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

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

4 Condensation: this systematic review summarises the evidence for interventions aiming to
5 reduce the incidence of adverse outcome in pregnancies with reduced fetal movement.

6 Short title: Effect of RFM awareness and clinical management on pregnancy outcome

7 AJOG at a Glance

8 A. Why was this study conducted?

- 9 • This study aimed to determine whether interventions aiming to encourage awareness of
10 reduced fetal movement and/or improve its subsequent clinical management reduce the
11 frequency of stillbirth or other adverse pregnancy outcomes

12 B. What are the key findings?

- 13 • The evidence is uncertain about the effect of encouraging awareness of fetal movement
14 or fetal movement counting on stillbirth compared with standard care
15 • Encouraging awareness of fetal movement may reduce NICU admissions and Apgar
16 scores <7 at five minutes of age, and may increase maternal fetal attachment and
17 decrease maternal anxiety compared with standard care

18 C. What does this study add to what is already known?

- 19 • Encouraging awareness of fetal movement may be associated with reduced adverse
20 neonatal outcomes without increased interventions in labour
21 • Meta-analysis is hampered by variation in outcome reporting and individual studies are
22 frequently underpowered to detect reductions in rare outcomes; studies from high-
23 burden settings are needed

24 Keywords – stillbirth, perinatal death, kick counting, ultrasound

25

26 **Abstract**

27 Objective

28 Reduced fetal movement (RFM), defined as a decrease in maternal perception of frequency or
29 strength of fetal movements, is a common reason for presentation to maternity care.

30 Observational studies demonstrate an association between RFM, stillbirth, and fetal growth
31 restriction related to placental insufficiency. However, individual intervention studies have
32 described varying results. This systematic review and meta-analysis aimed to determine whether
33 interventions aiming to encourage awareness of reduced fetal movement and/or improve its
34 subsequent clinical management reduce the frequency of stillbirth or other important secondary
35 outcomes.

36 Data sources

37 Searches were conducted in MEDLINE, EMBASE, CINAHL, The Cochrane Library, Web of
38 Science and Google Scholar. Guidelines, trial registries, and grey literature were also searched.
39 Databases were searched from inception to the 20th January 2022.

40 Study eligibility criteria

41 Randomised controlled trials (RCTs) and controlled non-randomised studies (NRS) were eligible
42 if they assessed interventions aiming to encourage awareness of fetal movement or fetal
43 movement counting and/or improve the subsequent clinical management of RFM. Eligible
44 populations were singleton pregnancies after 24 completed weeks of gestation. The primary
45 review outcome was stillbirth; a number of secondary maternal and neonatal outcomes were
46 specified in the review.

47 Study appraisal and synthesis methods

48 Risk of bias was assessed using Cochrane Risk of Bias 2 and ROBINS-I for RCTs and NRS
49 respectively. Variation due to heterogeneity was assessed using I². Data from studies employing
50 similar interventions was combined using random effects meta-analysis.

51 Results

52 1,609 citations were identified; 190 full text papers were evaluated against the inclusion criteria,
53 18 studies (16 RCTs and 2 NRS) were included.

54 The evidence is uncertain about the effect of encouraging awareness of fetal movement on
55 stillbirth compared with standard care (two studies, n=330,084); pooled aOR 1.19 (95% CI 0.96,
56 1.47). Interventions for encouraging awareness of fetal movement may be associated with a
57 reduction in NICU admissions and Apgar scores <7 at five minutes of age and may not be
58 associated with increases in caesarean section or induction of labour.

59 The evidence is uncertain about the effect of encouraging fetal movement counting on stillbirth
60 compared with standard care; pooled OR 0.69 (95% CI 0.18, 2.65), data from three RCTs
61 (n=70,584). Counting fetal movements may increase maternal fetal attachment and decrease
62 anxiety compared with standard care.

63 When comparing combined interventions of fetal movement awareness and subsequent clinical
64 management with standard care (one study, n=393,857) the evidence is uncertain about the
65 effect on stillbirth (aOR 0.86, 95% CI 0.70, 1.05).

