig. 3B, Fig. 3C). All included studies for neonatal death were retrospective, therefore a sensitivity analysis was not conducted (Fig. 3D).

Secondary outcomes

Table 4 and Supplemental File 3 presents the results for the pre-specified secondary outcomes. Women with RFM in pregnancy compared to women without RFM were more likely to have induction of labor (OR 1.81; 95% CI 1.50 to 2.18; 15 studies; 497018 participants; I^2=96%) instrumental birth (OR 1.14; 95% CI 1.03 to 1.25; 11 studies; 222827 participants; I^2=53%), caesarean section overall (OR 1.46; 95% CI 1.19 to 1.78; 16 studies; 472610 participants; I^2=95%), emergency caesarean section (OR 1.35; 95% CI 1.23 to 1.48; 12 studies; 246063 participants, I^2=55%), and metabolic acidosis (OR 1.33; 95% CI 1.15 to 1.54; 6 studies; 75166 participants;

Table 1
Summary of experimental conditions.

Lead Author & Year	Setting (Country)	Study Design	Study Period	Data Collection Methods	Inclusion/Exclusion Criteria	Definition of RFM	Timing of RFM G(gestation)	RFM (n)	No RFM (N)
Akelsson 2019	Sweden	prospective population-based cohort study	Jan 2014 - Dec 2014	Questionnaire and birth register	women who sought care due to decreased or altered fetal movements	decreased or altered fetal movements	≥28 weeks gestation	2683	26041
Aviram 2016	Israel	Retrospective	2008-2013	Medical record database	Singleton pregnancy admitted to delivery ward with spontaneous onset of labor, or for labor induction excluding pregnancies with known structural or chromosomal anomalies.	< 2 consecutive hours or a marked subjective complaint of movements pattern change	37 - 42 weeks'	825	37031
Binder 2018	UK	Retrospective	Jan 2008 - Oct 2015	Hospital obstetric and neonatal records	Singleton pregnancy excluding multiple pregnancies congenital anomaly or aneuploidy	Each visit to the fetal medicine unit was considered a RFM episode	≥ 36 weeks'	4500	1527
Bradford 2019	New Zealand	case-control	Feb 2012 - Dec 2015	Interviews	Cases were women who had experienced a singleton late stillbirth (≥28 weeks' gestation). Controls were women with ongoing singleton non-anomalous pregnancies randomly selected from hospital booking lists	Maternal perception	Not specified	145	588
Christou 2019	Afghanistan	Prospective national, population-based survey	2010	Questionnaires	Women aged 12-49 years, births within the last three years	Maternal perception	Not specified	162	13672
Daly 2011	Ireland	Retrospective	Calendar year	medical records	Singleton pregnancy	Maternal perception	28-42+² weeks'	524	7,338
Eng 2016	Australia	Retrospective	Jan 2007 - Dec 2011	medical records	Case-Stillbirth. Control- live birth after 34 weeks' gestation excluding Women in labor < 34 weeks	Not explicit	2 weeks prior to stillbirth	35	129
Eshragi 2020	Iran	prospective cohort	Not reported	Not reported	singleton pregnancy, ≥37 weeks gestation and persistent reduced fetal movement	Persistent reduced fetal movement	>37 weeks'	150	150
Harrington 1998	UK	Not specified	20 month period	Not specified	Women who presented to the FAU with a primary complaint of RFM	Not specified	Not explicit	435	6793
Heazell 2017	International	Case-Control	Sep 2012 - Aug 2014	Web-based survey	Cases -women ≥ 18 years, fluent in reading and writing English, delivered a singleton stillborn baby with no evidence of congenital anomaly at ≥ 28 weeks gestation < 30 days prior to completing the survey. Controls-pregnant (≥ 28 weeks) or had recently delivered a living baby less than 30 days before they completed the survey.	Maternal perception of fetal activity	>28 weeks'	88	545
Heazell 2018	UK	Case -Control	April 2014 - March 2016	interviewer-administered questionnaire	Women with a singleton, stillbirth at or after 28 weeks gestation without congenital anomaly. Controls were women with an ongoing pregnancy	changes in strength and frequency in the last two weeks prior to stillbirth	≥28 weeks'	86	875
Ho 2017	Australia	Prospective	Mar 2015-Nov 2015	medical records	Uncomplicated third-trimester pregnancies excluding known fetal anomaly	Maternal perception	26-40 weeks'	50	50
Holm Tveit 2009	Norway	Prospective Case-Control	Jun 2004-Oct 2005	medical records	Singleton pregnancy excluding stillbirths not initially identified by RFM	Self-reported perception	≥ 28 weeks'	2374	614

(*continued on next page*)

Table 1 (*continued*)

