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Review article

Risk factors for reduced fetal movements in pregnancy: A systematic review and meta-analysis

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ABSTRACT

Maternal perception of reduced fetal movements (RFM) is an important clinical marker to identify women at higher risk of adverse perinatal outcomes. Preventing and reducing stillbirths can only be achieved through better detection and management of women with RFM, however the characteristics of women who present with RFM in pregnancy vary. A systematic review was conducted to explore the risk factors associated with reduced fetal movements (RFM) in pregnancy.

PubMed, EMBASE, CINAHL, Maternity and Infant Care, PsycINFO and Science Citation Index were searched, from their inception date, for studies published up to 16th May 2019. Non-randomised observational studies reporting risk factors in pregnant women presenting with a primary complaint of RFM during pregnancy were included. The quality of the included studies was assessed with the Quality in Prognosis Studies (QUIPS) tool. Meta-analyses were performed using RevMan 5.3 software for each identified risk factor where two or more studies reported on the same risk factor. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed.

Twenty-seven studies reporting on risk factors for RFM during pregnancy were included. Women presenting with RFM during pregnancy are more likely to be Caucasian, smokers, and have an anterior placenta, oligohydramnios and polyhydramnios. No difference was found in parity or the mean age of women presenting with RFM and women who did not present with RFM. Previous caesarean section, postdates >42 weeks', and other medical conditions, including diabetes and hypertensive disorders were not predictive for RFM during pregnancy.

Modifiable and non-modifiable risk factors associated with RFM in pregnancy were identified. These results can be used to raise awareness of factors associated with RFM, and prompt women to attend their maternity care provider should concerns arise.

Contents

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Introduction

Stillbirth rate is a key indicator of maternal health and the quality of maternity care in pregnancy and birth. Over the past few years there have been calls for further reduction in stillbirth rates [1]. Up to 50% of women report a gradual decrease in fetal movement before intrauterine death [2–4]. Maternal perception of reduced fetal movements (RFM) is therefore an important clinical marker to identify women at higher risk of adverse perinatal outcomes. Preventing and reducing adverse outcomes can only be achieved through better detection and management of women with RFM, however the characteristics of women who present with RFM in pregnancy vary.

Risk factors for RFM are increasingly being investigated with several associated factors, including maternal age, BMI, parity, ethnicity, smoking, occupation, position of placenta and medications, reported across studies. Systematic reviews conducted on fetal movements in pregnancy to date have concentrated on methods of fetal movement counting to assess fetal well-being [5], management of reported RFM during pregnancy [6] and interventions to enhance maternal awareness of RFM [7].

Early identification by healthcare professionals of risk factors, both modifiable and non-modifiable, that are significantly associated with RFM could contribute to the prevention and reduction of adverse pregnancy, birth, fetal and neonatal outcomes. For this reason, we performed a systematic review to identify risk factors for RFM in pregnancy (the focus of this paper), and to assess pregnancy, labour and birth outcomes following RFM (to be reported separately). The protocol for the review is registered with the international prospective register of systematic reviews (PROSPERO) (ID: CRD42017082685). The Preferred Reporting Items for Systemic Reviews and Meta-analyses (PRISMA) guidelines (www.prisma-statement.org) were followed in reporting this systematic review.

Methods

Study design

In healthcare, prognosis relates to the probability or risk of an individual developing a particular state of health (outcome) over a specified time [8]. To evaluate the risk factors for RFM, non-randomised, observational studies published in English or Spanish, reporting on pregnant women with at least one episode of RFM $\geq$ 24 weeks gestation were included. For comparator analyses, data for non-exposed participants (women without RFM) were also required. Risk factors were not pre-specified, rather risk factors for RFM that were reported in two or more eligible studies were included in the review.

Search strategy

PubMed, EMBASE, CINAHL, Maternity and Infant Care, PsycINFO, and Science Citation Index were searched from inception to 23rd March 2018. This search was subsequently updated on 16th May 2019. No new studies reporting on risk factors were found in the updated search. The search strategy used in Pubmed was: ((fetal movement[MeSH Terms]) OR fetal movement*) OR foetal movement*) OR fetal activit*) OR foetal activit*) OR fetal movement*[Title/Abstract]) OR foetal movement*[Title/Abstract]) OR fetal activit*[Title/Abstract]) OR foetal activit*[Title/Abstract])) AND ((((reduc*) OR decreas*) OR decreas*[Title/Abstract]) OR reduc*[Title/Abstract]). The same search was adapted for use across the other databases. No filters were applied. Supplement 1 presents the complete search strategy. Retrieved records were imported and de-duplicated in Endnote X7. The reference lists of the included studies were also screened for additional potentially relevant studies. Retrieved citations were imported into Covidence (http://www.covidence.org) for screening and eligibility assessments.

Study selection

Title and abstracts of retrieved citations were independently screened by two review authors (LC & VS; LC & LG). Potentially eligible studies were forwarded for full text review. Full text papers were assessed independently by two authors (LC & VS and LC & LG) against the review's eligibility criteria. Any uncertainties during the study selection or data extraction process were resolved by discussion and consensus. 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.

Data extraction

A pre-specified data extraction form was developed to extract the relevant data from the included studies. Information was extracted from each included study, where available, by two reviewers independently (LC & VS and LC & LG), and checked for accuracy; author, year of publication, country of study, time of study, study design, inclusion/exclusion criteria, characteristics of cohort, description of RFM exposure, reported risk factors including definitions and methods of assessment, number of participants with and without the risk factor for RFM and no-RFM populations, 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).

If any data were missing, attempts were made to contact the authors for additional information.

Quality assessment of included studies

The quality of all included studies was assessed independently by two authors (LC & VS; LC & LG), using the Quality in Prognosis Studies (QUIPS) tool with recourse to discussion and consensus if required. 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 [9].

