New guidelines to improve pregnancy trials will pave way for novel therapies for women and babies

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Clinical trials in pregnant women are challenging but crucial for saving lives and the advancement of new therapies and treatments for mothers and babies.

Published in *Prenatal Diagnosis* today, the team present their research on developing a new severity grading system with key definitions and responses for 'adverse events (AE)' that can occur in pregnancy trials. The 12 maternal and 19 fetal definitions have been adopted by the Medical Dictionary for Regulatory Activities and it is hoped they will now be used by triallists, industry and other regulatory authorities.

The authors say the new terminology fills a vital gap in pregnancy research and will help further the development of new therapies for pregnant women, who are a neglected patient group.

The aim of the grading criteria is to ensure that when complications or emergencies occur in pregnant women participating in clinical trials, such as bleeding or the detection of a new structural abnormality in an unborn baby, it is recorded using a standard definition and then graded on a level of severity to give detailed information about the safety of the intervention being studied.

The research team note that the lack of regulatory language available until now may have contributed to the lack of investment in novel therapeutics for diseases that affect pregnant women.

Professor Anna David (Director, UCL Elizabeth Garrett Anderson Institute for Women's Health and NIHR UCLH BRC), who led the research, said: "Conducting clinical trials in pregnancy raises many challenges, primarily due to safety concerns for mother and fetus, and particularly when testing novel maternal and fetal therapies.

"We wanted to design a new set of criteria to help all those involved in

pregnancy trials so that we can develop new drugs and therapies for women and babies and further advance pregnancy research."

Dr. Gill Norman, a member of the Patient Public Engagement Group who co-developed the criteria, said: "This is an area of medicine where safety concerns are front and center. Having a framework to record and assess these feels like a big step forward in enabling the testing of different types of treatments for both pregnant women and their unborn babies. We hope it will help both the women who decide to take part in trials when pregnant and the clinical staff caring for them."

The research paper highlights that the recording and reporting of adverse events using standardized severity grading terminology allows for better comparisons of safety data between clinical trials. For the first-in-human or early-phase trials in particular, the grading is vital in determining what dose of medication can be safely offered to mothers.

Professor David explained: "A recent example of this phenomenon is the SARS-CoV-2 pandemic, a current and urgent situation in which the exclusion of pregnant and lactating women from many clinical trials of treatment or vaccination for COVID-19 has left a vacuum of information. This means that women and their healthcare providers have to make treatment decisions without the appropriate safety information."

Dr. Rebecca Spencer, NIHR Academic Clinical Lecturer who co-led the study added: "We believe this new system will greatly improve safety reporting for fetal and maternal clinical trials. Pregnancy research is so important because many of the problems that affect women and their babies during pregnancy still don't have safe and effective treatments. If we are going to do better for future generations then we need to make testing new treatments as safe as possible."

Mehali Patel, Senior Research Officer from Sands, (Stillbirth and

Neonatal Death Charity), said: "Sands welcomes the new guidelines for pregnancy trials. Research has the potential to change the lives of generations of mothers and babies, yet for too long people who are pregnant have been excluded from research. This has slowed progress in developing new therapies for use during pregnancy.

"We often hear from bereaved families about how little was known about what caused their baby's death and how few effective treatments were available to make a difference. These guidelines provide researchers with the language they need to open up pregnancy research and increase the potential to develop safe and effective therapies for pregnancy."

The authors say the strength of the grading criteria comes from working with multiple stakeholders across many countries. They highlight, however, that the new terminology should not be considered final or exhaustive and they will continue to improve these criteria with revised versions as more data is gathered from pregnancy trials and new treatments.

More information: Rebecca N Spencer et al, Development of standard definitions and grading for Maternal and Fetal Adverse Event Terminology, *Prenatal Diagnosis* (2021). DOI: 10.1002/pd.6047

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