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Opportunities and barriers for innovation at the interface of engineering and maternal-fetal medicine

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The development of safe and effective maternal-fetal therapeutics is significantly hindered by chronic underfunding, inequitable access to specialized care, and persistent sociopolitical stigmas surrounding women's health. Addressing these challenges will require interdisciplinary collaboration between clinicians, scientists, and engineers to design accessible therapeutics for maternal-fetal healthcare.

Many barriers exist to maternal-fetal healthcare including social constructs, complex regulatory attitudes, critical underfunding of research, and healthcare accessibility, which limit innovation and implementation of new technologies in the space. With increased attention and funding in the field, there are more opportunities now than ever to foster meaningful collaborations and leverage clinically approved therapeutic platforms to spur innovation in maternal-fetal medicine. In this commentary, we will discuss barriers and opportunities for interdisciplinary research that combine bioengineering with reproductive biology in an effort to make medicine more effective and accessible for pregnant patients and their offspring (Fig. 1).

Barriers to innovations in maternal-fetal medicine research

Social, ethical, and historical constructs surrounding drug implementation in pregnancy have resulted in limited therapeutic translation in the field. A notable and contributing historical event was the thalidomide tragedy in the 1950's and 1960's; thalidomide was prescribed to pregnant patients as a "cure" for morning sickness but was later found to cause severe birth defects in children born from these pregnancies. How did this happen? While the drug was shown to be non-toxic in animal testing, thalidomide was not tested in pregnant animals, nor was a controlled clinical trial performed in most countries before being approved for human use[1]. While the thalidomide incident led to more stringent drug testing and approval requirements, events like these have contributed to complex social and ethical constructs regarding testing and approving new medications for pregnant women. These challenges are compounded by the need to design therapeutics to treat two patients—both the mother and the fetus—without sacrificing safety and efficacy for either.

Historically, new drugs and devices have not been tested in pregnant females or even females of reproductive age (15–49 years of age). After the thalidomide tragedy, the U.S. Food and Drug Administration (FDA) issued guidance to exclude women of childbearing potential from clinical trials. Only after the National Institutes of Health (NIH) Revitalization Act of 1993 were there official mandates to include women and minority groups in all NIH-funded clinical research. The effects of these historical events still linger: as of 2025 more than 99% of U.S. drug trials still exclude pregnant patients[2], which reduces the amount of clinical data accessible to physicians in order to accurately prescribe medications to pregnant women. Beyond this challenge, recent research estimates there are substantial negative health outcomes due to omitting pregnant women from clinical drug trials[3]. The report states that if the initial randomized controlled trials for the COVID-19 vaccines had included pregnant women, a projected 20% of COVID-19–related maternal deaths and stillbirths in the U.S. would have been prevented from March to November 2021.

Besides the persisting effects of these historical events, manufacturing and drug product costs can also be prohibitive to therapeutic implementation for maternal-fetal medicine, but they are not the only barrier to access needing consideration. Infrastructure, facilities and trained staff are also a limitation; for example, maternal healthcare access is a major challenge across the globe, including in the United States. March of Dimes (a nonprofit organization that works to improve the health of mothers and babies) recently reported that 32.6% of U.S. counties are maternity care deserts, while in some states like ours, that rate is even higher (Texas, 46.5%)[4].

Women's health research has historically been underfunded[5] with pregnant patients being particularly underserved as maternal-fetal health research receives just a fraction of this small funding pool. Recent pushes from organizations like the Gates Foundation, ARPA-H, Wellcome Leap, and Nuttall Women's Health are working to help close the gap, providing significant opportunities for healthcare innovation in maternal-fetal medicine. With this increased attention and promise in funding, one remaining challenge for pregnancy healthcare lies in expediting the translation of biomedical research into clinically promising therapeutics. To execute on innovation and translation, increased collaboration will be essential to overcome siloing in academic departments and limited contact amongst basic scientists, engineers, and clinicians. Teams such as ours are asking: what design parameters should we consider during preclinical design and engineering to ensure new maternal-fetal medicines are accessible and implementable? We believe collaborative teams have strong potential for real-world impact in maternal-fetal medicine by pursuing creative solutions that can rapidly reach pregnant patients with restricted healthcare access. In the following sections, we will discuss engineering opportunities to establish physiologically-relevant models of women-specific microenvironments and tissues as well as the translational potential of rationally engineered therapeutics for maternal-fetal medicine.