Data analysis

Meta-analyses were conducted where feasible for each risk factor using Review Manager 5.3 software. Dichotomous data were summarised using odds ratio (OR) and 95% confidence intervals (CI). Continuous data were summarised using mean difference (MD) and 95% CI. Where statistical heterogeneity (I^2) was >50%, a random effects model was used. Where meta-analysis was not possible, a narrative summary of study results is provided. Publication bias was visually evaluated using a funnel plot where ten or more studies contributed data to a meta-analysis. To enable synthesis of all available evidence, all studies' data irrespective of study quality were included in meta-analyses.

Results

Study selection

The search returned a total of 3374 records. Following title and abstract screening, 158 records were forwarded for full-text screening. Of these, 118 were excluded. A review of the reference lists of retrieved papers did not identify any additional papers. One additional study [10], published in abstract format only by one of the review authors (VS) was also included and additional data provided as appropriate. This resulted in 41 records reporting on 37 studies for inclusion. The abstract and full report of one study were included because they reported additional data to each other [11]. Two papers reporting on the same study [12,13] and two abstracts of the same study [14,15] were also included. On further review of these 37 studies, ten studies reported on outcomes following RFM only and were subsequently excluded. This resulted in the inclusion of 27 studies [10–14,16–35] that reported on risk factors for RFM in pregnancy (Fig. 1).

Characteristics of included studies

Table 1 presents the summary characteristics of the 27 included studies. Nine studies were retrospective studies, eleven were prospective, and in seven studies the design was not clearly specified. Studies were conducted in Israel (7), UK (6), Ireland (3), Australia (1), Norway (2), South Africa (1), Sweden (1), India (1), Nigeria (1), United States (2), Iran (1) and Venezuela (1). Various definitions of RFM exposure were used. These included, maternal perception of RFM, self-reported RFM, <10 FM in 12 h, < 4 FM in one hour, <3 FM/half hour, RFM of at least two hours in the previous 12 h, <4 movements/hour for two consecutive hours, and any maternal concern leading to hospital examination. Five studies explicitly examined risk factors in women with RFM at ≥36 week's gestation while the remaining studies examined risk factors in women with RFM ≥ 24 weeks' gestation. Three studies reported on women presenting with RFM at a gestation >42 weeks. Twelve risk factors were identified across the 27 studies. These were, maternal age, body mass index, education level, ethnicity, parity, anterior placenta, smoking, postdates >42 weeks', abnormalities of amniotic fluid, diabetes, hypertensive disorders of pregnancy and antenatal bleeding.

Quality assessment

Table 2 provides an overview of the results of the risk of bias assessments. Only full text articles were assessed using the QUIPs tool.

Eighteen studies were rated low risk of bias for study participation (domain 1). Four studies were rated moderate risk of bias as the description of the sampling frame, recruitment and inclusion or exclusion criteria were not explicit or evident. One study [21] was rated high risk of bias as 61% of eligible participants only were evaluated, description of source population was not evident and inclusion/exclusion criteria were not clearly specified. All except three studies were rated low risk of bias for study attrition (domain 2). Three studies were rated moderate risk of bias as they did not report reasons for attrition or loss of participants to follow up. Nineteen studies were rated as low risk of bias for risk factor measurement (domain 3). Three studies were rated moderate risk of bias because the definitions/descriptions of the risk factors were unclear or because it was unclear if the risk factor measurement was valid or reliable. One study [29] was rated high risk of bias because no definition of the risk factor was reported. Seventeen studies were rated low risk of bias for domain 4 (outcome measurement). One study was rated moderate risk of bias and another high risk of bias as the definitions for outcome measurement were unclear or unreported. This domain was not applicable for the remaining four studies as these studies did not report on outcomes. Five studies were rated as high risk of bias for domain 5 (study confounding), due to no multivariate regression or no reporting of confounding within the paper. Studies were rated low risk of bias if the studies reported methods of case-controlling, matching or control groups (n = 14). Nineteen studies were rated low risk of bias for domain 6 (statistical analysis and presentation). One study was rated moderate risk of bias and three studies high risk of bias due to either no documentation of analytical strategy or insufficient presentation of data to assess the analytical strategy.

Findings

Twelve risk factors were identified. Five of these were found to be predictive of RFM in pregnancy: ethnicity, anterior placenta, smoking, oligohydramnios and polyhydramnios as shown in Table 3 and Fig. 2.

Ethnicity

Two studies reported on ethnicity as shown in Fig. 2. Both studies were rated low risk of bias. The overall results indicate that Caucasian women are more likely to present with RFM in pregnancy than non-Caucasian women (OR 2.59, 95% CI 2.40–2.80, 2 studies, 5365 participants, $I^2 = 0\%$).

Anterior placenta

Four studies examined position of the placenta as a risk factor for RFM during pregnancy. Three studies provided data for meta-analysis. Women who had an anterior placenta were more likely to present with RFM in pregnancy when compared to women who did not have an anterior positioned placenta (OR 1.31; 95% CI 1.11–1.55, 3 studies, 6852 participants, $I^2 = 0\%$) (Fig. 2).

