Article:
Heazell, AEP, Stacey, T orcid.org/0000-0003-2002-6200, O'Brien, LM et al. (2 more authors) (2018) Excessive Fetal Movements are a Sign of Fetal Compromise Which Merits Further Examination. Medical Hypotheses, 111. pp. 19-23. ISSN 0306-9877

https://doi.org/10.1016/j.mehy.2017.12.024

Excessive Fetal Movements are a Sign of Fetal Compromise Which Merits Further Examination

Alexander E P Heazell,[1,2] Tomasina Stacey,[3] Louise M. O'Brien.[4] Edwin A Mitchell,[5] Jane Warland.[6]

1. Maternal and Fetal Health Research Centre, School of Biological Sciences, Faculty of Biology, Medicine and Health, University of Manchester.

2. St. Mary's Hospital, Central Manchester University Hospitals NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, M13 9WL.

3. School of Healthcare, University of Leeds, University of Leeds Leeds: UK LS2 9JT

4. Sleep Disorders Center and Department of Obstetrics & Gynecology, University of Michigan, Ann Arbor, MI, USA

5. Department of Paediatrics: Child and Youth Health, University of Auckland, Auckland 1142, New Zealand.

6. Mothers, Babies and Families Research Group, School of Nursing and Midwifery, University of South Australia. 5001

Corresponding Author - Dr Alexander Heazell, Senior Clinical Lecturer in Obstetrics, Maternal and Fetal Health Research Centre, 5th floor (Research), University of Manchester, St Mary's Hospital, Oxford Road, Manchester, UK.

Telephone – +44 161 701 0889

Fax - +44 161 276 6134

Email – alexander.heazell@manchester.ac.uk

Word Count – 2,453 words

Abstract

Changes in fetal movement are associated with increased risk of stillbirth after 28 weeks of pregnancy. The majority of studies have focussed on maternal perception of reduced fetal movements, which is associated with stillbirth via placental dysfunction. Recent studies have also described an association between a single episode of excessive fetal movements and late stillbirth. We present a hypothesis that a sudden episode of excessive fetal activity indicates fetal compromise relating to underlying disturbance of the in utero environment, which if it persists can lead to fetal death. The origin of the excessive fetal movements is unknown; they may represent fetal seizures induced by asphyxia or infection, an attempt to release cord entanglement or a change in fetal behaviour (inducing signs of distress) in response to a noxious stimulus. It is also possible that an increase in maternal anxiety may lead to increased perception of fetal activity.

Current evidence regarding excessive fetal movements is sparse; there is no clinical guidance regarding how reporting of this symptom might relate to a fetus at risk and which management might reduce the risk of subsequent stillbirth. This could be addressed by prospective observational studies of mothers presenting with excessive fetal movements which could both explore the underlying pathophysiology and determine which investigations could identify fetal compromise in this population. The presence of fetal seizures or umbilical cord entanglement could be evaluated at the time of presentation by cardiotocography and ultrasonography of the fetus and cord. Exposure to infection or noxious stimuli could be evaluated by maternal history and measurement of maternal blood for inflammatory markers or toxins. Maternal anxiety could be assessed by validated anxiety scores. Fetal outcome following excessive fetal movements can be recorded after birth. In addition, the presence of perinatal asphyxia can be assessed using Apgar scores, assessment of fetal acidaemia or measurement of stress-related factors in umbilical cord blood. The placenta and cord can be systematically examined for signs of hypoxia, infection or umbilical cord compression. Such studies would provide evidence regarding the underlying cause of excessive fetal movement and

how this symptom might relate to in utero compromise and stillbirth. Ultimately, this approach will determine whether excessive fetal movements can be used alongside reduced fetal movements as a tool to reduce the perinatal mortality rate.