Lead Author & Year	Setting (Country)	Study Design	Study Period	Data Collection Methods	Inclusion/Exclusion Criteria	Definition of RFM	Timing of RFM G(gestation)	RFM (n)	No RFM (N)
Inukollu 2021	India	Prospective	Sept 2018 -Aug 2019	Not specified	Pregnant women presenting with RFM after 30 weeks of gestation	A subjective feeling of reduced fetal movements	>30 weeks'	100	100
Leader 1981	South Africa	Prospective Case-Control	Not specified	Not explicit	Women admitted to the wards of hospital	A day of no FMs or 2 successive days in week before of FM<10/day	26-42 weeks'	23	138
Levy 2020	Israel	Retrospective	Jan 2009 July 2019	medical records	singleton deliveries≥37 gestational weeks, isolated complaint of RFM,	Maternal perception	≥37 weeks	2762	10576
Linde 2017	Sweden	Not specified	2014	Questionnaire and medical records	All women with simplex pregnancy	Not explicit	Not explicit	2683	26041
McCarthy 2016	Ireland	Prospective	Apr 2013- Oct 2013	medical records	All women presenting with RFM excluding multiple pregnancies and congenital anomalies	Not explicit	> 28 weeks'	275	265
O'Sullivan 2009	UK	Retrospective	Jan 2007- Dec 2007	medical records	Women with a primary complaint of DFM & a viable fetus	Not explicit	After 24 weeks	203	3896
Olagbuji 2011	Nigeria	Case-Control	Jan 2006 - Dec 2009	Medical records	Study group: Women who had antenatal care and IOL at term for maternal perception of DFM. Control: next consecutive parturient matched for age & parity who had IOL for prolonged pregnancy excluding with other obstetric complications and contraindications to vaginal birth	Not explicit	Term	107	107
Pagani 2014	UK	Retrospective	Jan 2008 - Dec 2012	Electronic medical records	All singleton pregnancies excluding pregnancies with fetal anomalies or multiple gestations	Subjective perception	> 36 weeks	865	16926
Sadovsky 1974	Israel	Prospective	Not specified	Not clear	Not specified	< 3 movements/hr	2nd half of pregnancy	15	65
Sage 2012	US	Not specified	Oct 2010 - Sept 2011	Not explicit	All women who presented with initial complaint was DFM.	Not specified	3rd trimester	371	7224
Saglam 2021	Turkey	Case control matched	Sept 2018 - Jan 2020	Medical records	Women who complained of RFM in a singleton pregnancy after 32 weeks	Maternal perception	> 32 weeks'	42	126
Sheikh 2014	Iran	Prospective	Feb 2012 - March 2013	Questionnaire and medical records	Normotensive singleton uncomplicated pregnant women who gave birth to healthy term newborns excluding preterm birth, SGA, maternal smoking, opiate use, diabetes, hypertension, fetal anomaly or multiple gestations.	< 4 fetal movements/hour	> 28 weeks'	59	670
Sinha 2007	UK	Retrospective Matched	Jan 2004 - Aug 2004	Electronic charts/records	Women attending the DAU primarily with a history of RFM excluding pregnancies complicated with maternal medical complications, congenital fetal anomalies, or with previous CS	Not explicit	≥ 24 weeks	90	90

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Table 1 (*continued*)

Lead Author & Year	Setting (Country)	Study Design	Study Period	Data Collection Methods	Inclusion/Exclusion Criteria	Definition of RFM	Timing of RFM G(gestation)	RFM (n)	No RFM (N)
Skornick-Rapaport 2004	Israel	Not specified	Not specified	electronic medical records	Women with primary complaint of subjectively RFM	Not explicit	Not explicit	769	28119
Smith 2014	Ireland	Retrospective	Jan 2011-Dec 2011	medical records and annual report	All women with primary complaint of RFM	Maternal perception	≥28 weeks'	1008	16627
Stacey 2011	New Zealand	Retrospective Matched	July 2006- Jun 2009	Interviews	Women with a singleton, late stillbirth without congenital abnormality	changes in strength and frequency of movement,	> 28 weeks'	155	310
Sterpu 2020	Sweden	Retrospective cohort	Jan 2016 - Dec 2017	medical records	All singleton pregnancies presenting with RFM after 22 gestational weeks'	Maternal perception	> 22 weeks'	3243	11944
Tokoro 2022									
Turner 2021	Australia	Retrospective cohort	2009 - 2019	hospital database	Women with a single fetus without a known congenital anomaly presenting with RFM	Maternal perception	>28 weeks'	8821	92776
Valencia-Rincon 2017	Venezeula	Prospective Case-Control	Jun 2015-Apr 2017	medical records	Mothers over 18 years with normal pregnancy delivering at term excluding multiple pregnancy and any other complication of pregnancy	at least two hours of RFM in the previous 12hrs that differed from usual pattern	37-41 weeks'	93	550
Valentin 1987	Sweden	Not specified	Not specified	medical records	Not specified	FM counts fell below the individual lowest normal limit in two consecutive counting sessions (alarm signal)	Not explicit	158	1756
Warrander 2012	UK	Not specified	Aug 2009- Oct 2010	medical records	RFM and subsequently delivered within 7 days of presentation excluding fetal anomaly, multiple pregnancy or abnormal fetal heart rate on CTG	Subjective maternal perception of RFM for at least 12 hours	> 28 weeks	36	36
Whitty 1991	USA	Not specified	Jan 1985 - Apr 1990	Not explicit	All low risk patients presenting with a complaint of RFM	<four movements/hr for 2 consecutive hrs	< 36 weeks	223	623
Williams 2014	UK	Retrospective	2009-2012	medical records	Multifetal pregnancies and congenital anomalies were excluded	Any change in perceived quality or frequency of fetal movements	Not explicit	23621	108102
Winje 2012	Norway	Prospective	July 2009 - July 2011	medical records	All women with singleton pregnancies presenting with RFM	Maternal perception	last 7 days before birth	129	191
Yogev 2003	Israel	Prospective matched	Jan 1998 - Dec 2000	electronic medical records	Women with consistent reduced perception of FM excluding pregnancies with contraindication to induction of labor and vaginal delivery	< five fetal movements/day for 2 consecutive days	Not explicit	115	510
Zamstein 2019	Israel	Retrospective cohort	1991 - 2014	Databases	maternal complaint of DFM during advanced stages of pregnancies	Maternal perception	advanced stages of pregnancy	439	243243