66 Conclusions

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

74 Introduction

75 Reduced fetal movement

76 Reduced fetal movements (RFM) are defined as a decrease or change in maternal perception of a
77 baby's normal pattern of movements *in utero*.¹ Concerns about RFM are a frequent reason for
78 presentation at hospital, occurring in up to 15% of pregnancies.² Around 70% of pregnancies where
79 RFM has been reported have a normal outcome, but maternal perception of RFM is associated
80 with adverse outcomes such as stillbirth and fetal growth restriction.^{3,4-6} An individual participant
81 data meta-analysis with data from five studies (n=3,108) reported an adjusted odds ratio (aOR)
82 of 2.33 (95% CI 1.73 to 3.14) for stillbirth in pregnancies with a decreased frequency of fetal
83 movement in the last 2 weeks.⁷ Studies have demonstrated links between RFM and placental
84 pathology, particularly those relating to maternal vascular malperfusion.⁸⁻¹⁰ Thus, the association
85 between RFM, fetal growth restriction, and stillbirth is thought to represent fetal compensation
86 for placental insufficiency (where the placenta cannot meet the metabolic demands of the fetus)
87 or other fetal stressors, in an attempt to conserve energy and oxygen consumption.^{11,12}

88 Interventions for RFM

89 Interventions for RFM can be split into two categories: 1) those that aim to encourage awareness
90 of fetal movement and/or fetal movement counting by clinicians, other healthcare professionals,
91 or in people who are pregnant, and 2) those that employ subsequent clinical management when
92 there is concern about RFM in order to identify fetal compromise.¹³⁻¹⁵ Studies may employ one
93 or the other approach, or a combination. A diagram demonstrating how interventions might
94 work in clinical practice is shown in Supplementary file S1.

95 Several large randomised trials have shown insufficient evidence of an effect of interventions on
96 stillbirth in high income settings.^{13,16} Two systematic reviews from 2015 and 2016 reported no
97 clear evidence of harms or benefits for formal fetal movement counting or encouraging maternal
98 awareness of RFM respectively.^{17,18} A 2020 systematic review and meta-analysis of five
99 randomised trials of fetal movement counting reported a relative risk (RR) of 0.92 (95% CI 0.85
100 to 1.00) for perinatal death and 0.94 (95% CI 0.71 to 1.25) for stillbirth.¹⁹

101 Current guidance and management strategies for RFM

102 Current guidance is to contact a health professional or maternity unit if a baby is moving less
103 than usual or not at all.²⁰⁻²² Guidance with respect to formal fetal movement counting and
104 clinical management is variable, as is the quality of clinical practice guidelines, leading to variation
105 in care.^{23,24} Uncertainties persist despite recent publication of RCTs measuring the effects of
106 interventions for RFM.^{14,25} Conducting a systematic review including both randomised and non-
107 randomised studies will provide an updated view of available evidence and also maximise the
108 pool of evidence that has so far been synthesised.

109 Objectives

110 The primary objective was to determine whether encouraging awareness of fetal movement
111 and/or the subsequent clinical management of pregnancies with RFM affects adverse maternal
112 or perinatal outcomes, when compared to other management strategies or no management.

113 Secondary objectives were:

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

117 Methods

118 The protocol was registered with the International Prospective Register of Systematic Reviews
119 (PROSPERO) on 16/10/2020 (CRD 42018088635).²⁶ Reporting followed the PRISMA
120 Statement.²⁷

121 Eligibility criteria, information sources, search strategy

122 Studies of interventions that aimed to encourage clinician or maternal awareness of the pattern,
123 strength, and/or frequency of RFM in pregnancy and/or interventions for the subsequent
124 clinical management of RFM were included, delivered alone or in combination.

125 Studies were included if they reported data from singleton pregnancies after 24 completed weeks'
126 gestation presenting at least once in a hospital setting. Included definitions of RFM were those
127 based on maternal perception and/or confirmed by clinical assessment of fetal activity. The

128 gestational age threshold was set at 24 completed weeks as this is consistent with the current
129 definition of stillbirth in the UK.²⁸

130 Study types considered for inclusion were RCTs, quasi-RCTs and some NRS. To be eligible,
131 NRS needed to have a clearly reported mechanism of group formation, clearly defined inclusion
132 criteria, and clearly described methods of ascertainment of eligible patients and their recruitment.
133 Cross-sectional studies, case control studies, and cohort studies without clearly defined
134 comparator groups were not included as their internal validity was considered too poor for any
135 exploration of intervention effectiveness.