Introduction

Worldwide there are 2.6 million stillbirths each year [1]. The majority of stillbirths occur largely in low and middle-income countries (LMICs); in these settings stillbirths are frequently related to access to adequate care in pregnancy and labour [1]. In high-income countries (HICs) and settings where these issues have been addressed, other risk factors for stillbirth are being investigated to identify women at increased risk of stillbirth. Established risk factors include nulliparity, advanced maternal age, women from minority ethnic groups, hypertension, maternal obesity, and cigarette smoking [2]. Unfortunately, few of these risk factors are amenable to modification in pregnancy. This has led to exploration of modifiable risk factors that include maternal signs and symptoms. The mostly commonly studied maternal symptom to date is maternal perception of reduced fetal movements (RFM) [3]. RFM is hypothesised to be associated with adverse pregnancy outcome through placental dysfunction [4]. In combination with findings from confidential enquiries into antepartum stillbirths [5, 6], this observed association has led to the development of guidelines to improve information for women and standardise care following maternal perception of RFM [7].

In recent years a series of studies have been conducted to identify additional modifiable factors associated with stillbirth that can subsequently be used to direct intervention to reduce the incidence of stillbirth. These studies have largely been retrospective case-control studies exploring factors including: maternal sleep position, mother's experience of fetal movements, diet, exercise, and maternal intuition [8-10]. Other approaches have included cohort studies exploring the experience of mothers whose pregnancies have ended in stillbirth [11]. With regard to maternal perception of fetal movements these studies have confirmed the association between stillbirth and RFM (findings are summarised in Table 1). However, in addition to RFM, emerging data now suggest that excessive fetal movements are a risk factor for stillbirth.

The STARS cohort study of 1,714 women from more than 7 countries described excessive movement in 8.5% of respondents [11]. This increase was described as much more active or aggressive e.g. "the

day before he died he was especially busy and moving like crazy." The frequency of symptoms was consistent amongst respondents from the four main countries participating in the survey. The frequency of perception of excessive fetal movements was also similar to the 10% of respondents analysed in a questionnaire study of women who experienced a stillbirth in Sweden [12]. These movements were described as "very lively", "death-jerk", "intense" and "cramped". This period of excessive fetal movement was then followed by no movement or only limited movement. Interestingly, this symptom was more frequently reported after 37 weeks gestation (12% of respondents) compared to 28-36 weeks gestation (7%), suggesting that the excessive fetal movement is associated more frequently with late stillbirth [12].

Case-control studies have been employed to determine whether the frequency of such symptoms differs between pregnancies ending in stillbirth and those resulting in live births. The Auckland Stillbirth Study found that a single episode of 'more vigorous movement than normal' was 6-fold more common in women who had a stillbirth (being reported by 20.8% of mothers who had a stillbirth, Odds Ratio (OR) 6.81, 95% Confidence Interval (95% CI) 3.01-15.41) [13]. In contrast, women who had a stillbirth were less likely to perceive more than one episode of vigorous fetal activity (OR 0.58, 95% CI 0.33-1.03). Furthermore, a general perception of increased fetal movements was less frequently reported by women who had a stillbirth compared to controls (OR 0.24, 95% CI 0.12-0.50) [13]. In the STARS case-control study women who experienced a stillbirth were more likely to perceive one episode of vigorous activity described using words such as "crazy or frantic" (OR 4.59, 95% CI 2.38-8.89) and the controls more likely to report gradual increase or multiple episodes of increased activity described as "strong or powerful" [14].

These more recent observations reflect those in older studies between 1977-1983 when women were asked to keep a daily record of any perceived strong fetal movements [15]. Signs of fetal hyperactivity were diagnosed in 5% of women. Nine cases (19%) involved umbilical cord complications, but none of the infants were growth restricted or had evidence of compromise at

delivery (e.g. need for neonatal resuscitation), or had any signs of seizure disorders in the neonatal period. Consequently these authors concluded that excessive fetal movements was not a worrying sign [15]. Conversely, a study by Sadovsky et al. described that any "sudden, strong, vigorous movements with increased rate followed by cessation was almost invariably a sign of acute fetal distress and fetal death", the authors speculate that this may be the attempt of the fetus to release a complication if, for example, a cord entanglement was released then normal fetal movements would resume and if not, the episode ended in fetal death [16]. The discrepancy between these two authors' views demonstrates that further work is needed to determine the origins and implications of a sudden episode of excessive fetal movements.

The Hypothesis

A sudden episode of excessive fetal activity indicates fetal compromise relating to underlying disturbance of the environment in utero, which if it persists can lead to fetal death.