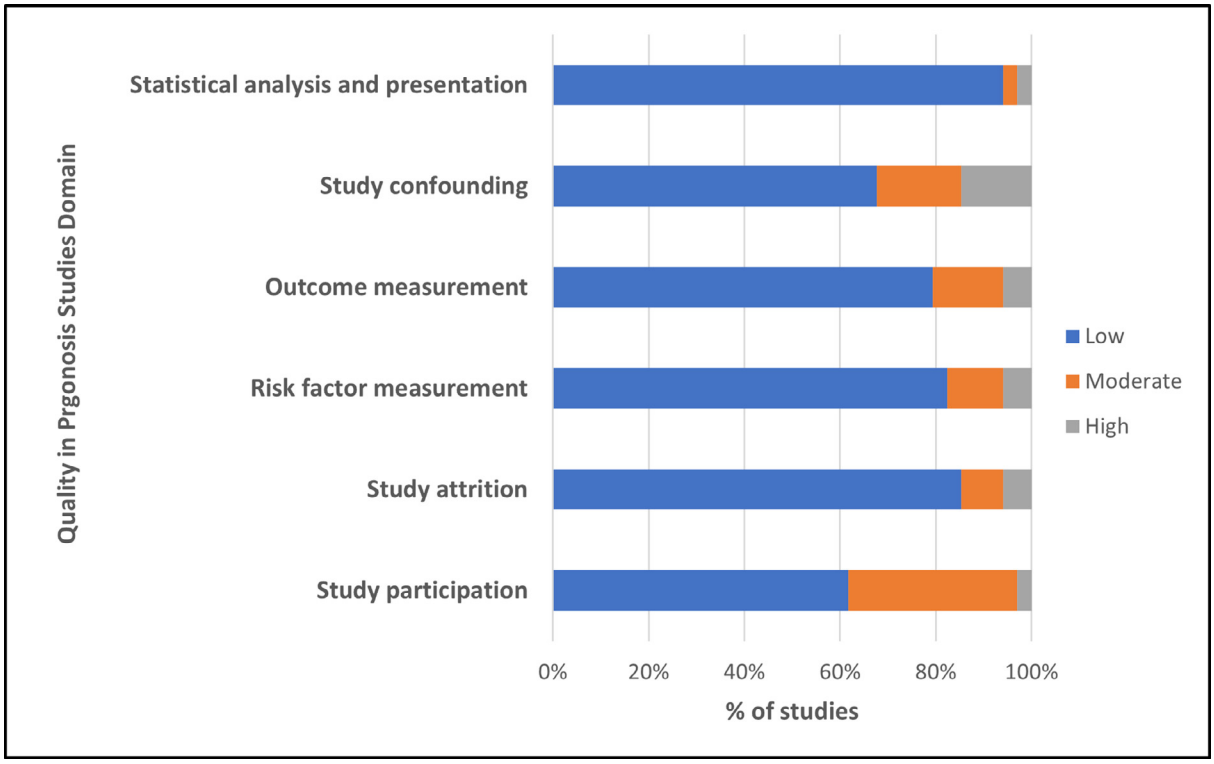

Fig. 2. Quality of the studies.

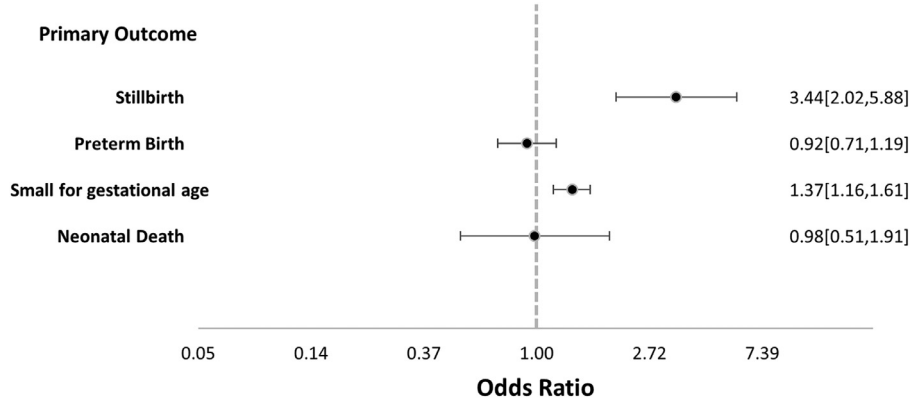

Fig. 3. Association between reduced fetal movements and adverse primary outcomes.

I^2=5%. No differences were found between groups in any of the remaining pre-specified secondary outcomes (meconium, planned caesarean section, apgar score <7 at 5 mins, birthweight, admission to NICU or gender).