136 Searches were performed in MEDLINE, EMBASE, CINAHL, The Cochrane Library, Web of
137 Science and Google Scholar (described in Supplementary file S2). Guidelines, trial registries, and
138 grey literature were also searched. Studies were included irrespective of publication status and
139 language of publication; the last search was on the 20th January 2022.

140 **Outcomes of interest**

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

152 **Study selection and data extraction**

153 Titles and abstracts of studies retrieved using our search strategy were screened by two authors
154 independently (DH and AH), disagreements were resolved by consulting a third author (JD or
155 TW). Full texts of included studies were obtained where possible and a standardised, pre-piloted

156 form was used to extract data. Data were extracted by two authors independently (combinations
157 of DH, MW, LH and AH) and discrepancies were amended through discussion.

158 Where possible, study protocols were obtained for more information on study design and to
159 determine whether data for all pre-specified outcomes were reported. Attempts were made to
160 contact study authors if no protocol was available, if any characteristics of the intervention were
161 unclear, or to enquire about unpublished data. TIDieR checklists²⁹ were used to extract
162 information from each study about the nature of the intervention.

163 **Assessment of risk of bias**

164 Risk of bias was assessed for randomised controlled trials using the Cochrane Risk of Bias 2
165 (RoB 2) tool,³⁰ for non-randomised studies the ROBINS-I tool was used.³¹ Two authors
166 independently assessed risk of bias and consultations took place in the case of any
167 disagreements.

168 **Assessment of heterogeneity and sensitivity analyses**

169 Clinical and methodological heterogeneity was assessed using extracted information from
170 studies. Heterogeneity was also quantitatively assessed using the Chi-squared statistic, χ^2 , as well
171 as the I-squared measure.³² Variation due to heterogeneity was classified as low ($I^2=0-40\%$),
172 moderate ($I^2=41-60\%$), substantial ($I^2=61-80\%$), or considerable ($I^2=81-100\%$).³³ Sensitivity
173 analyses were planned to determine whether effect sizes were influenced by risk of bias or study
174 inclusion criteria, described in the review protocol.

175 **Data synthesis**

176 Interventions were broadly classified using the categories in the review protocol²⁶ and these
177 categories were used to group studies for analyses (Supplementary file S3).

178 Adjusted effect estimates were presented from included studies where possible. When adjusted
179 values were unavailable, odds ratios (ORs) and their corresponding 95% confidence intervals
180 (95% CI) were calculated for binary outcomes. Where adjusted and unadjusted estimates were
181 provided for the same outcome and intervention groups, these were displayed as subgroups on
182 the forest plot.³⁴

183 Data were only combined after careful assessment of clinical and methodological features of
184 studies to ensure that pooled estimates would be meaningful. Binary data were combined using
185 the random effects method (DerSimonian and Laird inverse variance³⁵). For continuous
186 outcomes, the standardised mean difference (SMD) was calculated along with corresponding
187 95% CIs. Effect estimates for RCTs and NRS were calculated separately.

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

192 **Assessment of certainty of evidence**

193 GRADE^{36,37} was used to determine the certainty of the body of evidence by assessing study
194 design, inconsistency of results, indirectness of evidence, imprecision, and publication bias. This
195 assessment reflects the extent of confidence that the estimate is certain for any given finding, and
196 was carried out for all comparisons for the outcomes of stillbirth, perinatal death, and neonatal
197 death. Evidence from RCTs starts out as high certainty, evidence from NRS starts out as low
198 certainty,³⁸ this was then upgraded or downgraded after assessing the characteristics of included
199 studies.³⁹

200 **Results**

201 **Study selection and characteristics of included studies**

202 The literature search identified 1,609 citations. These were screened based on their titles and
203 abstracts, resulting in 18 included studies (Figure 1). These studies are described in Table 1.
204 Additional data, study protocols, and/or further detail about the study were obtained from five
205 authors.^{14,40–43}