Evaluation of the hypothesis

One possible explanation for excessive fetal activity is that it represents fetal seizures. Evidence of intrauterine seizures is limited to case reports describing fetal seizures visualised by real-time ultrasound and cardiotocography in labour [17, 18]. In one case, there was evidence of intrauterine and neonatal seizures but no evidence of perinatal asphyxia (the most frequency cause of neonatal seizures) [19]. A more recent case report describes an otherwise uncomplicated pregnancy until the night before birth when the mother described unusual fetal movements which she interpreted as seizures. The following morning an ultrasound scan showed jerky, dysrhythmic fetal movements with no evidence of spontaneous activity. Consequently, an emergency Caesarean section was performed and the cord was found to be tightly around the infants' neck. Although there was no evidence of perinatal asphyxia (umbilical arterial pH = 7.30 (normal ≥7.20) or low birth weight the infant continued to have seizures and died on the fourth day of life [20]. The authors were unable to

determine the cause of seizures in this case, but hypothesised that these were due to cerebral hypoxia. This was explored using an animal model in which seizures were hypothesised to occur 7-13 hours after a hypoxic insult [21]. The authors then reviewed nine infants who had seizures in the neonatal period and estimated the timing of the cerebral insult. Infants who had an insult before labour had seizures before 12 hours of life, in contrast to those who had a hypoxic event in labour or at the time of delivery. This suggests that if excessive activity represents seizures *in utero* then the insult may have occurred prior to the onset of seizure activity.

If excessive fetal activity represents seizures then this may reflect the aetiology of the underlying insult. Linde described that symptoms of excessive fetal movements were more common in cases of stillbirth occurring after 37 weeks [12]. Stillbirths after 37 weeks are more likely to be due to an infection (39.5% vs. 29.2%, p <0.001), umbilical cord complication (18.8% vs. 13.1%, p <0.05), or unexplained cases (14.5% vs. 10.7%, p=0.06) [22]. These findings are similar to the Stillbirth Collaborative Research Network study of 500 stillbirths, which found stillbirths at or after 37 weeks were more likely to result from infection (11.9% vs. 5.6% at 28-31 weeks), umbilical cord complications (14.3% vs. 5.6% at 28-31 weeks), and less likely to be associated with maternal hypertensive disorders (2.8% vs. 16.7% at 28-31 weeks) [23]. Thus, if an episode of excessive fetal movements is more frequent in women who have a stillbirth in late pregnancy then it may be more likely to reflect complications secondary to infection or umbilical cord complications, in contrast to the pattern of RFM, which is associated with placental dysfunction, fetal growth restriction, and stillbirth.

An alternative explanation is that excessive fetal movement represents fetal behaviour in response to a stressful stimulus. One case series describes a fetal homologue of crying in 10 out of 124 pregnancies exposed to vibroacoustic stimulation [24, 25]. Some of the mothers whose fetuses exhibited this behaviour were exposed to tobacco smoke or cocaine. However, the study was not adequately powered to determine an association between fetal crying and exposure to noxious

environments. Other stressors may also alter fetal behaviour, for example one study of 29 women with uncomplicated normal pregnancies recorded fetal behaviour in different maternal positions [26], finding that fetuses are more likely to be in a state of 'fetal quiescence' when the mother is supine compared to lateral positions. Therefore, it is hypothesised that fetuses adapt their behaviour in response to mild stressors (such as maternal supine position) but a prolonged or profound unpleasant or noxious stimulus could result in a change in fetal behaviour, which is perceived as excessive fetal movements.

It is also possible that perception of excessive fetal movements results from heightened maternal anxiety. The large international cohort study reported some of the cohort perceived that all was not well with the pregnancy [11]. In some cases this feeling arose early in the pregnancy and well before any other maternal or pregnancy complications. If this feeling were present, women may pay increased attention to their baby's movements. This idea is supported by observations in a group of 30 women; those with higher anxiety scores, as measured by the Beck Anxiety Inventory, took significantly less time to perceive 10 fetal movements The authors suggested that either maternal behaviour or mood affects fetal movements or that baby's behaviour alters maternal anxiety state [27]. Importantly, a difference in maternal anxiety would not explain the difference in stillbirth seen between a single episode of excessive movement and more frequent episodes of heightened activity, which is less common in mothers who experienced a stillbirth.