Publication bias

Upon inspection of the funnel plots for outcomes such as preterm birth, small for gestational age, induction of labor and instrumental birth, there was evidence of either publication bias, suggesting that smaller studies with large effects may be underrepresented or there is selective outcome reporting amongst studies (Supplementary File 4).

Discussion

There are no systematic reviews on pregnancy outcomes in women presenting with reduced fetal movements. This comprehensive systematic review and meta-analysis, including 39 studies, is the first systematic review that the authors are aware of that provides a comprehensive examination of the impact of RFM on a broad range of perinatal outcomes. The results demonstrate that RFM presents a significant burden for pregnancy and birth adversity, especially for stillbirth and SGA.

Our review did not find an association between RFM and preterm birth or neonatal deaths. The number of NNDs, however were very few across the groups in only eight studies (11 of 17,787 versus 102 of 151,201. This could be explained by the fact that over the past decades there have been many advances in antenatal and neonatal critical care resulting in a reduction in neonatal deaths.

This systematic review also confirms that when women present with RFM in pregnancy they are more likely to have increased intervention such as induction of labor, caesarean section and instrumental birth. It is acknowledged that there is a paucity of evidence to direct the clinical management of women presenting with RFM (Hofmeyr & Novikova, 2012). Current international guidance on the

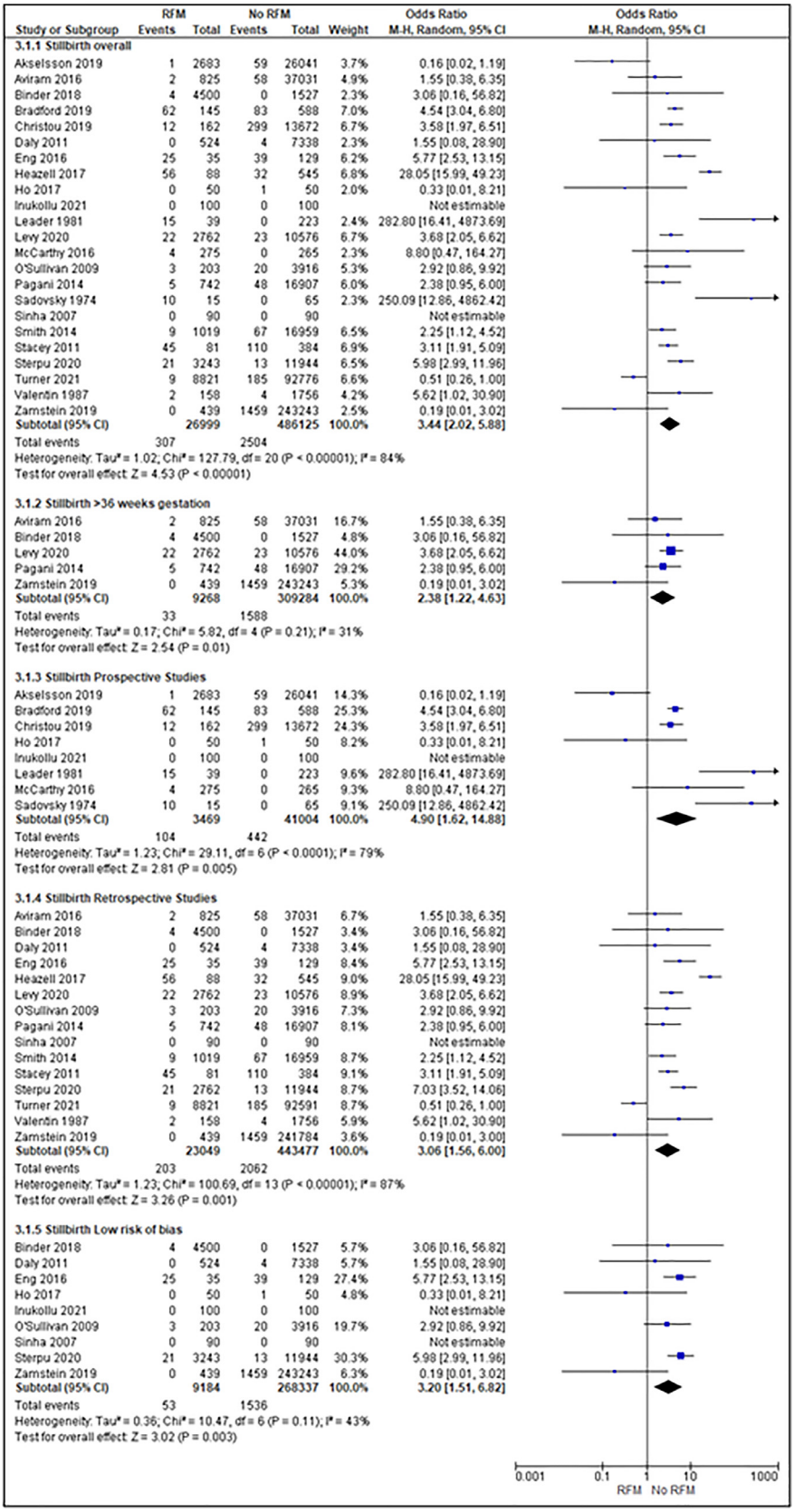

Fig. 3A. Stillbirth forest plots.