206 In total, 16 RCTs and two NRS were included. Of the RCTs, 12 focused on interventions aiming
207 to encourage fetal movement counting and/or awareness of the frequency, strength, or pattern
208 of fetal movement healthcare professionals and/or people who are pregnant, three focused on
209 the subsequent clinical management of RFM after identification, and one employed a
210 combination of these. Of the NRS, one compared an intervention to encourage maternal

211 awareness of RFM with standard care and the other compared two interventions for the
212 subsequent clinical management of RFM. One ongoing trial was identified.⁴⁴

213 Risk of bias of included studies

214 Nine of the 16 included RCTs were rated as at low risk of bias; the other seven RCTs were rated
215 as at high risk (Table 2). Concerns were mainly due to deviations from the intended
216 intervention,^{13,16,43,45,46} low intervention fidelity, or adequacy of the randomisation process.^{13,47–50}
217 Of the two NRS, one study was rated as at moderate risk of bias⁵¹ and the other at critical risk⁵²
218 (Table 3). All NRS were judged to be of at least moderate risk of bias for confounding.

219 Synthesis of results

220 INTERVENTIONS FOR ENCOURAGING AWARENESS OF FETAL MOVEMENT

221 [GROUP ONE]

222 Encouraging awareness of fetal movement compared with standard care (two RCTs; 330,084 223 participants)

224 Data were available from two RCTs. Akselsson et al. (n=39,865) compared the Mindfetalness
225 intervention, aimed at encouraging maternal awareness of the pattern of fetal movements, with
226 standard care.¹⁴ Flenady et al (n=290,219) compared an intervention to encourage awareness of
227 fetal movement (using a mobile phone app for pregnant women and an educational programme
228 for clinicians) with standard care.⁴³

229 *Primary outcome*

230 *Stillbirth*

231 The evidence is uncertain about the effect of encouraging awareness of fetal movement on
232 stillbirth when compared with standard care; pooling aORs from both studies gave an aOR of
233 1.19 (95% CI 0.96 to 1.47; I² 0.0, p=0.929). Evidence is of very low certainty, downgraded once
234 for imprecision as the confidence interval fails to exclude important benefits and harms as well
235 as no effect, once due to risk of bias (one study contributing most of the weight of the analysis
236 was rated as being at high risk of bias⁴³), and once for indirectness as evidence is from high
237 income countries only (Figure 2).

238 *Secondary outcomes*239 *Neonatal death*

240 The evidence is uncertain about the effect of encouraging awareness of fetal movement on
241 neonatal death when compared with standard care; pooling aORs from both studies gave an
242 aOR of 0.80 (95% CI 0.54 to 1.20; I^2 0.0, $p=0.780$). Evidence is of very low certainty,
243 downgraded once for imprecision as the confidence interval includes both benefit of the
244 intervention and standard care, once for risk of bias as above, and once for indirectness as above
245 (Figure 3).

246 *Perinatal death*

247 There is insufficient current evidence of a difference in the effectiveness of encouraging
248 awareness of fetal movement when compared with standard care; pooling ORs calculated using
249 the raw data from both studies gave an OR of 0.88 (95% CI 0.77 to 0.99). Flenady et al. also
250 reported an aOR of 1.07 (95% CI 0.86 to 1.31) for perinatal death (Figure 4).

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

254 *Other secondary outcomes*

255 Interventions for encouraging awareness of fetal movement may be associated with a reduction
256 in NICU admissions; there may also be reductions in Apgar scores <7 at five minutes of age,
257 caesarean section, and induction of labour (Figure 5).

258 Encouraging maternal awareness of RFM compared with standard care (one NRS; 140
259 participants)

260 Data for this comparison were available from one study and stillbirth data were not reported,⁵³
261 the results of this study can be seen in Supplementary file S4.

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

264 Eight RCTs compared encouraging fetal movement counting with standard care (as defined by
265 each study); four were rated as being at low risk of bias,⁵⁴⁻⁵⁷ the other four as high risk.^{13,47,58,59}

266 Further details of these studies can be seen in Table 1. None of these studies presented adjusted
267 effect estimates.

