Improved stillbirth risk stratification, an urgent global need. (Mini-commentary on BJOG-20-0453.R1)

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Mini-commentary on BJOG-20-0453.R1: Can risk prediction models help us individualise stillbirth prevention? A systematic review and critical appraisal of published risk models

Improved stillbirth risk stratification, an urgent global need

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Stillbirth is among the most devastating pregnancy complications and is also one of the hardest complications to predict. Traditionally, stillbirth risk stratification has incorporated maternal demographic characteristics such as age and ethnicity as well as medical and pregnancy conditions including multiple gestation, chronic hypertension and pregestational diabetes. While these are clear risk factors for stillbirth, they are nonspecific and are often present in live births. Thus, tailoring an antenatal surveillance strategy to this poorly defined and heterogenous population at increased risk of stillbirth is difficult and can result in unnecessary obstetric intervention and health system costs. Townsend et al have synthesized existing stillbirth risk prediction models to address the need for a better method by which to identify those pregnancies at highest risk for stillbirth (BJOG 2020 xxxx).

In this report, the variables most used in stillbirth risk prediction systems included maternal ethnicity, body mass index (BMI), uterine artery Doppler, pregnancy-associated plasma protein (PAPP-A) and placental growth factor (PlGF). Biomarkers that can be assessed prospectively at earlier gestational ages are attractive candidates for stillbirth risk prediction as this may facilitate recognition of an at-risk pregnancy that would otherwise not be identified. Individually these biomarkers have poor positive predictive values for pregnancies ultimately ending in stillbirth. (Dugoff et al. Am J Obstet Gynecol 2004;191:1446e51; Heazell AEP et al. Cochrane Database Syst Rev 2015;11:CD011202.) To address this, maternal demographic and medical characteristics have been combined with ultrasound and biochemical markers into multivariable models. However, as Townsend and colleagues show, these models are prone to bias and lack external validation which limits their clinical utility.

Important steps in improving stillbirth risk prediction and identification of those pregnancies which would benefit from obstetric intervention include novel biomarker discovery and high- quality stillbirth evaluation and data collection. A large proportion of stillbirths are associated with placental dysfunction and research into biomarkers of placental insufficiency is ongoing. (Cleaton et al. Nat Genet 2016 Dec;48(12):1473-1480; Chaiworapongsa T, et al. Am J Obstet Gynecol 2013;208(4):287.) This research is an important step

toward better understanding the mechanisms of placentally-mediated stillbirths and developing better risk identification tools.

Large variation in stillbirth definitions and evaluation exist due to differences in resources, as well as practice variation within the same resource setting, resulting in discordant datasets and incompletely characterized stillbirth cases. This heterogeneity in practice is problematic, as even with complete evaluation, up to a quarter of stillbirths remain unexplained. (Stillbirth Collaborative Research Network Writing Group. JAMA 2011;306:2459e68.) As pointed out by Townsend et al (BJOG 2020 xxxx), this variation in practice makes external validation of a stillbirth risk prediction model exceedingly difficult due to heterogeneous populations and datasets. Given the global need to reduce stillbirth, collaboration among groups with ongoing collection of uniform and standardized stillbirth data is an imperative step forward to improving care for those at highest risk and reducing unnecessary obstetric intervention.

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