How could the hypothesis be investigated?

The utility of excessive fetal movements as a warning sign for stillbirth will depend upon what this symptom relates to and whether this leaves any time to intervene to prevent fetal death. These questions can be addressed by using a methodological approach employed to the study of women with RFM [28, 29]. The associations and underpinning aetiology of exaggerated fetal movements could be explored by conducting a cohort study of women with this symptom. Given the reported association with abnormalities seen on cardiotocography and ultrasonography [17-20], fetal

compromise associated with infection or placental dysfunction would need to be excluded using these methods. An observational study could then record any additional alterations in fetal activity occurring prior to delivery as well as the neonatal outcome. However, special attention should be paid to the identification of noxious stimuli, infection or umbilical cord complications or seizure disorders (see Figure 1). Information could be collected regarding potential noxious exposures such as tobacco smoke, prescribed and non-prescribed drugs and maternal sleep position.

After delivery, the placenta and umbilical cord could be collected and examined to look for evidence of umbilical cord compression, infection, or placental insufficiency (Figure 1). Morphological and histopathological studies have highlighted that different causes of stillbirth have different placental phenotypes. For example, Ryan et al. found that umbilical cord accident was associated with fetal thrombotic vasculopathy specific features: dilated fetal vessels, thrombosis in fetal vessels, and avascular or near-avascular chorionic villi [30]. Ptacek et al. found that stillbirths associated with umbilical cord complications had increased syncytial nuclear aggregates (syncytial knots), decreased proliferation and increased numbers of avascular villi, but no changes in the number of blood vessels, leukocytes or trophoblast area [31]. Thus, detailed examination of the placenta and cord may give information about the underlying aetiology. As abnormal placental phenotypes can be seen in pregnancies with an apparently healthy infant [32] it is important to compare the histopathological and morphological assessment of placentas from women with excessive fetal movements to those from women who have normal fetal movements.

Evidence for fetal compromise could also be inferred from measurements of biomarkers in umbilical cord blood. Various biomarkers of fetal compromise have been proposed including: umbilical cord pH, erythropoietin, S100B, endothelin-1 and nucleated red blood cells [33-36]. Umbilical artery pH relates to the risk of perinatal asphyxia, the most common cause of neonatal seizures [37]. Exploration of these biomarkers in women with excessive fetal movements could provide further data to determine underlying pathological processes associated with such movements. It would also

give an insight into whether a single period of excessive fetal movements represents an inevitable pathway to perinatal asphyxia, neurological damage and death, or whether there is a period during which intervention may prevent an adverse outcome. Understanding the underlying associations and mechanisms of this symptom is essential to developing tests to identify fetal compromise in this population. As studies describing increased fetal activity have noted that infants are usually an appropriate size for gestational age [15], ultrasonography to identify a small or large for gestational age baby are unlikely to give useful information about prognosis.

Presently, there is little clinical data regarding excessive fetal movements. A questionnaire study of 225 women in two tertiary centres in Nigeria found that 47% of women had knowledge about excessive fetal activity compared to 31.1% for reduced fetal movements; this increased knowledge may be the reason that a higher proportion of women expressed concern about excessive movement compared to significantly reduced movements (31.1% vs. 21.8%). Further clinical studies are required to more accurately describe incidence of excessive fetal movements, the features of excessive fetal movements that should alert care professionals and differentiate between a healthy, active baby and a period of exaggerated or excessive fetal movement [38]. This information would allow more specific information to be given to women to avoid additional maternal anxiety.