268 *Stillbirth*

269 The evidence is uncertain about the effect of encouraging fetal movement counting on the
270 proportion of stillbirths when compared with standard care, pooling unadjusted data from three
271 RCTs (n =70,584)^{13,54,59} gave an OR of 0.69, 95% CI (0.18 to 2.65) (I² 53.1%) (Figure 6).

272 Evidence is of very low certainty, downgraded three times: once due to imprecision (the 95% CI
273 fails to exclude important benefit or harm), once due to the inconsistency of the evidence due to
274 clinical heterogeneity (study populations and definitions of standard care across these
275 populations are likely to differ), and once as two studies (contributing to over 70% of the weight
276 of the analysis) were at high risk of bias.

277 *Secondary outcomes*

278 Three randomised studies (n=406) presented data for maternal-fetal attachment; two studies^{47,57}
279 used the Cranley maternal-fetal attachment (MFA) scale, the third⁵⁵ used the Condon maternal
280 antenatal attachment scale (MAAS). Maternal-fetal attachment scores may be higher, indicating
281 greater attachment, in fetal movement counting groups compared with standard care; meta-
282 analysis gave a pooled SMD of 1.22 (95% CI 1.01 to 1.43; I² 48.0%, p=0.146) (Figure 7).

283 Three randomised studies (n=281) presented data on maternal anxiety measured using the
284 Spielberger state trait anxiety index (STAI), trait scores^{58,60} or the Cambridge worry scale.⁶¹
285 Another RCT could not be included in this analysis as it presented only p values and no data.⁴⁸
286 Pooling data from three studies suggested that maternal anxiety scores, and therefore anxiety
287 itself, during pregnancy may be lower in those offered fetal movement counting; pooled SMD of
288 -0.16 (95% CI -0.24 to -0.08; I² 66.2%, p=0.052) (Figure 7)

289 Data for other secondary outcomes are shown in Supplementary file S4. It was only possible to
290 calculate effect sizes from one study;⁶¹ there is insufficient evidence of any effects on other
291 secondary outcomes as confidence intervals are wide and overlap zero.

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

293 One RCT in a low risk obstetric population compared fetal movement counting from 29 weeks'
294 gestation to blood tests for oestriol and human placental lactogen (hPL) starting at 33 weeks.⁵⁰

295 *Stillbirth*

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

302 *Secondary outcomes*

303 Data for secondary outcomes can be seen in the supplementary file; there is no current evidence
304 of any effects as confidence intervals are wide and include both benefits and harms.

305 Other fetal movement counting comparisons (one study; 1,400 participants)

306 One RCT compared two fetal movement counting methods;⁴⁶ this study reported no relevant
307 outcome data (Supplementary file S4).

308 INTERVENTIONS FOR THE SUBSEQUENT CLINICAL MANAGEMENT OF RFM
309 [GROUP TWO]

310 Universal ultrasound screening for RFM compared with ultrasound when indicated (one NRS;
311 579 participants)

312 One NRS compared universal CTG and ultrasound screening with universal CTG and targeted
313 ultrasound (for biophysical profile) only if indicated.⁵² This was a retrospective observational
314 study with 579 participants, who all self-reported RFM after 26 weeks of gestation.

315 *Stillbirth*

316 The evidence is uncertain about the effect of universal ultrasound screening on the proportion of
317 stillbirths in RFM pregnancies compared with targeted ultrasound; OR 0.53 (95% CI 0.05 to

318 5.86). Evidence is of very low certainty, downgraded once due to serious and critical risk of bias
319 in this study and once due to imprecision (95% CIs fail to exclude important benefits or harms).
320 No further outcomes relevant to the review were reported.

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

323 One RCT compared intensive management (ultrasound scan, serum hPL, expedited birth if
324 indicated by these tests) with standard care for presentations with RFM after 36 weeks' gestation
325 (n=120).⁶² A second RCT (n=216) compared standard care and a biomarker blood test (sFlt-
326 1/PIGF), where the result of the blood test indicated whether expedited birth was offered, with
327 standard care alone in presentations with RFM after 36 weeks' gestation.⁶³ No data for our
328 primary outcome of stillbirth were reported; we did not pool data for secondary analyses due to
329 differences in the interventions. Effect sizes for secondary outcomes can be seen in
330 Supplementary file S4.

