Fetal movement trials: where is the evidence in settings with high-burden of stillbirths?

Natasha Housseine[1], Joyce Browne[1], nanna maaloe[2], Sam Ali[3], brenda dmello[4], Muzdalifat Abeid[5], Tarek Meguid[6], Marcus Rijken[1], and Hussein Kidanto[5]

[1]UMC Utrecht
[2]Affiliation not available
[3]Makerere University College of Health Sciences
[4]Comprehensive Community Based Rehabilitation in Tanzania
[5]Aga Khan University - Tanzania
[6]University of Cape Town

March 13, 2022

BJOG Commentary

Title: Fetal movement trials: where is the evidence in settings with high burden of stillbirths?

Authors:

Natasha Housseine[1,2], natasha.housseine@aku.edu, natasha.housseine@outlook.com

Joyce Browne[2], J.L.Browne@umcutrecht.nl

Nanna Maaløe[3] nannam@sund.ku.dk

Sam Ali[2,4], alisambecker@gmail.com

Brenda Sequeira Dmello[1,5] brenda.dmello@ccbrt.or.tz

Muzdalifat Abeid[1], muzdalifat.abeid@aku.edu

Tarek Meguid[6], tarekmeguid@gmail.com

Marcus J Rijken[2,7,8], mrijken2@umcutrecht.nl

Hussein Kidanto[1], hussein.kidanto@aku.edu

Affiliations

1. Aga Khan University, Medical College East Africa, Dar es Salaam campus
2. Julius Global Health, Julius Centre for Health Sciences and Primary Care, University Medical Centre Utrecht, Utrecht University, The Netherlands
3. Global Health Section, Department of Public Health, University of Copenhagen, Denmark
4. Research Department, Ernest Cook Ultrasound Research and Education Institute (ECUREI), P.O. Box 7161, Kampala, Uganda
5. Comprehensive Community Based Rehabilitation in Tanzania, Dar es salaam, Tanzania
6. Child Health Unit, Department of Paediatrics and Child Health, University of Cape Town, Cape Town, South Africa
7. Vrouw en Baby department, University Medical Centre Utrecht, Utrecht University, The Netherlands

8. Obstetric department, Amsterdam University Medical Center, Amsterdam, The Netherlands

Corresponding author:

Natasha Housseine

The Aga Khan University

Medical College

Ufukoni Road, P. O. Box 38129, Dar es salaam, Tanzania

Telephone: +255 745 338 950

Fetal movement (FM) is a sign of fetal life and wellbeing that is felt by the pregnant woman, and reduced FM is known to precede stillbirths (1,2). Therefore, women may be instructed to monitor and report if movements are fewer than usual (2). In high-income countries, there has been a renewed interest in FM with a recent wave of large-scale randomised controlled clinical trials investigating FM as a potential stillbirth reduction strategy. As published in BJOG, My Baby's Fetal Movement trial was carried out in Australia/New Zealand, and the Mindfetalness trial in Sweden (3,4). Also, the AFFIRM trial published in the Lancet was conducted in UK and the CEPRA study is ongoing in the Netherlands, UK and Australia (5). None of the completed trials, however, found significant reductions in stillbirths, and they showed conflicting results on some potential harmful consequences such as increased rates of obstetric interventions. In this commentary, we reflect on these trials through a global lens, and we urgently call for more trials; but this time in settings suffering from the vast majority (98%) of the world's 2 million annual stillbirths.

Importantly, the global applicability of these trials from high-income countries should be considered. The studies above are conducted in populations with pre-existing high awareness about the importance of reduced FM and easily accessible advanced fetal monitoring opportunities. Moreover, these settings are examples of countries providing the world's highest-level programs of early detection and timely management of obstetric complications associated with risk of stillbirth, such as growth restriction and pre-eclampsia. In fact, women in these high-resource settings are already alerted about potential pregnancy complications to an extent where additional alerting might cause more harm than good, with over-use of interventions and an unnecessary stressful pregnancy. In low- and middle-income countries (LMICs), most women are still provided inadequate antenatal care and lack health information to report reduced FM movement. Antenatal clinics are often overcrowded, understaffed, and lack essential supplies and clinical guidelines including for investigating and managing high risk pregnancies and abnormal FMs (2). Recent estimates show stillbirth rates as high as 22 per 1000 per total births in the Sub-Saharan African region, compared to less than 3 per 1000 in HICs(6). We propose for consideration that these trials may be demonstrating a lack of evidence rather than a lack of effectiveness and we hypothesise that in LMICs, a similar RCT with a low-cost, low-tech strategy would be likely to demonstrate a positive effect.