Conclusion

Currently, there have been no prospective studies to determine the incidence of excessive fetal movements in the general obstetric population. The literature describes the application of standard investigations such as cardiotocography (non-stress test) and ultrasound assessment of fetal biometry, liquor volume and umbilical artery Doppler. However, these investigations have limited evidence for the reduction of perinatal mortality [39-42]. The uncertainty regarding excessive fetal movements is emphasised by the exclusion of this symptom from guidelines focussed on RFM to reduce perinatal mortality and morbidity [7] and the need to differentiate a single episode of excessive fetal activity from a gradual increase in fetal movements. A better appreciation regarding

the origins of and outcomes following a single sudden episode of excessive fetal movements would enable studies to determine whether encouraging women to present with this symptom and instituting appropriate investigations and intervention could reduce perinatal mortality and morbidity. This would also provide a template to translate findings from case-control studies to identify modifiable risk factors for stillbirth into improved perinatal outcome.

Conflicts of Interest Statement

The authors have no conflicts of interest to declare.

References

1. Lawn, J.E., et al., *Stillbirths: rates, risk factors, and acceleration towards 2030.* Lancet, 2016. **387**(10018): p. 587-603.
2. Flenady, V., et al., *Stillbirths: recall to action in high-income countries.* Lancet, 2016. **387**(10019): p. 691-702.
3. Heazell, A.E. and J.F. Froen, *Methods of fetal movement counting and the detection of fetal compromise.* J Obstet Gynaecol, 2008. **28**(2): p. 147-54.
4. Warrander, L.K. and A.E. Heazell, *Identifying placental dysfunction in women with reduced fetal movements can be used to predict patients at increased risk of pregnancy complications.* Med Hypotheses, 2011. **76**(1): p. 17-20.
5. Confidential Enquiry into Stillbirths and Deaths in Infancy, *8th Annual Report, 1 January–31 December 1999.* 2001, Maternal and Child Health Research Consortium: London.
6. Draper, E.S., et al., *MBRRACE-UK Perinatal Confidential Enquiry: Term, singleton, normally formed, antepartum stillbirth.* 2015, The Infant Mortality and Morbidty Studies, Department of Health Sciences, University of Leicester: Leicester.
7. Royal College Of Obstetricians and Gynaecologists, *Management of Reduced Fetal Movements.* 2011, RCOG: London.
8. Stacey, T., et al., *The Auckland Stillbirth study, a case-control study exploring modifiable risk factors for third trimester stillbirth: methods and rationale.* Aust N Z J Obstet Gynaecol, 2011. **51**(1): p. 3-8.
9. Platts, J., et al., *The Midland and North of England Stillbirth Study (MiNESS).* BMC Pregnancy Childbirth, 2014. **14**: p. 171.
10. Gordon, A., et al., *Sleep position, fetal growth restriction, and late-pregnancy stillbirth: the Sydney stillbirth study.* Obstet Gynecol, 2015. **125**(2): p. 347-55.
11. Warland, J., et al., *An international internet survey of the experiences of 1,714 mothers with a late stillbirth: the STARS cohort study.* BMC Pregnancy Childbirth, 2015. **15**: p. 172.
12. Linde, A., K. Pettersson, and I. Radestad, *Women's Experiences of Fetal Movements before the Confirmation of Fetal Death--Contractions Misinterpreted as Fetal Movement.* Birth, 2015. **42**(2): p. 189-94.
13. Stacey, T., et al., *Maternal perception of fetal activity and late stillbirth risk: findings from the Auckland Stillbirth Study.* Birth, 2011. **38**(4): p. 311-6.
14. Heazell, A.E., et al., *Stillbirth is Associated with Perceived Alterations in Fetal Activity – Findings from an International Case Control Study.* BMC Pregnancy and Childbirth, 2017. **In Press**.
15. Rayburn, W.F., P.R. Rayburn, and L.L. Gabel, *Excessive fetal activity: another worrisome sign?* South Med J, 1983. **76**(2): p. 163-5.
16. Sadovsky, E. and W.Z. Polishuk, *Fetal movements in utero: nature, assessment, prognostic value, timing of delivery.* Obstet Gynecol, 1977. **50**(1): p. 49-55.
17. Landy, H.J., A.N. Khoury, and P.S. Heyl, *Antenatal ultrasonographic diagnosis of fetal seizure activity.* Am J Obstet Gynecol, 1989. **161**(2): p. 308.
18. Ingemarsson, I. and J.A. Spencer, *Fetal seizure activity associated with lethal cerebral damage at birth: two cases.* Acta Obstet Gynecol Scand, 1998. **77**(1): p. 127-9.
19. Maouris, P.G., *Spontaneous fetal seizures in utero.* Am J Obstet Gynecol, 1987. **157**(4 Pt 1): p. 1009-10.
20. Osiovich, H. and K. Barrington, *Prenatal ultrasound diagnosis of seizures.* Am J Perinatol, 1996. **13**(8): p. 499-501.
21. Filan, P., et al., *The relationship between the onset of electrographic seizure activity after birth and the time of cerebral injury in utero.* BJOG, 2005. **112**(4): p. 504-7.
22. Stormdal Bring, H., et al., *Causes of stillbirth at different gestational ages in singleton pregnancies.* Acta Obstet Gynecol Scand, 2014. **93**(1): p. 86-92.