331 COMBINED INTERVENTIONS FOR ENCOURAGING AWARENESS OF FETAL
332 MOVEMENT AND ITS SUBSEQUENT CLINICAL MANAGEMENT [GROUP THREE]

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

335 Norman et al. conducted a stepped wedge RCT in 33 hospitals comparing education of pregnant
336 women and clinicians, along with a clinical management plan including CTG and ultrasound for
337 all presentations with RFM, with standard care.¹⁶

338 *Stillbirth*

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

344 *Perinatal death*

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

349 *Secondary outcomes*

350 In the intervention group, this study reported statistically significant increases in the number of
351 Apgar scores <7 at five minutes, caesarean section, emergency caesarean section, and NICU
352 admission and statistically significant reductions in induction of labour and the proportion of
353 SGA babies (Supplementary file S4). However, conclusions that can be drawn from these results
354 are limited by the high risk of bias. Data were used from a corrected version of the online
355 supplementary appendix.⁶⁴

356 **Other planned analyses and changes from protocol**

357 We planned on presenting data as RRs, however, due to the data that were available (adjusted
358 estimates were available as ORs only) we presented all data as ORs to minimise confusion. The
359 majority of studies did not present adjusted effect estimates, although these were used where
360 available. Planned sensitivity analyses were not possible due to the number of studies at overall
361 low risk of bias and low number of included studies in each comparison. Comparisons between
362 RCTs and NRS were not possible. Other intervention comparison groups, such as hormone
363 analyses, were added after extracting data from all studies.

364 **Comment**

365 **Main findings**

366 Current evidence is insufficient for understanding the effects of interventions for encouraging
367 awareness of fetal movement or fetal movement counting on stillbirth, neonatal death or
368 perinatal death, when compared with standard care. This may be in part due to the relative rarity
369 of these severe outcomes in high-resource settings and the size of the trials that have evaluated
370 them rather than the interventions themselves.

371 Meta-analysis indicates that interventions for encouraging awareness of fetal movement may
372 lower NICU admissions. NICU admission is a more common outcome than perinatal death, so

373 it may be that the sample size is more likely to detect an effect on this outcome. From a clinical
374 standpoint, lower NICU admissions, lower frequency of Apgar scores <7 at 5 minutes, and no
375 increases in other outcomes such as caesarean section or induction of labour indicates that the
376 effects of these interventions are all acting in the same direction along the proposed clinical
377 pathway. Thus, acting on presentations with RFM is able to reduce the number of babies that
378 end up in NICU (i.e. those that are unwell but not at immediate risk of death) but is not always
379 able to save those babies that are at immediate risk of death as in some cases RFM may be too
380 late an indicator

381 Our analyses also show that interventions for encouraging fetal movement counting may result
382 in higher maternal-fetal attachment and lower maternal anxiety when compared with standard
383 care, although the risk of bias of the included studies must be considered, as well as whether the
384 degrees of difference seen in the standardised measures are clinically significant.

385 Importantly, there have been few studies of the subsequent clinical management of RFM, and no
386 conclusions can be drawn as to whether ultrasound screening or blood tests of placental markers
387 are likely to be of benefit. The link between reduced fetal movements, placental insufficiency,
388 and stillbirth is well established; the challenge is whether this link can be modified and
389 demonstrated by trials.

390 **Strengths and limitations**

391 This is the most comprehensive systematic review and meta-analysis of interventions for RFM,
392 including both RCTs and the most appropriate NRS while still employing strict inclusion criteria,
393 and conducted in accordance with a published protocol. This review builds on earlier work by
394 widening the inclusion criteria for both study design and the types of intervention that were
395 included, as well as by extracting data for a larger range of outcomes.^{17,65} Validity has been
396 maintained by only including robust study designs, only comparing interventions that we judged
397 to be similar using the TIDieR checklist, and applying GRADE to our findings. We were also
398 able to obtain unpublished data from study authors to conduct analyses that would otherwise not
399 have been possible.

