Another Consequence of Overturning *Roe*: Imperiling Progress on Clinical Research in Pregnancy

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In recent years, tremendous progress has been made toward recognizing the need for improved medical knowledge for pregnant people, a population group that has long been excluded from clinical trials and suffered the harms that result from a poor evidence base to inform care (Lyerly, Little, and Faden 2008). From the National Institutes of Health (NIH) to the Food and Drug Administration (FDA), federal agencies have signaled strong support for closing knowledge gaps in pregnancy, in part through advancing responsible inclusion of pregnant individuals in clinical research (e.g., FDA 2018; PRGLAC 2018). As evidence of progress, a new National Academies report on improving representation in clinical trials emphasizes that a more equitable research enterprise would be responsive to the clinical needs of pregnant people (NASEM 2022).

Yet this hard-won progress is now in jeopardy as the U.S. contemplates a post-*Roe* landscape. Indeed, as Paltrow, Harris, and Marshall (2022) so powerfully illustrate, the consequences of abortion restrictions extend far beyond abortion access and care. Here, we highlight another potential consequence of ending *Roe* beyond abortion access: interrupting—or reversing—critical progress around biomedical research in pregnancy.

Debates about abortion have long shaped approaches to biomedical research and its regulation. The 1970s were a time of major transformation in both reproductive rights and research ethics in the United States. When *Roe* was decided in 1973, the field of bioethics was just taking shape. The year before *Roe* saw the Tuskegee study exposed, and the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research began its work in 1974. *Roe* provided key context to the deliberations of the Commission, which promptly took up the issue of research involving the fetus (National Commission 1975). The basis of research protections as we know them today was developed during this decade, at a time when the right to abortion had recently been codified, if hotly debated.

More than a cultural backdrop, concerns about abortion were central to the development of federal regulations governing biomedical research with women and pregnant people. In 1975, federal “protections” were added—Subpart B of 45 CFR 46—that restricted pregnant women from being involved in research if specific criteria are not met (DHEW 1975). In 1977, the FDA

recommended that *all* women “of childbearing potential” be excluded from early-phase clinical trials (FDA 1977). These changes promulgated the notion of the fetus as uniquely vulnerable to research harms. After the highly publicized episode of thalidomide in the 1960s, which epitomized the possibility of drug-related harm to pregnancies, the debates over *Roe* furthered the rise of a protectionist ethic with regard to women’s participation in research (Johnson and Fee 1994) and had a “chilling effect” on all research that involved women of reproductive age (McCarthy 1994).

Even as legalization of abortion informed a research agenda that emphasized the vulnerability of the fetus and the need to protect it from research-related harm, access to safe abortion has been the (contested) presumption against which research with women—pregnant or not—has taken place. Indeed, it is worth remembering that *all* research regulations in the U.S.—Common Rule, Subpart B, etc.— have been devised and deployed in the context of abortion being legal. We fear that the changing legal landscape in the U.S. threatens progress in addressing key evidence gaps in the care of women and pregnant people. Just as *Roe* had consequences for the evolution of research with women and pregnant individuals, so, too, will its reversal.

One concern is the impact of abortion restrictions on interventional research in pregnancy—trials designed to characterize dosing, efficacy, and safety of drugs to treat or prevent maternal disease. These trials almost always are therapeutically oriented, aimed at improving outcomes for the pregnant person and the fetus. Yet such trials have long been stymied by the fear of fetal harm, such as possible drug-related birth defects or miscarriage risks, even where the risks of untreated disease are significant for the pregnant person, fetus, or both. For example, despite strong advocacy from research and bioethics communities, pregnant people were excluded from trials that led to authorization of COVID-19 vaccines, even though they constitute a high-risk group. It is easy to imagine that in a legal context where fetal harm is more likely to result in criminal penalties, especially among women of color (Paltrow, Harris, and Marshall 2022), the research community might conclude that a study with pregnant persons is too risky to justify—to funders, to research oversight boards, or to pregnant persons themselves. The changing legal reality may also expand liability concerns which already cast a dark shadow across research. In short, the overturning of *Roe* could be another barrier to the inclusion of pregnant persons in ethically responsible and urgently needed biomedical research aimed at optimizing health outcomes for childbearing people and their children.