23. Stillbirth Collaborative Research Network, *Causes of death among stillbirths*. JAMA, 2011. **306**(22): p. 2459-68.
24. Gingras, J.L., et al., *Effects of maternal cigarette smoking and cocaine use in pregnancy on fetal response to vibroacoustic stimulation and habituation*. Acta Paediatr, 2004. **93**(11): p. 1479-85.
25. Gingras, J.L., E.A. Mitchell, and K.E. Grattan, *Fetal homologue of infant crying*. Arch Dis Child Fetal Neonatal Ed, 2005. **90**(5): p. F415-8.
26. Stone, P.R., et al., *Effect of maternal position on fetal behavioural state and heart rate variability in healthy late gestation pregnancy*. J Physiol, 2017. **595**(4): p. 1213-1221.
27. Pimenta, B.S., et al., *Maternal anxiety and fetal movement patterns in late pregnancy*. J Matern Fetal Neonatal Med, 2016. **29**(12): p. 2008-12.
28. Warrander, L.K., et al., *Maternal perception of reduced fetal movements is associated with altered placental structure and function*. PLoS One, 2012. **7**(4): p. e34851.
29. Dutton, P.J., et al., *Predictors of poor perinatal outcome following maternal perception of reduced fetal movements--a prospective cohort study*. PLoS One, 2012. **7**(7): p. e39784.
30. Ryan, W.D., et al., *Placental histologic criteria for diagnosis of cord accident: sensitivity and specificity*. Pediatr Dev Pathol, 2012. **15**(4): p. 275-80.
31. Ptacek, I., et al., *Quantitative assessment of placental morphology may identify specific causes of stillbirth*. BMC Clin Pathol, 2016. **16**: p. 1.
32. Pathak, S., et al., *Frequency and clinical significance of placental histological lesions in an unselected population at or near term*. Virchows Arch, 2011. **459**(6): p. 565-72.
33. Loukovaara, M., et al., *Amniotic fluid S100B protein and erythropoietin in pregnancies at risk for fetal hypoxia*. Eur J Obstet Gynecol Reprod Biol, 2009. **142**(2): p. 115-8.
34. Ostlund, E., et al., *Fetal erythropoietin and endothelin-1: relation to hypoxia and intrauterine growth retardation*. Acta Obstet Gynecol Scand, 2000. **79**(4): p. 276-82.
35. Gazzolo, D., et al., *Urinary S100B protein measurements: A tool for the early identification of hypoxic-ischemic encephalopathy in asphyxiated full-term infants*. Crit Care Med, 2004. **32**(1): p. 131-6.
36. Boskabadi, H., et al., *Nucleated red blood cells count as a prognostic biomarker in predicting the complications of asphyxia in neonates*. J Matern Fetal Neonatal Med, 2016: p. 1-6.
37. Georgieva, A., M. Moulden, and C.W. Redman, *Umbilical cord gases in relation to the neonatal condition: the EveREst plot*. Eur J Obstet Gynecol Reprod Biol, 2013. **168**(2): p. 155-60.
38. Olagbuji, B.N., et al., *Maternal understanding of fetal movement in third trimester: a means for fetal monitoring and reducing stillbirth*. Niger J Clin Pract, 2014. **17**(4): p. 489-94.
39. Alfirevic, Z., T. Stampalija, and G.M. Gyte, *Fetal and umbilical Doppler ultrasound in high-risk pregnancies*. Cochrane Database Syst Rev, 2010(1): p. CD007529.
40. Alfirevic, Z., T. Stampalija, and N. Medley, *Fetal and umbilical Doppler ultrasound in normal pregnancy*. Cochrane Database Syst Rev, 2015(4): p. CD001450.
41. Bricker, L., N. Medley, and J.J. Pratt, *Routine ultrasound in late pregnancy (after 24 weeks' gestation)*. Cochrane Database Syst Rev, 2015(6): p. CD001451.
42. Grivell, R.M., et al., *Antenatal cardiotocography for fetal assessment*. Cochrane Database Syst Rev, 2015(9): p. CD007863.