Smoking

Only one of five included studies found a significant association between smoking and RFM, however meta-analysed results

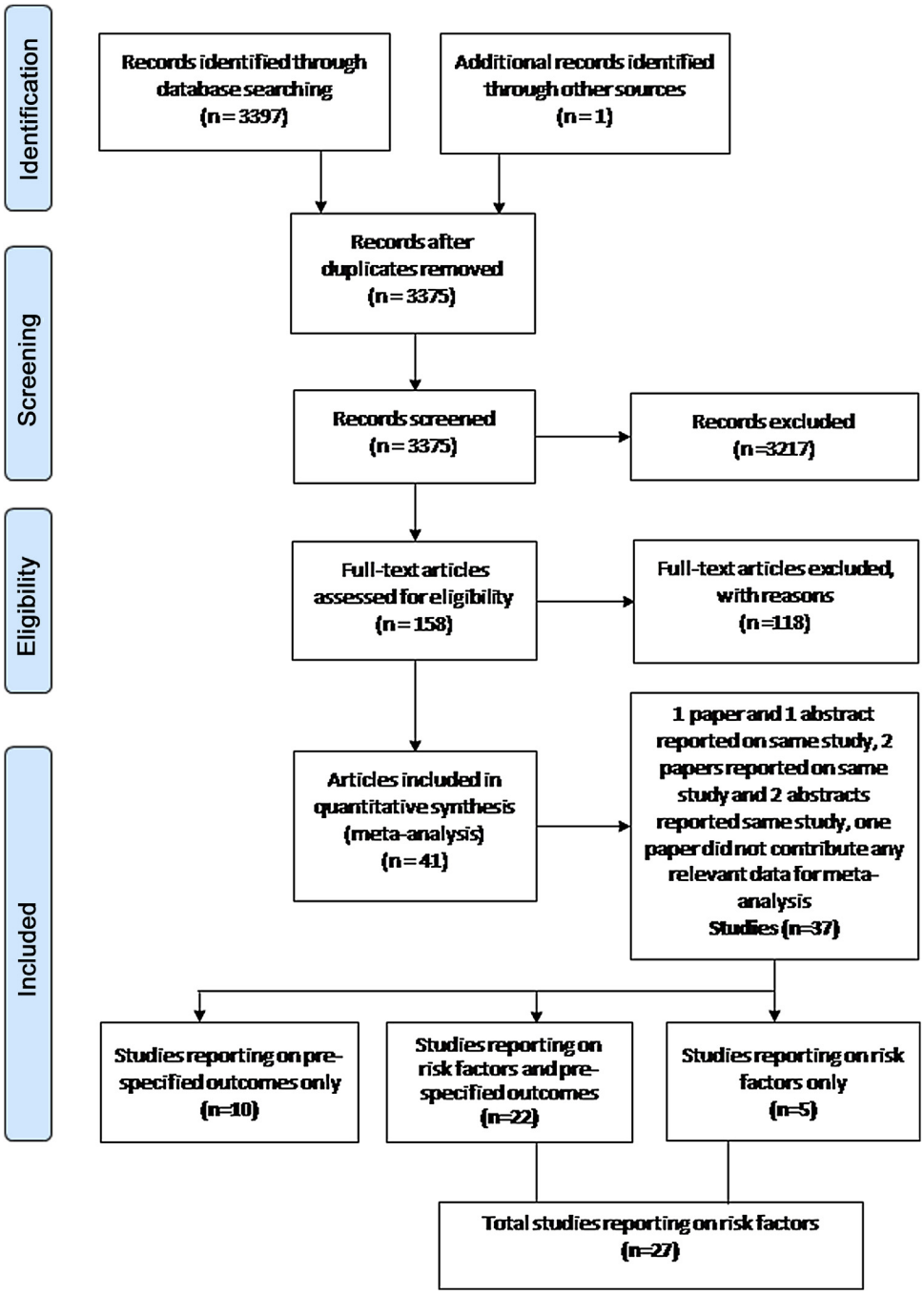

Fig. 1. Study selection flow chart.

identified smoking as a risk factor for RFM (OR 1.18, 95% CI 1.02–1.35; 5studies; 29,557 participants, $I^2 = 4\%$) (Fig. 2). All studies had low risk of bias.

Oligohydramnios

Five studies reported oligohydramnios as a risk factor for women presenting with RFM in pregnancy. Three of these studies contributed data for meta-analysis. The results showed that oligohydramnios is more associated with women with RFM in pregnancy (OR 4.04 95% CI 3.29–4.97, 3 studies; 39,407 participants, $I^2 = 0\%$) (Fig. 2). The majority of the data in this analysis, however, are from one large retrospective cohort study [16] and a second study [27] was conducted nearly 40 years ago and rated moderate risk of bias.

Polyhydramnios

Four studies reported polyhydramnios as shown in Fig. 2. Overall results indicate that women who present with RFM in pregnancy are twice as likely to have polyhydramnios when compared with women who do not have RFM (OR 2.01, 95% CI 1.44–2.81; 4 studies; 39,487 participants, $I^2 = 28\%$). Caution should be applied to these findings, however, as two of the studies included were conducted 40–50 years ago and rated moderate to high risk of bias. The majority of the data are from one large cohort

Table 1
Characteristics of Included Studies.