400 Importantly, many included studies were not adequately powered to measure the effects of
401 interventions on stillbirth. We were only able to pool data from five studies (n=400,668)
402 containing 962 stillbirths, leading to potential fragility of the meta-analyses. Several uncontrolled

403 before and after studies have been conducted to measure the effect of guideline implementation
404 for RFM on adverse outcomes.^{15,41,66} However, this study design means that it is not possible to
405 attribute any differences in outcome to the intervention. Our analyses were also limited by
406 drawing evidence from high income countries only; consequently, all analyses were downgraded.

407 **Implications for future research**

408 Interventions

409 Interventions for RFM should be multifaceted; encouraging awareness of RFM can only prevent
410 adverse outcomes if combined with effective clinical management. Likewise, clinical
411 management can only prevent fetal death in the event of timely presentation with RFM. Studies
412 should consider the prognostic accuracy of clinical tests such as ultrasound - the accuracy of
413 which has been shown to be lacking for predicting stillbirth.⁶⁷

414 In addition to this, the expected adherence to and acceptability of interventions needs to be
415 considered, as well as whether they will reach the people who need them the most; for example
416 those at higher risk of adverse outcome due to socioeconomic factors, who are often less able
417 and/or more reluctant to go to hospital if they suspect something is wrong.⁶⁸

418 Sample size

419 A 2015 confidential enquiry showed that there was suboptimal management of RFM in 25% of
420 antepartum stillbirths.⁶⁹ An intervention that is 50% effective would reduce antepartum stillbirth
421 in these pregnancies by 12.5%. Using these numbers and a stillbirth rate of 4 in 1,000, a trial
422 would require over 230,000 participants in each arm.

423 NRS may be an easier way to achieve necessary sample sizes and retrospective designs may also
424 give more accurate reflections of standard care. Trials across multiple centres would allow for
425 larger sample sizes and detection of potential variation in effectiveness by country and income
426 setting. Crucially, this would also allow the effects of interventions in low-resource settings,
427 where incidences of severe outcomes are normally higher (and the link between RFM and
428 stillbirth may be stronger⁷⁰), to be examined. Current evidence suggests that interventions are
429 unlikely to cause harm, although this is yet to be tested in lower resource settings. Interventions
430 for awareness and kick counting are easiest to implement and come with fewer associated costs.

431 Stillbirth rates

432 Study stillbirth rates varied, due to the study settings and years in which they took place
433 (Supplementary file S5). Notably, in several large trials, stillbirth rates in both the control and
434 intervention groups were lower than the population stillbirth rates during the study period;^{13,14}
435 this may be due to trial effects,⁷¹ variation in the quality of guidelines in individual maternity
436 units,²⁴ or under-representation of minority ethnic groups.⁷² Changes in population stillbirth rates
437 over the course of the trial, as seen in some of our included studies,^{16,43} also need to be
438 accounted for as this could mean that any decreases in stillbirth rate associated with the
439 interventions themselves are difficult to detect.

440 Outcome measurement

441 There was wide variation in measured outcomes of included studies, which impedes meta-
442 analysis. A core outcome set to be used in studies of encouraging awareness and/or evaluating
443 the clinical management of RFM is currently being developed to ensure that future studies
444 measure the most important outcomes, and to reduce the need for review authors to obtain
445 unpublished data.⁷³

446 **Conclusions**

447 Using evidence from both RCT and NRS it is uncertain whether interventions to encourage
448 maternal awareness of fetal movement over and above standard care affect the rate of stillbirth
449 or perinatal death. Included studies varied in population stillbirth rates and adherence to the
450 interventions, which may affect whether the true effect of the intervention is measurable. Further
451 research is necessary as people who are pregnant are likely to present with concerns about their
452 babies' movements which need to be investigated and responded to appropriately. Thus, high
453 quality controlled studies including those from low-resource settings are needed to provide
454 evidence of, or refute, the effectiveness of common and novel clinical management strategies for
455 presentations for RFM.

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640

641 **Supporting information**

642 S1 – Logic model for the effects of RFM interventions

643 S2 – Search strategies

644 S3 – Classification of interventions

645 S4 – Additional data from studies where pooled analyses were not possible

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646 S5 – Stillbirth rates in included studies