Importance of employing physiologically-relevant models

Selecting suitable experimental models in biomedical research is critical for evaluating therapeutic technologies and can improve access by both

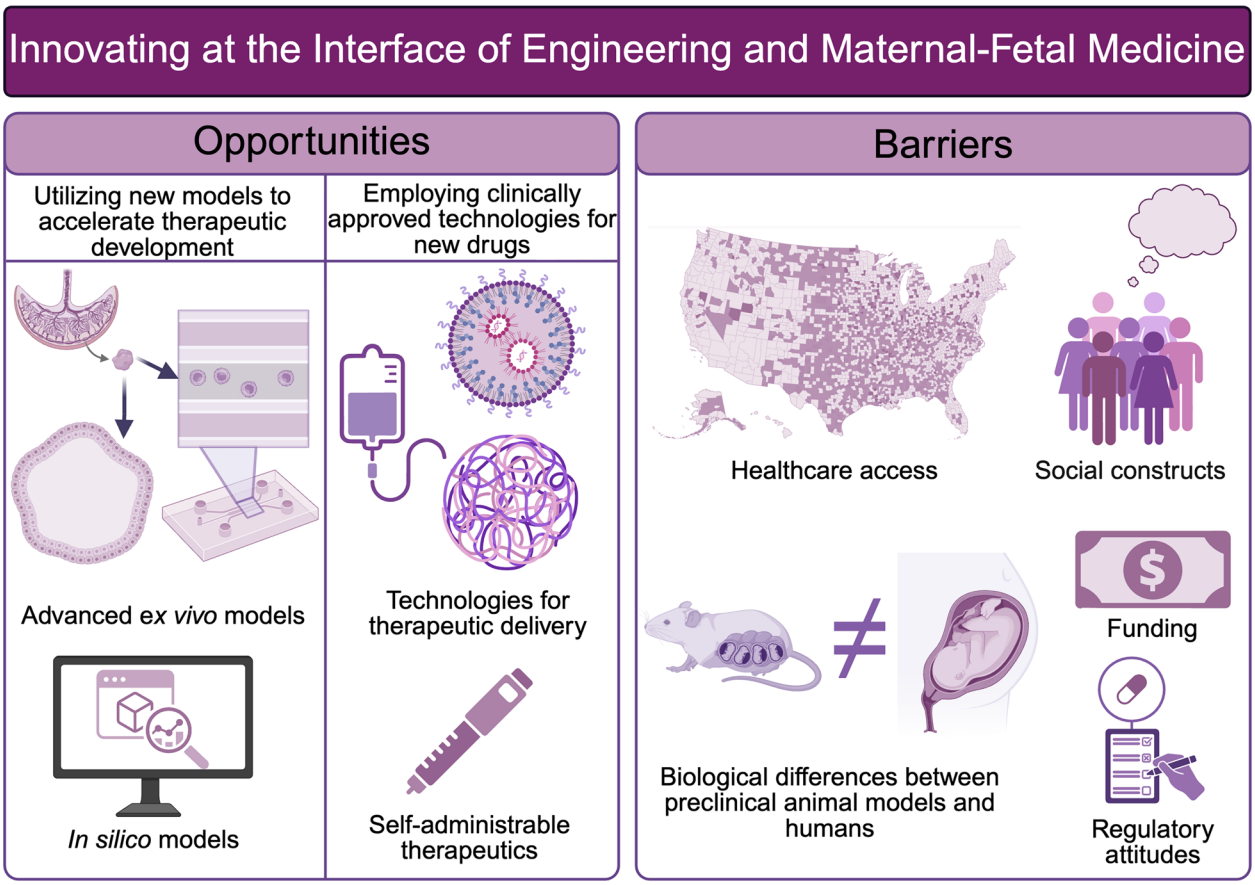

Fig. 1 | Opportunities and barriers to innovate at the interface of engineering and maternal-fetal medicine. Opportunities include cost reduction and increased accessibility approaches such as implementing advanced models and existing drug technologies with regulatory approvals to accelerate therapeutic development. Barriers to innovation include social stigmas, funding, regulatory attitudes towards maternal-fetal health, restricted healthcare access, and biological limitations with pregnant animal models, all of which make translation challenging. Created in BioRender. Howlett, T. (2026) https://BioRender.com/1zfdvrs.

speeding up and bringing down the cost of preclinical development. However, major physiological differences exist among humans and other species, especially in the context of pregnancy; these differences can pose substantial challenges when utilizing animal models for therapeutic assessments. For example, humans have a distinct placental structure compared to many of the commonly used laboratory animals such as mice and rats. One difference lies in the cellular barriers that separate maternal and fetal blood spaces in the placenta, making it difficult to assess and compare drug transport across the placenta between species. Similarly, differences in placental tissue invasion into the uterine environment and degree of spiral artery remodeling make it hard to model and study placental disorders like preeclampsia in the preclinical setting[6]. While animal models are informative and suggest future therapeutic potential, these physiological differences can make translating maternal-fetal medicines tested on non-human models quite challenging and therefore require utilization of complementary models.

To address these challenges, recent efforts have sought to shift preclinical research away from sole reliance on traditional in vitro and ex vivo models by incorporating more advanced and physiologically-relevant human-based models to study and understand maternal-fetal health. Agencies like the U.S. NIH and FDA are advocating for human-based models to replace and reduce the use of animals and a similar regulatory outlook is occurring in Europe, with a goal to eventually phase out animal tests. Yet rationally designed, physiologically-relevant, and easy-to-implement models for studying maternal-fetal health are still being developed[7]. Increasing interdisciplinary collaborations will be key to accomplish these new goals and to promote therapeutic innovation in maternal-fetal health.