Lead Author & Year	Setting (Country)	Study Design	Study Period	Inclusion/Exclusion Criteria	Definition of RFM	Timing of RFM *gestation*	RFM (n)	No RFM (N)
Aviram 2016	Israel	Retrospective	2008-2013	Singleton pregnancy admitted to delivery ward with spontaneous onset of labour, or for labour 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	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
Daly 2011	Ireland	Retrospective	Calendar year (not specified)	Singleton pregnancy	Maternal perception	28-42+[2] weeks'	524	7,338
Ho 2017	Australia	Prospective Matched	Mar 2015-Nov 2015	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	Singleton pregnancy excluding stillbirths not initially identified by RFM	Self-reported perception	≥ 28 weeks'	2374	614
Leader 1981	South Africa	Prospective Case-Control	Not specified	Not explicit	A day of no FMs or 2 successive days in week before birth of FM < 10/day	26-42 weeks	23	138
Linde 2017	Sweden	Not specified	2014	All women with simplex pregnancy	Not explicit	Not explicit	2683	26041
McCarthy 2016	Ireland	Prospective	Apr 2013- Oct 2013	All women presenting with RFM excluding multiple pregnancies and congenital anomalies	Not explicit	> 28 weeks'	275	265
Mohr Sasson 2016	Israel	Retrospective	2011–2013	All women that visited the ER due to RFM Control group-women who presented for different causes	Not explicit	24-42 weeks'	399	4493
O'Sullivan 2009	UK	Retrospective	Jan 2007- Dec 2007	Women with a primary complaint of DFM & a viable fetus	Not explicit	After 24 weeks	203	3896
Olagbuji 2011	Nigeria	Case-Control Matched	Jan 2006 - Dec 2009	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	All singleton pregnancies excluding pregnancies with fetal anomalies or multiple gestations	Subjective perception	> 36 weeks	865	16926
Sadovsky 1974	Israel	Prospective	Not specified	Not specified	< 3 movements/hr	2nd half of pregnancy	15	65
Sadovsky 1981	Israel	Not specified	Nov 1976 -Apr 1980	Women admitted to High risk pregnancy unit	Total absence or less than 10 FM per 12 hours	27-41 weeks'	55	767
Sage	US	Not specified	Oct 2010 - Sept 2011	All women who presented with initial complaint was DFM.	Not specified	3rd trimester	371	7224
Sheikh 2014	Iran	Prospective	Feb 2012 - March 2013	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
Simon 1986	Israel	Not specified	Not specified	Women with mild and severe cases of rheumatic heart disease	< three FM/half hour, recording was extended to 1, 2 or more hours /day. The number of FM was calculated for 12 hours	≥ 25 weeks	5	156
Sinha 2007	UK	Retrospective Matched	Jan 2004 - Aug 2004	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
Skornick-Rapaport 2004	Israel	Not specified	Not specified	Women with primary complaint of subjectively RFM.	Not explicit	Not explicit	769	28119
Smith 2014	Ireland	Retrospective	Jan 2011-Dec 2011	All women with primary complaint of RFM	Maternal perception	≥28 weeks'	1008	16627
Tuffnell	UK	Prospective	Jan 1989- Oct 1989	All women reporting RFM	Maternal perception	Not explicit	180	1051
Valencia-Rincon 2017	Venezeula	Prospective Case-Control	Jun 2015-Apr 2017	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 12 hrs that differed from usual pattern	37-41 weeks'	93	550
Warrander 2012	UK	Not specified	Aug 2009- Oct 2010	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

Table 1 (*Continued*)

Lead Author & Year	Setting (Country)	Study Design	Study Period	Inclusion/Exclusion Criteria	Definition of RFM	Timing of RFM *gestation*	RFM (n)	No RFM (N)
Whitty 1991	USA	Not specified	Jan 1985 - Apr 1990	All low risk patients presenting with a complaint of RFM	<four movements/hr for 2 consecutive hrs	< 36 weeks	223	623
Winje 2012	Norway	Prospective	July 2009 - July 2011	All women with singleton pregnancies presenting with RFM	Any maternal concern leading to a hospital examination	last 7 days before birth	129	191
Yogev 2003	Israel	Prospective	Jan 1998 - Dec 2000	Women with consistent reduced perception of FM excluding pregnancies with contraindication to induction of labour and vaginal delivery	< five fetal movements/day for 2 consecutive days	Not explicit	115	510

Table 2
Quality Assessment of Included Studies.

Reference (Author/Year)	Study Participation	Study Attrition	Risk Factor Management	Outcome Measurement	Study Confounding	Statistical Analysis & Presentation
Aviram et al, 2016	Moderate	Low	Low	Low	Low	Low
Binder et al, 2018	Low	Low	Low	Low	Low	Low
Daly et al, 2011	Low	Low	Low	Low	High	Low
Ho et al, 2018	Low	Low	Low	Low	Low	Low
Holm Tveit et al, 2009	Low	Low	Low	Low	Low	Low
Leader et al, 1981	High	Low	Low	Moderate	Unknown	Low
Linde et al, 2017	Abstract					
McCarthy et al, 2016	Low	Low	Low	Low	Low	Moderate
Mohr Sasson et al, 2016	Low	Moderate	Low	Low	Low	Low
Naz et al, 2010	Low	Low	Low	Not applicable	Unknown	Low
Olagbuji et al, 2011	Low	Low	Low	Low	Low	Low
O'Sullivan et al, 2009	Low	Low	Low	Low	Low	Low
Pagani et al, 2014	Low	Moderate	Low	Low	Low	Low
Sadovsky et al, 1981	Low	Low	Moderate	Not applicable	High	High
Sadovsky et al, 1974	Moderate	Low	Moderate	High	High	High
Sage and Fretts, 2012	Abstract					
Sheikh et al, 2014	Low	Low	Low	Low	Low	Low
Simon et al, 1985	Moderate	Low	High	Not applicable	High	High
Sinha et al, 2007	Low	Low	Low	Low	Low	Low
Skornick-Rapport et al,	Abstract					
Smith et al, 2014	Abstract					
Tuffnell et al, 1991	Low	Low	Moderate	Not applicable	Low	Low
Valencia-Rincon et al, 2017	Moderate	Moderate	Low	Low	Moderate	Low
Warrander et al, 2012	Low	Low	Low	Low	Moderate	Low
Whitty et al, 1991	Low	Low	Low	Low	High	Low
Winje et al, 2012	Low	Low	Low	Low	Low	Low
Yogev et al, 2003	Low	Low	Low	Low	Low	Low

Table 3
Risk Factors for RFM during pregnancy.