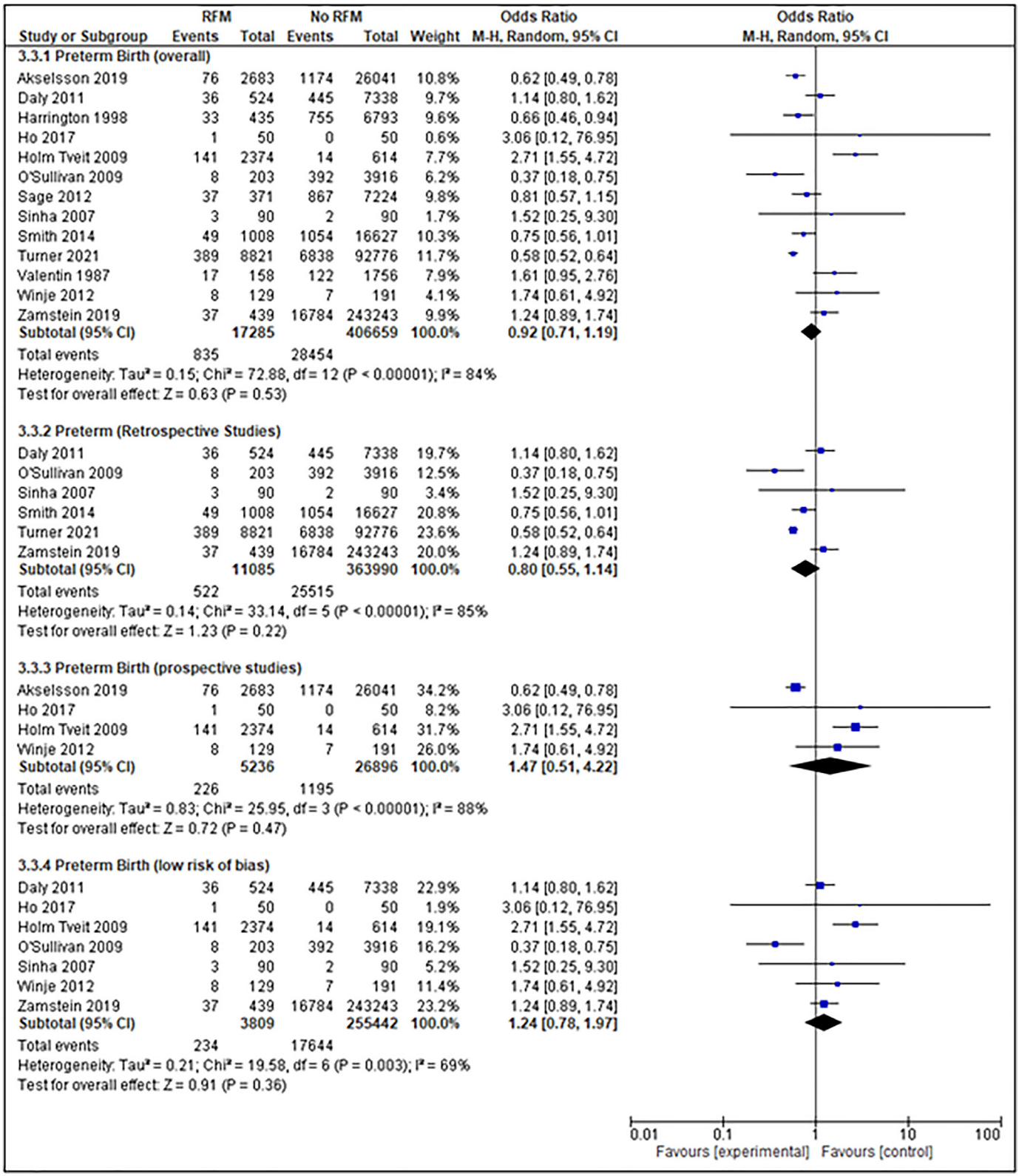

Fig. 3B. Preterm birth forest plots.

management of RFM is based on level 2 evidence (case-control study) conducted over a decade ago (Royal College of Obstetricians and Gynaecology, 2011). It is possible that in the absence of robust higher-level evidence to support standard management policies for women presenting with RFM, varied clinical management will continue. Recently, a large, stepped wedged, cluster RCT conducted in the UK and Ireland that compared a care package for pregnant women and clinician that increased the awareness of prompt reporting of RFM and used a standardized management protocol, including timely delivery for RFM, with standard care, did not sig-

