Understanding pregnancy: Accelerating the development of new therapies for pregnancy-specific conditions - Executive summary

During pregnancy, women and pregnant individuals who do not identify as women[1] can develop a range of pregnancy-specific conditions, such as pre-eclampsia and gestational diabetes, that can adversely affect both their own health and that of the developing fetus during the pregnancy. These conditions can affect the lifelong health of both mother and child. Despite the danger that these conditions present to mother and baby, there are few approved, safe and effective medicines to treat them, and limited investment in novel therapy development.

The lack of safe and effective medicines for pregnancy-specific conditions reflects significant challenges along the entire drug discovery and development pathway, which includes the need to minimise the risk to both women and their unborn babies in research studies and clinical trials. These challenges complicate preclinical research into the physiology of healthy pregnancy, the mechanisms of disease of pregnancy-specific conditions, and potential therapeutic interventions. Preclinical evidence is essential for identifying candidate treatments for pregnancy-specific conditions and for designing clinical trials to test their safety and efficacy.

To map out key barriers and potential enablers of preclinical research and experimental medicine to support the development of new medicines for pregnancy-specific conditions, the Academy of Medical Sciences, Birmingham Health Partners, and Concept Foundation organised a multi-sectoral FORUM workshop in September 2023. People with lived experience joined representatives from academia, the commercial sector, clinical practice (including doctors and midwives), regulatory authorities, funding bodies, charities, and patient advocacy groups at the meeting.

Participants highlighted that stimulating more early-stage research on pregnancy-specific conditions could improve understanding of disease mechanisms, identify new targets for medicine development, and develop methods for better evaluating safety, toxicity, and dosage prior to early-stage clinical trials. Such advances could invigorate medicine development for pregnancy-specific conditions and drive renewed commercial interest in the development of treatments. The workshop did not focus on the specific challenges of running clinical trials in pregnancy; however, participants discussed the need for evidence from preclinical research and experimental medicine to support the design and approval of clinical trials for candidate medicines for pregnancy-specific conditions, and inform recruitment of trial participants.

Participants proposed next steps (outlined in the full report) around the following priorities:

1. **A cross-sectoral and cross-speciality network or coalition, including women with lived experience, to provide a platform for collaboration and to coordinate efforts to promote the development of new medicines for pregnancy-specific conditions.**
2. **Additional interdisciplinary research and cross-sector collaboration to address key knowledge gaps (including the biology of the placenta, of the early stages of pregnancy, and of pregnancy-specific conditions), to enable appropriate use of animal models and physiologically based pharmacokinetic (PBPK) modelling, and to leverage routinely collected health data and patient samples.** Combining preclinical

[1] The Academy acknowledges that not all pregnant people identify as women. While the terms 'woman' and 'mother' are used here, many of the learnings from the workshop about obstetric/pregnancy-specific conditions are expected to be widely applicable. It is recognised that there will be specific experiences and challenges associated with obstetric conditions among pregnant individuals who do not identify as women that were not explored at the workshop given the lack of specific research in this area.

data from different research tools, including multiple species, could provide a powerful approach to overcome the limitations presented by any individual model for the study of pregnancy. Access to human tissue for this research is essential as many features of human pregnancy and pregnancy-specific conditions are not present in animals. However, most biological samples from pregnant women are from healthy, late-stage pregnancies. To enable pregnancy research, participants proposed the establishment of a biobank that collects biological samples linked with relevant health data from pregnant women, including those with pregnancy-specific conditions. Participants also noted that linking the health data of mother and child is important (e.g. for research into the long-term impacts of pregnancy-specific conditions and their treatments).

3. **The establishment of a more enabling environment for research in pregnancy, for example through development of a stronger research base and a more supportive regulatory environment.** The additional regulatory challenges for proving safety of medicines for both the pregnant woman and the fetus using traditional approaches and experimental models have acted as a deterrent to commercial investment. Given the diversity of novel tools being developed for pregnancy research, participants suggested a cross-sector workshop to explore the regulatory acceptability of novel experimental models. Participants also highlighted that research into pregnancy-related conditions, and women's health more generally, is underfunded, which affects the sustainability of the workforce, and should be seen as a greater public health priority.
4. **Greater engagement with women to raise awareness of the importance of research into pregnancy and of opportunities to participate in this research,** including when women contact the healthcare system. Such opportunities could include blood/tissue donation, allowing access to health records for research, and participation in interventional studies. Participants felt that the opportunity to participate in research should be a routine part of care of pregnant women, whilst ensuring that such opportunities are presented sensitively. Participants strongly felt that efforts are needed to ensure equitable opportunity for research participation (for example, by working with community-based organisations to build trust and engage underserved communities).
5. **Education and training of healthcare professionals, including midwives, to promote research in pregnancy.** Healthcare professionals often do not encourage women, particularly pregnant women, to participate in research, perhaps due to perceived risk and/or lack of awareness of potential benefits. Participants proposed a survey of attitudes of healthcare professionals to pregnancy research to explore the reason for any reluctance. Informed by the results, participants suggested the Royal Colleges would be well placed to facilitate relevant education and training.
6. **Advocacy to secure greater prioritisation of research in pregnancy (and women's health more generally) by policymakers, funders, and higher education institutions.** As well as highlighting disease burdens, medical needs and long-term impacts (economic as well as health), participants suggested that advocacy strategies should develop strong positive messaging, including by highlighting evidence-based success stories.

There was a strong appetite amongst participants to maintain momentum and continue the cross-sector conversations begun at the workshop. Greater prioritisation of research in pregnancy, increased funding, and dialogue with regulatory authorities could reshape the landscape for research in pregnancy and promote translation of research findings into much-needed treatments for pregnancy-specific conditions.