Risk Factor	No. of Studies	No. of participants	OR (95% CI)	I^2
Ethnicity (Caucasian versus Non-Caucasian)	2	5365	2.59 (2.40-2.80)	0%
Anterior placenta	3	6852	1.31 (1.11-1.55)	0%
Smoking	5	29557	1.18 (1.02-1.35)	4%
Oligohydramnios	3	39407	4.04 (3.29-4.97)	0%
Polyhydramnios	4	39487	2.01 (1.44-2.81)	28%

study limited by its retrospective design and selection bias of participants [16].

Risk factors not predictive of RFM

We found no association between previous caesarean, post-dates pregnancy, hypertensive disorders of pregnancy, diabetes or antenatal bleeding as shown in Table 4 and Supplement 2. Few studies reported on these risk factors. Statistical heterogeneity in these analyses was high, and therefore the findings should be interpreted with some caution.

Parity

Twenty-two studies reported on parity. Amongst women with RFM, seventeen studies found no difference in RFM related to parity (nulliparous women versus multiparous women (OR 1.26 95% CI 0.88–1.81; 17 studies, 11,368 participants, $I^2 = 97\%$) (Fig. 3). Five studies provided continuous data that could not be pooled for meta-analysis. Four of these studies [16,23,25,35] also found that the rates of RFM were comparable between nulliparous and multiparous women. Only one study [22] reported that primipara more often seek care for RFM ($p < 0.001$).

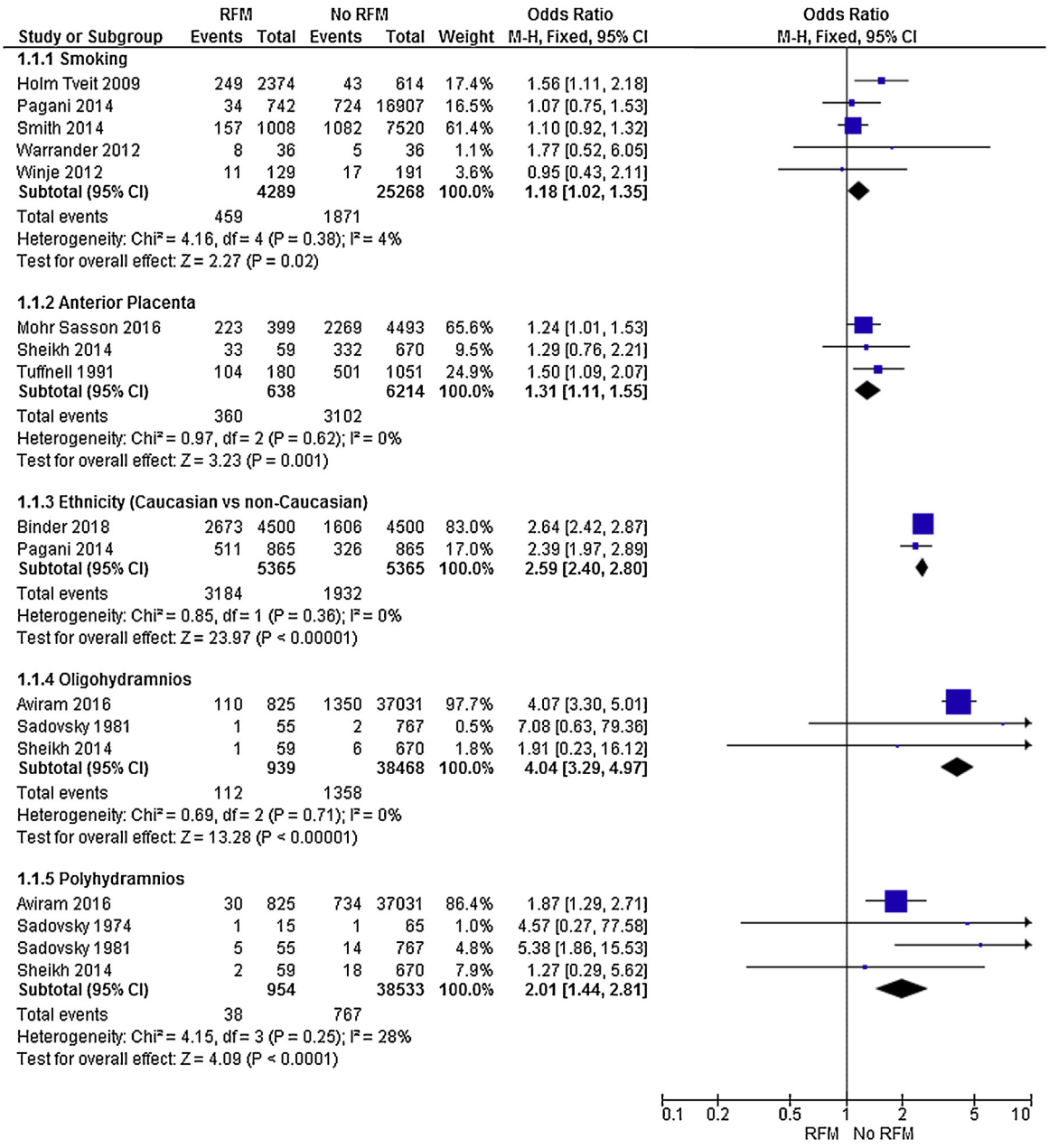

Fig. 2. Risk factors for RFM in pregnancy forest plots.

Table 4
Risk factors not predictive of RFM during pregnancy.