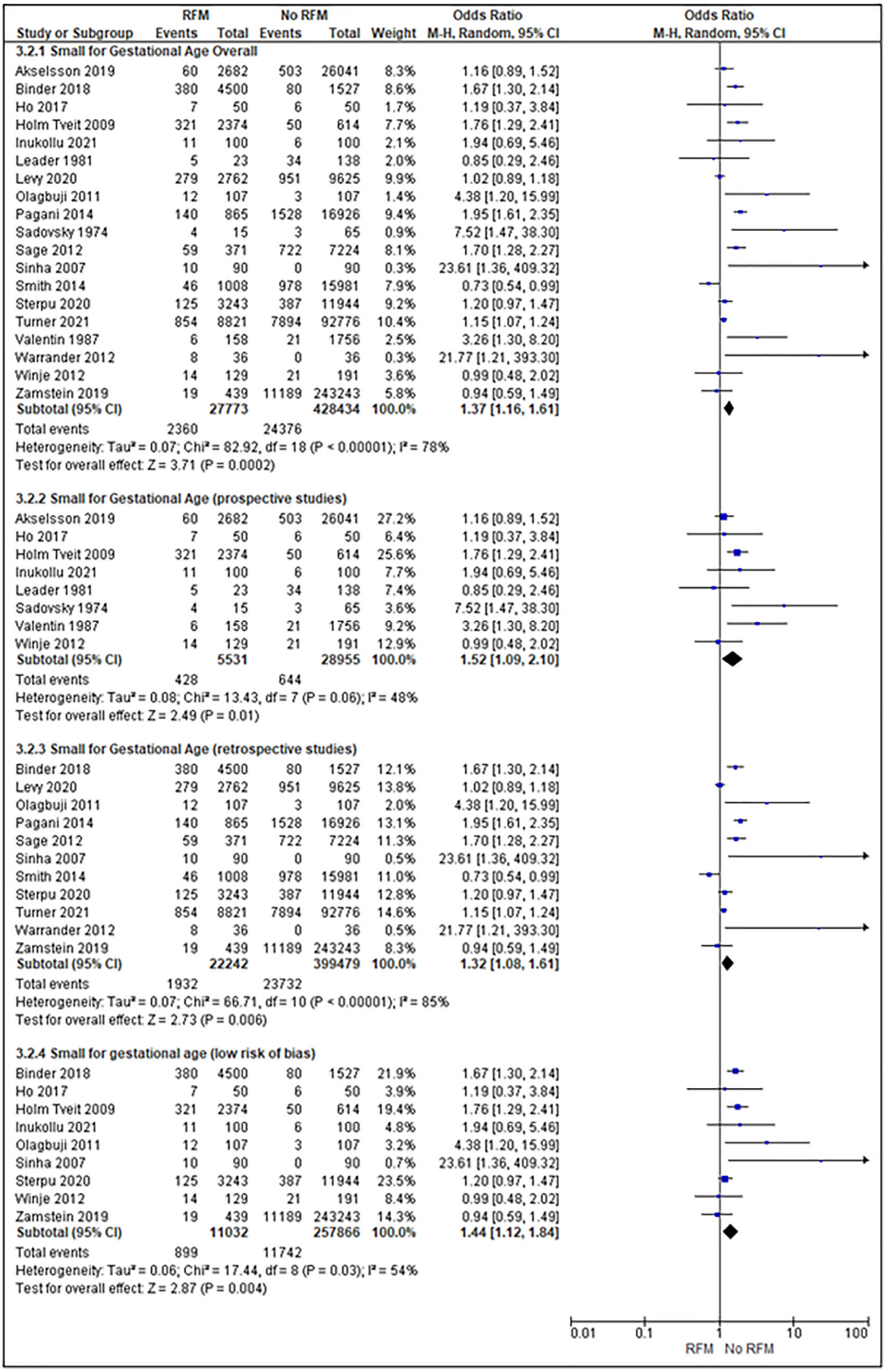

Fig. 3C. Small for gestational age forest plot.

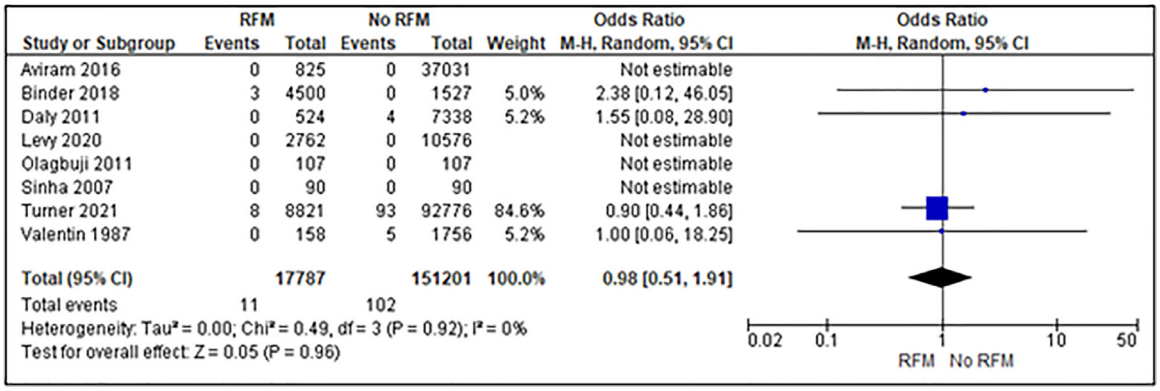

Fig. 3D. Neonatal Death forest plot.

Table 2
Quality of studies using the QUIPS tool.