For example, an interdisciplinary team of bioengineers and an OB-GYN physician scientist has engineered placenta-on-a-chip models that recapitulate human placental physiology while also employing primary human cells in the chip design[8]. This model gives researchers the ability to study human placental invasion and implantation in the lab, a process that can be difficult to study in animals because of the physiological differences mentioned above. Advanced ex vivo models allow more direct assessments of therapeutic efficacy on their intended target cell type, allowing researchers to more accurately predict human tissue responses and increase translational impact compared to animal models.

Throughout the model design process, it is important to consider the balance between model complexity—to accurately recapitulate human physiology—and capacity for utilization in non-expert labs. Many of these engineered systems for maternal-fetal health may be difficult to deploy for teams lacking access to primary human clinical samples, thereby limiting their broad utility as state-of-the-art models. Along with advanced physical

models, in silico or computer-based models can serve as valuable predictors for drug and therapeutic performance in vivo, accelerating research efforts by allowing bench scientists to focus only on lead therapeutic candidates. While this area is relatively under-explored, teams have worked to build in silico models of placental tissue, opening the door for tremendous impacts of computational workflows on maternal-fetal medicine[9].

Engineering therapeutic technologies with translational promise

To make a translational impact, there are additional design considerations beyond those that impact therapeutic efficacy that may be important to identify early in the design process, such as stability, ease of administration, and cost. As pregnancy disorders like preeclampsia and preterm birth have greater incidence rates and healthcare burdens in low- and middle-income countries (LMICs), considerations for cost and stability become especially relevant. Engineering thermal stability into therapeutic solutions greatly increases accessibility and can contribute to cost reduction if cold chain storage and transportation can be bypassed. This was particularly challenging for the COVID-19 mRNA vaccines manufactured by Moderna and Pfizer/BioNTech which required complicated cold storage and transportation, significantly impacting their rapid deployment in LMICs. Working with materials that can be lyophilized (freeze-dried) or have incorporated excipients to promote long-term stability at ambient temperatures can enable distribution to a much larger patient population across the globe.