Risk Factor	No. of Studies	No. of Participants	OR (95% CI) MD (95% CI)	I^2
Maternal age	6	6635	0.11 (-0.62-0.83)**	51%
Maternal age >35years versus ≤35 years	5	2887	0.18 (0.01-2.15)*	99%
BMI ≥ 25 kg/m^2	2	3088	1.24 (0.62-2.46)*	54%
BMI ≥ 35 kg/m^2	3	4992	0.87 (0.44-1.72)*	86%
Parity (Primiparous versus Multiparous)	17	11368	1.26 (0.88-1.81)*	97%
Previous CS	2	30260	0.86 (0.48-1.53)*	92%
Postdates >42 weeks	3	301	1.14 (0.40-3.24)	0%
Diabetes	4	38197	1.16 (0.87-1.55)	48%
Chronic Hypertension	2	38119	1.58 (0.90-2.78)	0%
Gestational Hypertension	4	38390	0.87 (0.32-2.39)*	54%
Pre-eclampsia	2	353	1.02 (0.36-2.84)	0%
Antenatal Bleeding	2	983	0.35 (0.03-4.62)*	54%

* Random Effect Model.
** MD Mean Difference; BMI Body Mass Index; CS Caesarean Section.

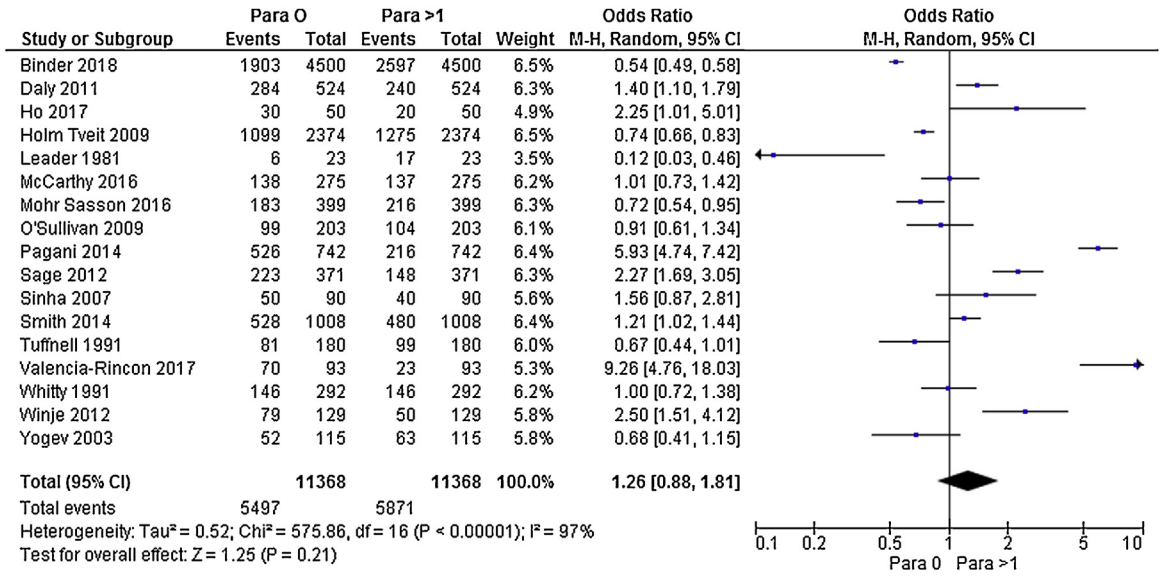

Fig. 3. Parity (primparous versus multiparous) Random Effect Model.

Maternal age

Eighteen studies reported on maternal age as a risk factor for RFM. Continuous data from six studies found no difference in the average age of women presenting with RFM and women who did not present with RFM during pregnancy (MD 0.11, 95% CI -0.62-0.83; 6 studies; 6635 participants, $I^2 = 51\%$) (Fig. 4). Five other studies [12,16,24,30,33] that could not be meta-analysed also demonstrated that age was not predictive of RFM. Five studies [11,19,20,28,36] provided data for meta-analysis based on age ≥35 years and age <35 years of age (Fig. 5). Although fewer women aged ≥35 years' present with RFM when compared to women aged <35 years, the difference was not statistically significant. Two other studies [17,22] also report that women presenting with RFM were younger ($p < 0.01$ and $p = 0.005$ respectively).

Body mass index

Eleven studies reported on BMI as a risk factor for RFM. Data from four studies reporting specific categories of BMI were pooled in a meta-analysis. Neither a BMI ≥ 25 (OR 1.24, 95% CI 0.62–2.46, 2 studies; 3088 participants, $I^2 = 54\%$) nor BMI ≥ 35 kg/ m^2 (OR 0.87 95% CI 0.44–1.72, 3 studies; 13,520 participants, $I^2 = 86\%$) were identified as risk factors for RFM. Of the other eight studies, four reported no differences in RFM and no RFM groups based on BMI [17,24,32,33], three reported higher rates of RFM in women with

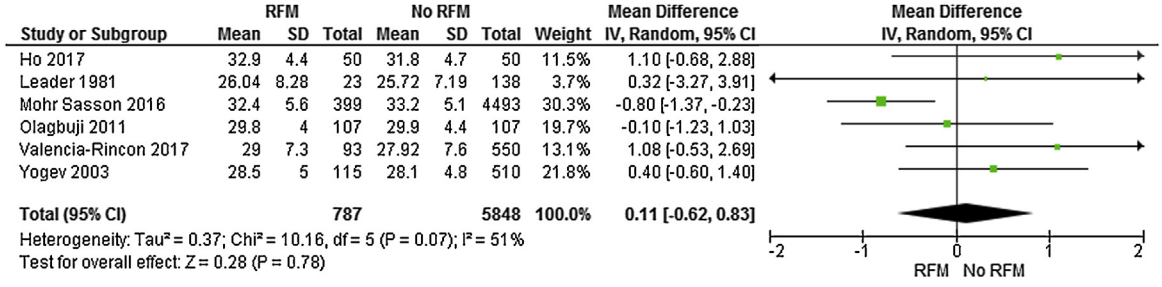

Fig. 4. Maternal age (Random Effect Model).