Lead Author & Year	Study Participation	Study Attrition	Risk Factor Management	Outcome Measurement	Study Confounding	Statistical Analysis & Presentation
Akelsson 2019	Low	Low	Low	Moderate	Moderate	Low
Aviram 2016	Moderate	Low	Low	Low	Low	Low
Binder 2018	Low	Low	Low	Low	Low	Low
Bradford 2019	Moderate	Low	Moderate	Low	Low	Low
Christou 2019	Low	Low	High	Low	Low	Low
Daly 2011	Low	Low	Low	Low	Low	Low
Eng 2016	Low	Low	Low	Low	Low	Low
Eshragi 2020	Moderate	Low	Moderate	Low	Moderate	Low
Harrington 1998	Moderate	Low	Low	Moderate	High	Low
Heazell 2017	Moderate	Low	Moderate	Moderate	Low	Low
Heazell 2018	Moderate	High	Low	Low	Low	Low
Ho 2018	Low	Low	Low	Low	Low	Low
Holm Tveit 2009	Low	Low	Low	Low	Low	Low
Inukollu 2021	Low	Low	Low	Low	Low	Low
Leader 1981	High	Low	Low	Moderate	High	Low
Levy 2020	Moderate	High	Low	Low	Moderate	Low
Levy 2020 (b)	Moderate	Low	Low	Low	Low	Low
Linde 2017	Abstract					
McCarthy 2016	Low	Low	Low	Low	Low	Moderate
O'Sullivan 2009	Low	Low	Low	Low	Low	Low
Olagbuji 2011	Low	Low	Low	Low	Low	Low
Pagani 2014	Low	Moderate	Low	Low	Low	Low
Sadovsky 1974	Moderate	Low	Moderate	High	High	High
Sage 2012	Abstract					
Saglam 2021	Moderate	Moderate	High	High	Moderate	Low
Sheikh 2014	Low	Low	Low	Low	Low	Low
Sinha 2007	Low	Low	Low	Low	Low	Low
Skornick-Rapaport 2004	Abstract					
Smith 2014	Abstract					
Stacey 2011	Moderate	Low	Low	Low	Low	Low
Sterpu 2020	Low	Low	Low	Low	Low	Low
Turner 2021	Low	Low	Low	Moderate	Low	Low
Valencia-Rincon 2017	Moderate	Moderate	Low	Low	Moderate	Low
Valentin 1987	Moderate	Low	Low	Low	High	Low
Warrander 2012	Low	Low	Low	Low	Moderate	Low
Whitty 1991	Low	Low	Low	Low	High	Low
Williams 2014	Abstract					
Winje 2012	Low	Low	Low	Low	Low	Low
Yogev 2003	Low	Low	Low	Low	Low	Low
Zamstein 2019	Low	Low	Low	Low	Low	Low
–	–	–	–	–	–	–

nificantly reduce the incidence of stillbirth but did increase the frequency of labor induction and birth by caesarean section and longer neonatal unit stay (Norman et al., 2018). Interestingly, compliance to the intervention package protocol was inconsistent with less than 40% of maternity units adhering to the overall package. Similar challenges have been experienced in other intervention studies to increase awareness of fetal movements (Akselsson et al., 2020; Flenady et al., 2022; Grant, Elbourne, Valentin, & Alexander, 1989). Several studies have also highlighted variation in maternity care professionals' views in relation to fetal movement screening and assessment (Flenady et al., 2009; Heazell, Green, Wright, Flenady, & Froen, 2008; Smith, Begley, & Devane, 2014; Smyth et al., 2016; Unterscheider, Horgan, Greene, & Higgins, 2010; Warland & Glover, 2017). This poses the question if management of RFM by experienced clinicians will be difficult to change. It is inevitable that clinicians will actively respond to any suspicion of fetal compromise by timely elective or caesarean birth in an effort to prevent an adverse event.

Table 3
Risk of adverse primary outcomes in women with RFM during pregnancy.

Outcome/Stratification	No. of Studies	No. of participants	OR (95% CI)	I^2
Stillbirth				
Overall	23	513124	3.44 (2.02, 5.88)	84%
Stillbirth ≥36 weeks gestation	5	318552	2.38 (1.22, 4.63)	31%
Retrospective studies only	15	466526	3.06 (1.56, 6.00)	87%
Prospective studies only	8	44473	4.90 (1.62, 14.88)	79%
Low Risk of Bias Studies	9	277521	3.20 (1.51, 6.82)	43%
Small for Gestational Age				
Overall	19	456207	1.37 (1.16, 1.61)	78%
Retrospective studies only	11	421721	1.32 (1.08, 1.61)	85%
Prospective studies only	8	34286	1.52 (1.09, 2.10)	48%
Low Risk of Bias Studies	9	268898	1.44 (1.12, 1.84)	54%
Preterm Birth				
Overall	13	423944	0.92 (0.71, 1.19)	84%
Retrospective studies only	6	375075	0.80 (0.55, 1.14)	85%
Prospective studies only	4	32132	1.47 (0.51, 4.22)	88%
Low Risk of Bias Studies	7	259251	1.24 (0.78, 1.97)	69%
Neonatal Death				
Overall	8	168988	0.99 (0.52, 1.90)	0%

CI, confidence interval; OR, odds ratio.

Table 4
Meta-analysis of secondary outcomes associated with RFM.