Figure Legend

Figure 1 – Potential causes of excessive fetal movements and how these could be investigated in pregnancy and after birth in women presenting to maternity services with a primary complaint of excessive fetal movements.

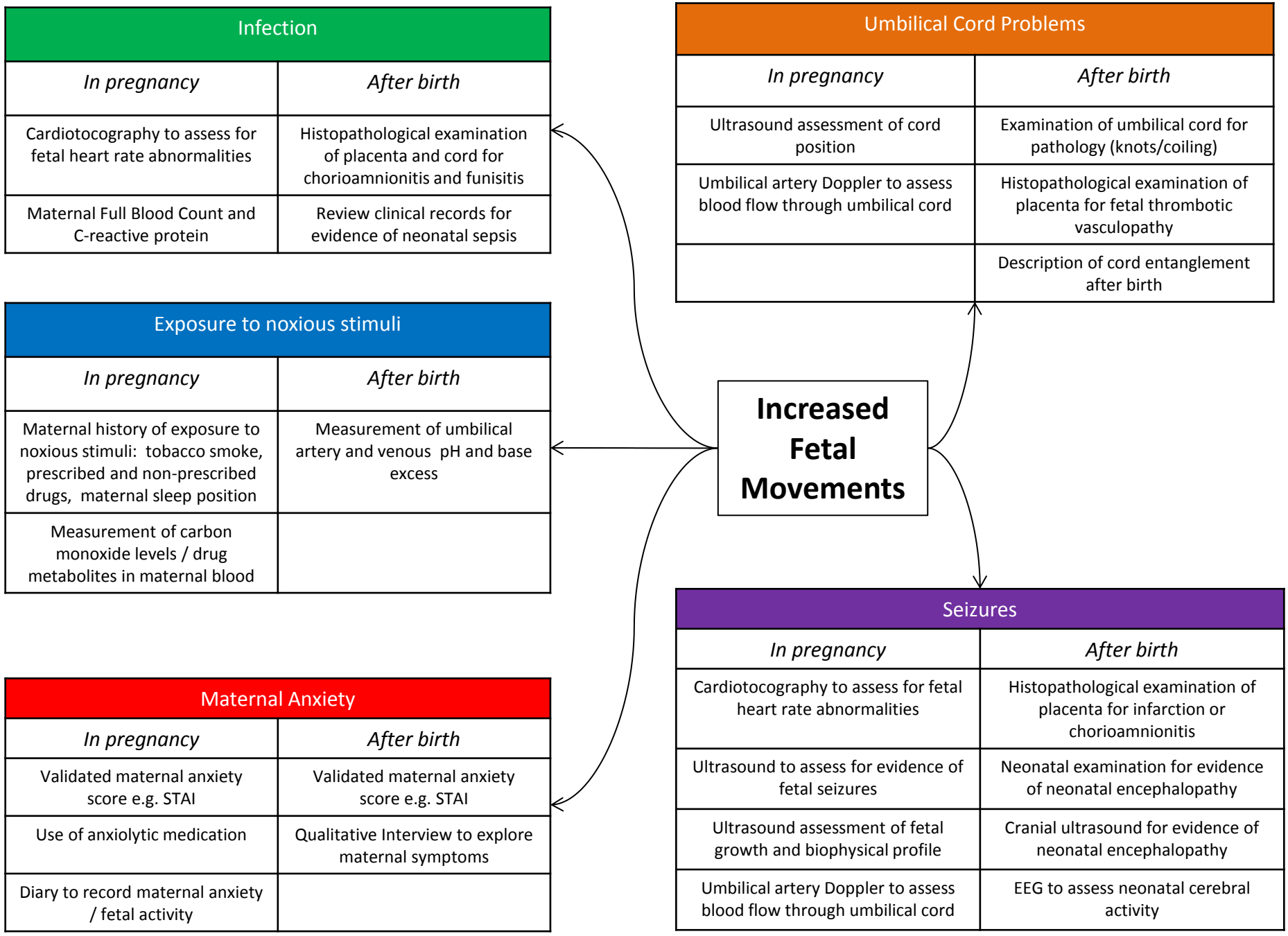
Infection
In pregnancy
After birth
Cardiotocography to assess for fetal heart rate abnormalities
Histopathological examination of placenta and cord for chorioamnionitis and funisitis
Maternal Full Blood Count and C-reactive protein
Review clinical records for evidence of neonatal sepsis
Umbilical Cord Problems
In pregnancy
After birth
Ultrasound assessment of cord position
Examination of umbilical cord for pathology (knots/coiling)
Umbilical artery Doppler to assess blood flow through umbilical cord
Histopathological examination of placenta for fetal thrombotic vasculopathy
Description of cord entanglement after birth
Exposure to noxious stimuli
In pregnancy
After birth
Maternal history of exposure to noxious stimuli: tobacco smoke, prescribed and non-prescribed drugs, maternal sleep position
Measurement of umbilical artery and venous pH and base excess
Measurement of carbon monoxide levels / drug metabolites in maternal blood
Increased Fetal Movements
Maternal Anxiety
In pregnancy
After birth
Validated maternal anxiety score e.g. STAI
Validated maternal anxiety score e.g. STAI
Use of anxiolytic medication
Qualitative Interview to explore maternal symptoms
Diary to record maternal anxiety / fetal activity
Seizures
In pregnancy
After birth
Cardiotocography to assess for fetal heart rate abnormalities
Histopathological examination of placenta for infarction or chorioamnionitis
Ultrasound to assess for evidence of fetal seizures
Neonatal examination for evidence of neonatal encephalopathy
Ultrasound assessment of fetal growth and biophysical profile
Cranial ultrasound for evidence of neonatal encephalopathy
Umbilical artery Doppler to assess blood flow through umbilical cord
EEG to assess neonatal cerebral activity