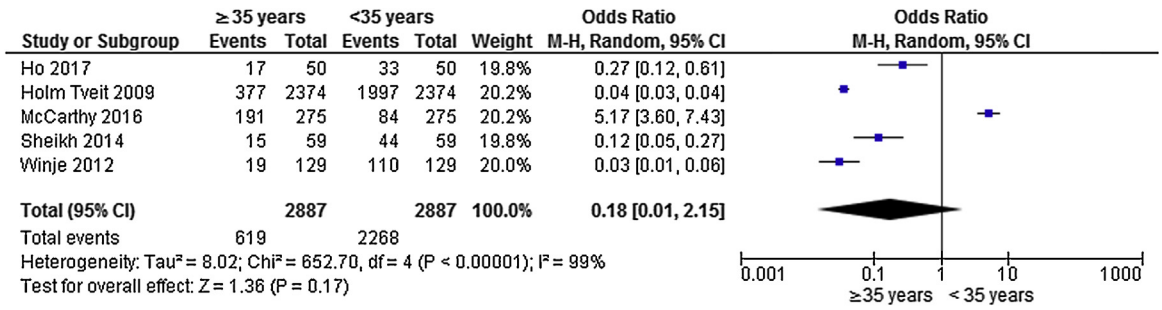

Fig. 5. Maternal age ≥35 years versus <35 years (Random Effect Model).

Table 5
Body Mass Index (BMI).

Study	RFM Group	No RFM Group	OR 95%CI	Significancep value
Binder et al (2018)	Median 24.6 (IQR 21.9-28.3), n = 4500	Median 24.5 (IQR 22.0-28.8), n = 1527		ns
Warrander et al. (2012)	Mean 24.4 (SD 18.1-45.6 kg/m^2), n = 36	Mean 24.6 (SD 17.8-41.9 kg/m^2), n = 36		ns
McCarthy et al. (2016)	BMI over 30 kg/m^2, n = 63	No data available		
O'Sullivan et al. (2009)	Mean 23.8 (range 17.4-45.7 kg/m^2), n = 203, p = 0.7		1.01 (0.95-1.07)	ns
Valencia-Rincon et al (2017)	Mean 26.1 (SD ±5.1 kg/ m^2), n = 93	Mean 27.0 (SD ±6.2 kg/ m^2), n = 550		ns
Pagani et al (2014)	BMI ≥ 35 kg/ m^2		2.10 (1.49-2.95)	p < 0.001
Linde et al (2017)	BMI (30-34.9 kg/ m^2)			P < 0.001
Holm Tveit (2009)	BMI >25 kg/ m^2		1.2 (1.3-2.0)	P < 0.001

OR Odds Ratio; IQR Interquartile Range; ns not significant; SD standard deviation.

higher BMI's [12,20,22] and one study [11] reporting on the RFM group only, stated that nearly one quarter of women with RFM (n = 275) had a BMI over 30 kg/m^2. Table 5 summaries the results for BMI.

Publication Bias

Visual inspection of a funnel plot for parity (17 studies) showed a gap in the middle and bottom left and right of the plot suggesting that smaller studies with large effects may be underrepresented (Fig. 6).

Discussion

Maternal perception of RFM is associated with adverse pregnancy and birth outcomes such as stillbirth and small for gestational age (SGA). It is important therefore to better understand maternal perception of RFM and attempt to identify pregnancies at higher risk of adverse outcomes. This review sought to identify risk factors associated with RFM in pregnancy, and, as far as we are aware, is the first systematic review and meta-analysis conducted to do so.

International guidelines on RFM recommend that women should be advised by maternity care providers about the factors that may hinder their perception of fetal movements and attend for assessment as soon as possible should they perceive RFM [37]. Awareness of the importance of fetal movements in pregnancy as a measure of fetal well-being is prevalent amongst midwives and obstetricians, however there is notable variation in their knowledge of risk factors associated with RFM. Less than 60% of practitioners in Ireland and UK identified the association between RFM and anterior placenta while nearly 60% considered maternal obesity to be a significant factor [38–40].

Our systematic review highlights that there remains inconsistency regarding the definition of RFM with many studies reporting varying RFM time and alert limits. Knowledge and understanding of fetal activity are also inconsistent. Irish and Australian midwives and obstetricians described <10 movements in 12 h as the best definition of RFM [38,40], while <10 movements in 24 h is commonly accepted by practitioners in the UK [39] despite the recommendation that maternal perception of a reduction in the strength or frequency of fetal movements be used to define RFM [37]. There is currently no evidence that a structured definition of RFM is of greater value than maternal perception of RFM. Lack of a clinically proven definition of what constitutes normal fetal activity impedes screening by maternity care professionals and subsequent management. Therefore, maternal perception of a reduction or change in fetal movements should be considered clinically important and therefore women with a concern about RFM should be advised to contact their healthcare provider immediately.

Findings regarding ethnicity should be interpreted with caution as it may be explained by the fact that both retrospective studies were conducted within the same tertiary Fetal Medicine Unit in the UK where the population is mainly Caucasian. Women of Asian and Afro-Caribbean origin are more likely to have a pregnancy complicated by SGA than present with RFM, while in contrast, Caucasian women are more likely to present with RFM than have a pregnancy complicated by SGA [13]. It is therefore possible that there may be a difference in social behaviour and/or access to maternity care amongst ethnic groups [13]. Further research on ethnicity and RFM is therefore warranted.