Yet, until now, there has not been a single high-quality study assessing the effect of FM interventions on perinatal deaths in LMICs (2,7). The authors of the robust above-mentioned trials did not consider the well-known major differences in clinical context globally as a limitation in generalizing their findings. In fact, the latest My Baby's Fetal Movement trial was not even published open access, limiting access to less privileged clinicians, researchers and policy makers (4). This lack of a global perspective on the international health crisis of preventable stillbirths is an epistemic injustice and a missed opportunity (8). It is crucial that the lack of generic applicability of these trials' findings are stressed, and that their high-resource contexts are carefully considered when applying the results in development of clinical guidelines and future research priorities. Notably, it has been seen too often how the unbalanced evidence production from HICs has over-influenced clinical practice also in LMICs (9). For instance, it appears that the breech trials from HICs have had considerable impact on practice also in LMICs with increased use of caesarean section in case of breech presentation. However, the risk ratios of vaginal breech births versus caesarean sections differ dramatically between high-resource and low-resource settings with lower surgical safety in LMICs (10,11).

Meanwhile, it must be stressed that future FM trials in LMICs can learn from the HIC trials. In particular, the rigorous, but practical study designs are highly relevant in LMICs as well: cluster (stepped wedge) randomised designs, which allows to evaluate an intervention in the real-life context of health care. These practical designs can stimulate evidence generation in low-resource settings facing the highest burden of stillbirths , and they can take the diverse contexts and resources into account by embedding qualitative and cost-effectiveness components (12). Similarly, challenges encountered in these trials can also be incorporated in the design of LMIC-based studies. For example, in including ways to ensure uptake of the intervention, e.g., by in-depth exploration of how different elements interact to influence attitude, behaviour and practice in a formative phase, and use of multiple modalities to deliver the intervention. Notably, low-dose high frequency training with facility-based follow-up is more likely to work, especially in these settings (13) Steps also need to be taken to minimize contamination during trials. , Lastly, it is crucial to ensure that the findings are accessible to the global audience, and, as population health interventions are strongly influenced by context, that this includes a thorough description of the context in which the intervention was conceived, developed, implemented and evaluated (9).

Future LMIC-based FM studies should be designed to consider the clinical reality of settings with a high-volume of pregnant women, low resources, and overwhelmed frontline health workers, contributing to poor quality care and data. Moreover, pregnant women migrate through different health facilities during the pregnancy continuum introducing follow-up challenges. This requires both strengthening routine data and innovative data collection systems. As such, any new care package needs to be seamlessly integrated into existing systems of care, be perceived by providers and pregnant women as beneficial and not to increase burden on healthcare workers. This means in-depth understanding of the complex adaptive system of care provision during pregnancy and childbirth, and co-creation of tailored interventions with the users to locally achievable standards.

Finally, while reduced FM can be obtained easily in any setting as a general screening, reduced FM must be complemented by an effective diagnostic and management strategy to improve perinatal outcomes. There is lack of such diagnostic tools to correctly identify the fetuses truly at risk for adverse outcomes and imminent intrauterine fetal death in all settings but especially in LMICs. However, antenatal (Doppler) ultrasound has proven itself as a useful tool for detecting and monitoring of high-risk pregnancies particularly in growth restricted fetuses. Notably, measuring abnormal fetal blood flow in Doppler ultrasound studies is a promising approach, also in LMIC settings, and need to be further tested (14,15).

Unfortunately, maternal perception of FM is still too often the *only* signal of complications in absence of regular high quality antenatal checks – and there are too many babies' lives lost by ignoring this essential danger sign. Given the burden of need and the context-specific realities that determine interventions' effectiveness, we hope these recent waves of FM trials will continue into LMICs.