Table 1 – Summary of recent studies investigating the association of reduced fetal movements and excessive fetal movements with stillbirth.

Study Identifier	Study type	Question	Women who experienced stillbirth		Women with live births		Unadjusted Odds Ratio	
			Reduced Fetal Movements (%)	Excessive Fetal Movements (%)	Reduced Fetal Movements (%)	Excessive Fetal Movements (%)	Reduced Fetal Movements	Excessive Fetal Movements
Rayburn et al. 1983	Cohort	Participants kept diaries during pregnancy	-	-	-	47 (5%)	-	-
Stacey et al. 2011	Case-Control	Participants were asked to describe their baby's movements, in particular whether any change in frequency or strength had occurred AND whether they had perceived vigorous movement	45 (29.0%)	32 (20.8%)	36 (11.6%)	16 (5.2%)	2.16 (1.24–3.77)	4.51 (2.23–9.10)
Warland et al. 2015	Cohort	Once you were aware of your baby's usual pattern of movements was there any time that your baby's movements were unusual?"	522 (30.5%)	146 (8.5%)	-	-	-	-
Linde et al. 2015	Cohort	How do you remember the fetal movement during the48 hours that preceded the diagnosis of intrauterine death?"	106 (69%)	22 (10%)	-	-	-	-
Heazell et al. 2017	Case-Control	Once you were aware of your baby's usual pattern of movements was there any time that your baby's movements were unusual?"	56 (40%)	42 (30.4%)	32 (8.4%)	24 (6.7%)	12.9 (7.17-23.4)	4.24 (2.36-7.62)

Re – Submission to Medical Hypotheses - Excessive Fetal Movements are a Sign of Fetal Compromise Which Merits Further Examination

Conflicts of Interest Statement

The authors have no conflicts of interest to declare.