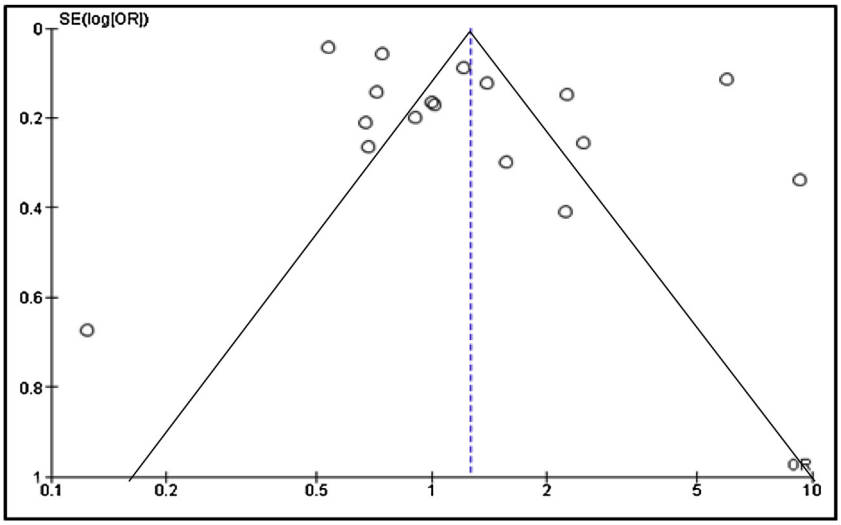

Fig. 6. Funnel plot (parity).

An anterior placenta acts as a barrier, hindering direct contact between the fetus and the uterus or abdominal wall. The clinical significance of RFM in pregnancies with anterior placental location remains to be determined. Studies have however found an association between an anterior positioned placenta and intra-uterine growth restriction [41,42] suggesting that clinicians also need to pay attention to fetal growth in their assessment of women with RFM and anterior placenta.

There is no known reason why smoking might inhibit the perception of fetal movements, indicating that it is the effects of smoking that affects the fetus. A systematic review of sixteen studies found that maternal smoking during pregnancy is associated with reduced fetal size and growth from the second trimester [43]. Smoking during pregnancy is also linked with various pregnancy complications such as miscarriage, pre-eclampsia, pre-term birth and low-birth weight, suggesting reduced oxygen-carrying capacity of maternal blood and reduced uteroplacental blood flow, as a consequence of high carboxyhaemoglobin levels from inhaled carbon monoxide [44]. Smoking is a modifiable risk factor; therefore, modification of this lifestyle factor may contribute to reduction in women presenting with RFM in pregnancy. Support for cessation of smoking should be advocated in routine antenatal care.

A significant correlation between decreased amniotic fluid volume and RFM has previously been found [45]. Placental insufficiency may result in a reduction in fetal renal perfusion leading to oligohydramnios. 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 symphysis fundal height (SFH) performed to assess growth and amniotic fluid. SFH is a common practice of fetal growth assessment that has been shown to have a positive predictive value of 60% and a negative predictive value of 76.8% for adverse outcomes in women with RFM [46] and may be helpful for clinicians in selecting women who should undergo further assessment and investigation.

Polyhydramnios is associated with increased risk of perinatal morbidity and mortality including diabetes, fetal anomalies and fetal macrosomia. If abnormalities of amniotic fluid exist upon initial clinical assessment for RFM in pregnancy, it seems appropriate that further investigations such as ultrasound should be performed to detect any possible underlying aetiology.

Advanced maternal age in pregnancy, a woman over 35 years of age, is a growing trend within high-income countries and is associated with increased risk of obesity, diabetes, infertility and stillbirth [47]. This review however did not find any association between advancing maternal age and RFM.

We found no difference between the rates of RFM in primigravidae and multigravidae. It is known that multiparous women perceive fetal movements earlier in pregnancy than nulliparous women. Many individual studies maintain that RFM is more prevalent among nulliparous women, who tend to be more focused on fetal movements, therefore will promptly seek reassurance if any change or reduction in fetal movements occurs. Multiparous women however are more familiar with the sensation of fetal movements. The similar rate of RFM among these two groups found in this review may be explained by other factors such as maternal weight, placental location and amniotic fluid volume. It was not possible to perform subgroup analysis according to parity.

While there is increased reporting of RFM amongst obese pregnant women, we were unable to find evidence that increased body mass index is associated with RFM in pregnancy. Few studies, however, reporting fetal movement perception in women who have a BMI > 35 kg/m2 were identified, and are thus warranted.

This systematic review also highlights the variation in the reporting of risk factors in studies on RFM. Very few recent studies have been conducted to review the association of medical conditions such as diabetes and hypertensive disorders of pregnancy with RFM. Further research of these potential risk factors will enhance the ability to compare, combine and contrast risk factors from other individual studies resulting in further clinical applicability and knowledge for decision making regarding RFM in pregnancy.

Evidence based and accurate information is necessary to improve management of women with RFM during pregnancy. It is important to note that current international guidelines [37] predate recent studies on RFM, and these studies are therefore not included. It is timely now that guidelines should be updated considering this current review of risk factors and other recent research on RFM. Pregnancy, birth and neonatal outcomes following RFM during pregnancy can only improve if appropriate care is given.

In conclusion, this systematic review and meta-analysis provides an evaluation of what is currently known about maternal characteristics associated with RFM during pregnancy. There is a dearth of robust observational studies comparing risk factors that may contribute to RFM in pregnancy. Studies that have examined potential risk factors are demonstrating conflicting results possibly due to divergent research designs, small sample size, incompleteness of data for control group, and selection bias of participants. Further investigation of maternal characteristics, risk factors and fetal factors associated with RFM is warranted. Assessment of predictive factors for RFM during pregnancy, through well designed observational studies could further aid clinicians to identify pregnancies at higher risk of adverse perinatal outcomes and aid decision making regarding need for further investigation and treatment when a woman presents with RFM during pregnancy.

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.

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.ejogrb.2019.09.028.

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