Once a therapeutic is distributed to an area, there may not be a healthcare professional available to administer it. Self-administrable technologies are a potential solution to making advanced therapeutics more translatable and accessible, especially in lower access areas, as they lessen the need for advanced medical facilities and trained staff for implementation. For self-administration and selective drug targeting to the female reproductive tract, vaginal delivery is a promising administration route that teams are currently exploring for the treatment of pregnancy disorders such as preterm birth[10].

One approach for reducing drug product costs relies on employing materials with established regulatory, manufacturing, and distribution processes. FDA-approved delivery technologies—like nanoparticles with the capacity for modular cargo swapping—that have demonstrated strong clinical efficacy and have robust manufacturing procedures allow newer formulas to be produced with minimal investment in new manufacturing infrastructure. Considering mRNA therapeutics specifically and the engineered delivery technologies—lipid nanoparticles—that are used to transport mRNA into the body, this platform offers significant translational promise for maternal-fetal medicine. Due to their implementation during the COVID-19 pandemic, there is an extensive body of literature, including meta-analyses and clinical data, that point to the safety and efficacy of COVID-19 mRNA vaccines for use during pregnancy[11]. These data suggest a strong potential for accelerated translation of mRNA-based drugs for maternal-fetal health to the clinic. Groups such as ours are working to redesign and repurpose this FDA-approved delivery technology to treat pregnancy disorders like preeclampsia[12].

Expansion of mRNA therapeutics into maternal-fetal medicine is just one example of how recognizing similarities across diverse scientific disciplines can contribute to expediting research, closing the healthcare gap sooner for pregnant patients. In these instances, strong collaborations amongst teams that engineer new therapeutics and those with expertise in reproductive and maternal-fetal biology can enable repurposing of existing therapies for understudied conditions. Recent advances in this space include efforts for maternal-fetal autoimmune diseases[13], which are rare and dangerous due to a lack of therapeutic options. Therapeutic antibodies are well-established in the clinic for many autoimmune conditions, and these successes could provide a framework for developing treatments for pregnancy disorders like fetal/neonatal alloimmune thrombocytopenia. In pregnant patients with this condition, fetal platelets are targeted by the mothers' immune system leading to platelet destruction. One monoclonal antibody therapy recently approved for generalized myasthenia gravis is currently being tested to target the maternal immune system for preventing fetal platelet destruction in this autoimmune disorder of pregnancy. Similar redesign and repurposing of therapeutic antibodies could be translationally impactful to develop treatments for other maternal-fetal conditions with immune implications.

As we notice recent growth with dedicated women's health funding, teams will have the opportunity to play catch-up by identifying new pregnancy biomarkers to serve as therapeutic targets in maternal-fetal diseases. With new therapeutic targets comes the opportunity for translation-focused research seeking to repurpose safe and effective technologies for pregnant patients. Simultaneously, we must ensure that efforts are dedicated towards designing, engineering, and testing drugs that people will want and are able to take while pregnant. To achieve these goals, the field must foster new opportunities for collaborative conversations amongst engineers, physician scientists, patients, regulatory officials, and providers; we believe these conversations must happen early in the design process to help steer maternal-fetal medicine research in a meaningful way. To initiate this process, researchers should prioritize cross-disciplinary literature review in conjunction with needfinding to identify collaborative relationships with a strong potential for research synergism. Teams from diverse disciplines must recognize both the unmet needs and the state-of-the-art approaches across their collective fields in order to pursue truly interdisciplinary research for maternal-fetal health.

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Competing interests

K.L.S. has filed a patent application related to one of the studies discussed in this article. The other authors declare no competing interests.

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