Outcome	No. of Studies —	Events in women with RFM —	Events in women with no RFM	OR (95% CI)	I^2
Induction of Labor	15	8024/23742	113176/473276	1.81 (1.50, 2.18)	96%
Meconium	4	1492/9918	15896/130480	1.09 (0.86, 1.37)	53%
Instrumental Birth	11	2359/18635	27558/209192	1.14 (1.03, 1.25)	53%
Caesarean Section Overall	16	5626/21319	88813/451291	1.46 (1.19, 1.78)	95%
Planned CS	7	2108/15638	24722/142242	0.77 (0.68, 0.86)	54%
Emergency CS	12	2894/20665	27167/225398	1.35 (1.23, 1.48)	55%
Birthweight (kgs)	10	13083	348931	-18.65 (-60.09, 22.78)	88%‡
Apgar Score <7 at 5 mins	18	447/21652	8420/467849	1.18 (0.77, 1.79)	87%
Metabolic acidosis	6	325/8779	993/66387	1.33 (1.15, 1.54)	5%
Admission to NICU	14	383/9562	5993/118727	0.87 (0.62, 1.23)	79%
Gender-Male	5	3074/6187	56087/109812	0.93 (0.81, 1.06)	73%

CI, confidence interval; OR, odds ratio; ‡mean difference (MD), CS, caesarean section.

Recent large case control studies have consistently demonstrated an association between RFM and risk of stillbirth (Heazell et al., 2018; Heazell et al., 2017; Stacey et al., 2011) and more recently small for gestational age (Norman et al., 2019; Sterpu et al., 2020). Studies have shown that a change in the strength and frequency of fetal movement causes an 'alarm signal' for women, prompting them to seek immediate medical advice. Opportunities are therefore established for further investigation for detection of any additional fetal complications such as oligohydramnios, fetal growth restriction or non-reassuring fetal cardiotocograph, thus prompting early intervention to prevent fetal death. Maternal perception of a reduction or change in fetal movements should consequently be considered clinically important and so women with a concern about RFM should continue to be advised to contact their healthcare provider immediately. SGA and stillbirth are attributed to placental insufficiency (Silver, 2018). The risk of stillbirth in pregnancies with growth restriction identified antenatally is 1% compared to an over 8-fold increase risk of stillbirth in pregnancies with unrecognized growth restriction (Gardosi, Madurasinghe, Williams, Malik, & Francis, 2013) suggesting that early detection of fetal growth and placental insufficiency can substantially reduce the risk of stillbirth. Symphysis-fundal height (SFH) measurement has been found to be an effective screening tool for SGA, which may indicate growth restriction due to placental insufficiency (Heazell, Sumathi, & Bhatti, 2005). This information is important for midwives and obstetricians when deciding on the investigations necessary for women who present with RFM in pregnancy, suggesting that at a minimum, women with RFM should have a clinical examination that includes an abdominal palpation and measurement of SFH performed to assess growth and amniotic fluid. It may also assist clinicians in selecting women who should undergo further assessment and investigation, such as ultrasound assessment of growth and umbilical artery doppler. There is also increasing evidence that the use of cerebro-placental ratio (the ratio of the umbilical artery pulsatility index over the middle cerebral artery pulsatility index) may be an alternative measurement for identifying fetuses at high risk of adverse perinatal outcome (Dunn, Sherrell, & Kumar, 2017). A low cerebro-placental ratio is associated with increased risk of adverse neonatal outcomes in women with RFM (Binder et al., 2018; Eshraghi et al., 2020).

Strengths of this review include the rigorous methods in which it was undertaken. All relevant evidence published in English or Spanish since the 1970's was included; therefore, there is a possibility that we may have missed studies published in other languages. Temporal changes to practices and local clinical guidelines for the management of RFM could have impacted on results of individual studies. However, over three quarters of included studies were published in the last decade, thus the available evidence largely reflects current practices. It is noteworthy that only two studies (Christou et al., 2019; Olagbuji et al., 2011) from low-income countries met the inclusion criteria. Therefore, our results are primarily relevant for medium-high income countries only.

This systematic review is based on data from observational studies which are at higher risk of confounding factors compared to randomised controlled trials. We also estimated unadjusted effect sizes which may have overestimated risks. Several included studies either did not control for the same confounders or control at all for the effect of confounders. Heterogeneity was moderate for a number of outcomes and should be taken into account when interpreting the results. Practice variations in the management of women presenting with RFM were not always reported in included studies, which may represent an unexplored source of heterogeneity. Moreover, we note inconsistencies in the definition of RFM used in the studies, however over 60% of included studies used 'maternal perception of reduced fetal movements' as the exposure criteria. The criteria on which outcomes were defined and measured varied. In addition, the reporting of outcomes varied significantly across studies. The various definitions used therefore pose a methodological difficulty when attempting to interpret and accurately evaluate associations between adverse perinatal outcomes. It is therefore necessary to reach a consensus on the definition and classification for adverse pregnancy outcomes to be comparable. The development of a core outcome set relating to RFM is welcome (Hayes et al., 2021). Standardizing a set of outcomes that should be measured and reported in all studies will optimise data synthesis of individual studies and interpretation of the research evidence surrounding RFM (Hayes et al., 2021). For further updates of this systematic review, we will consult the COS currently in development, once available, to ensure that all outcomes in the COS are included.

Conclusion

This review, involving thirty-nine studies and 724,826 participants has found that stillbirth and SGA, induction of labor, assisted vaginal birth and caesarean section are increased with RFM in pregnancy. This information provides clinicians, and others, with comprehensive evidence on RFM risks which will help clinicians make informed decisions when treating pregnant women with RFM.

Recommendations for research

Future reviews quantifying the risk of adverse perinatal outcomes in women who present more than once with RFM during pregnancy is warranted.

Ethical Approval

As this work was a review of published literature, ethical approval was not required.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.midw.2022.103524.

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