Contribution to Authorship

NH conceived and wrote the first draft. JB, NM and MJR contributed to subsequent drafting of the manuscript. All authors revised the commentary for important intellectual content and approved the final version to be published and agree to be accountable for all aspects of the work.

Details of ethics approval

No ethics approval applicable for this commentary

Funding

There was no financial support for this commentary

Disclosure of interests

Reference

1. Bekiou A, Gourounti K. Reduced Fetal Movements and Perinatal Mortality. Mater Sociomed. 2020;32(3).

2. Hayes DJL, Smyth R, Heazell AEP. Investigating the significance and current state of knowledge and practice of absent or reduced fetal movements in low and lower middle-income countries : a scoping review. 2019;3:1–12.

3. Akselsson A, Lindgren H, Georgsson S, Pettersson K, Steineck G, Skokic V, et al. Mindfetalness to increase women's awareness of fetal movements and pregnancy outcomes: a cluster-randomised controlled trial including 39 865 women. BJOG An Int J Obstet Gynaecol. 2020 Jun 1;127(7):829–37.

4. Flenady V, Gardener G, Ellwood D, Coory M, Weller M, Warrilow KA, et al. My Baby's Movements: a stepped-wedge cluster-randomised controlled trial of a fetal movement awareness intervention to reduce stillbirths. BJOG An Int J Obstet Gynaecol. 2022 Jan 1;129(1):29–41.

5. Norman JE, Heazell AEP, Rodriguez A, Weir CJ, Stock SJE, Calderwood CJ, et al. Awareness of fetal movements and care package to reduce fetal mortality (AFFIRM): a stepped wedge, cluster-randomised trial. www.thelancet.com. 2018;392.

6. Hug L, You D, Blencowe H, Mishra A, Wang Z, Fix MJ, et al. Global, regional, and national estimates and trends in stillbirths from 2000 to 2019: a systematic assessment. Lancet. 2021 Aug 28;398(10302):772–85.

7. Bellussi F, Po' G, Livi A, Saccone G, De Vivo V, Oliver EA, et al. Fetal Movement Counting and Perinatal Mortality: A Systematic Review and Meta-analysis. Obstet Gynecol. 2020 Feb 1;135(2):453–62.

8. Bhakuni H, Abimbola S. Epistemic injustice in academic global health. Lancet Glob Heal. 2021;9:e1465–70.

9. Maaløe N, Ørtved AMR, Sørensen JB, Sequeira Dmello B, van den Akker T, Kujabi ML, et al. The injustice of unfit clinical practice guidelines in low-resource realities. Lancet Glob Heal. 2021;9(6):e875–9.

10. van Roosmalen J, Meguid T. The dilemma of vaginal breech delivery worldwide. Lancet. 2014;338(9932):

11. Sobhy S, Arroyo-Manzano D, Murugesu N, Karthikeyan G, Kumar V, Kaur I, et al. Maternal and perinatal mortality and complications associated with caesarean section in low-income and middle-income countries: a systematic review and meta-analysis. Lancet. 2019 May 11;393(10184):1973–82.

12. Maaløe N, Housseine N, Sørensen JB, Obel J, Sequeira DMello B, Kujabi ML, et al. Scaling up context-tailored clinical guidelines and training to improve childbirth care in urban, low-resource maternity units in Tanzania: A protocol for a stepped-wedged cluster randomized trial with embedded qualitative and economic analyses (The Parto. Heal Action. 2022;In press.

13. Atukunda IT, Conecker GA. Effect of a low-dose, high-frequency training approach on stillbirths and early neonatal deaths: a before-and-after study in 12 districts of Uganda. Lancet Glob Heal. 2017 Apr 1;5:S12.

14. Damhuis SE, Ganzevoort W, Duijnhoven RG, Groen H, Kumar S, Heazell AEP, et al. The CErebro Placental RAtio as indicator for delivery following perception of reduced fetal movements, protocol for an international cluster randomised clinical trial; the CEPRA study.

15. Ali S, Kawooya MG, Byamugisha J, Kakibogo IM, Biira EA, Kagimu AN, et al. Middle cerebral arterial flow redistribution is an indicator for intrauterine fetal compromise in late pregnancy in low-resource settings: a prospective cohort study. BJOG An Int J Obstet Gynaecol. 2022 Feb 4;