Criminalization aside, restrictions on abortion raise other ethical concerns for such trials. For instance, a trial participant may desire termination of pregnancy in the rare circumstance where participation in the study is associated either with fetal harm or with prolonging a pregnancy where maternal health is in danger (e.g., severe pre-eclampsia). Indeed, current guidelines from the Council for International Organizations of Medical Sciences (CIOMS 2016) state, “Research with pregnant women must be conducted only in settings where these women can be guaranteed access to a safe, legal abortion.” Though controversial, given their potential to restrict biomedical research in pregnancy in settings where it is needed most, such guidelines reflect the ethical complexities of conducting research where reproductive rights are constrained. Should *Roe* be overturned, questions will undoubtedly be raised about whether it is

ethical to conduct a study where fetal risk in humans is unknown (as it is for more than 90% of drugs on the market, and for all drugs in development), or whether interventions that might prolong a dangerous pregnancy can be ethically studied.

A second concern is the impact that overturning *Roe* will have on the ethics of maternal-fetal therapy intervention trials. Such trials usually focus on optimizing pediatric outcomes either through medical or surgical intervention during pregnancy. They have been critical to developing an evidence base for maternal-fetal surgery through carefully designed studies, such as the MOMS (management of myelomeningocele) study that characterized risks and benefits of pre-birth closure of fetal neural tube defects. But the ethical conduct of such trials depends, if implicitly, on access to safe abortion. For one, informed consent for such trials has relied on there being three options for a pregnant person to consider: termination, neonatal (post-delivery) intervention, and maternal-fetal surgery. Absent the option to end an affected pregnancy, some individuals considering participation will be unwillingly pregnant—and arguably already deciding about participation from a position in which autonomy has been violated (Lyerly, Verite, and Marshall 2022). Additionally, there is reason to worry that if such procedures were shown to be beneficial to the child, maternal-fetal surgery could become another context for coerced intervention, even as such surgeries entail substantial risk to the women who undergo them.

The third—and obvious—consequence of overturning *Roe* will be further limits on research involving pregnancies that will not continue. Regardless of its legality, pregnant people will continue to seek abortion; clinical research is critical to ensure high-quality care (Harris 2016). Moreover, research on fetal tissue obtained after abortion or miscarriage has led to important advances in medicine and science, including vaccine development and understanding and treatment of disease. Data indicate that individuals who have been pregnant support fetal tissue research in general; many consider it a way to make meaning of reproductive loss (Spach et al. 2021).

Finally, it is critical to note that overturning *Roe* is likely to affect research with women more generally. The default exclusion of women from most clinical research gave way to new imperatives in the 1990s, when the NIH and the FDA developed guidance recognizing the importance of including women and minorities in clinical trials. Though evidence gaps remain, progress has been made in gender parity, made possible in large part by studies that require use of effective contraception. As many have suggested, abortion restrictions are likely to be followed by proscriptions on contraceptives such as intrauterine devices and post-coital methods. As such, almost *all* biomedical research that involves women of reproductive age is in peril in a post-*Roe* context.

We and others have argued elsewhere that the absence of research puts women, pregnant people, and their children in harm's way: they may be given medications that are unsafe for them or the fetus; they may be given the wrong dose of medication leading to toxicity or undertreatment; or they may be denied access to critically needed treatment or prevention. To the extent that overturning *Roe* threatens research, it further threatens the health and safety of

women, pregnant people, and children. Additionally, without data to inform safety, pregnant people may seek to end pregnancies out of concern that they have used a drug or vaccine that is unsafe for the fetus, as has been observed with rubella (Lyerly, Robin, and Jaffe 2017). Restricting abortion while condemning women to a poor evidence base redoubles the violation overturning *Roe* entails—a clear violation of reproductive justice.

Such backward movement would dampen other recent advances in regulatory and cultural understandings of pregnant women. In the revised Common Rule, pregnant women, as a category, were removed from the "vulnerable populations" list, a longstanding designation in research regulations that was used as a basis for denying pregnant people access to clinical research studies. This welcome change acknowledged that pregnant people do not have diminished capacity to consent to research; they are capable individuals who can determine their own needs and risk tolerance. Abortion restrictions fly in the face of the fact that women can make decisions for themselves. In circumstances where women's rights are broadly circumscribed and gestation is enforced—where women are unable to protect their interests or access medical care, where their bodily integrity is routinely threatened—vulnerability is a potent concern (see CIOMS 2016; Macklin 2012). Rather than being a settled matter, the labeling of pregnant people on the whole as "vulnerable" may unfortunately be debatable yet again in a post-*Roe* world.

As Paltrow, Harris, and Marshall note, "*Roe* protects all pregnant women, not just those seeking abortion." It took fifty years to get to the point of widespread consensus for the need to improve the biomedical knowledge base for pregnant people. If research in pregnancy is obstructed anew, evidence gaps will also continue, and women, pregnant people, and fetuses will be worse off—exposed to medical care uninformed by adequate evidence. In a post-*Roe* world, pregnant people will face the double injustice of lack of access to reproductive care and lack of medical knowledge that should inform it.

FUNDING

Waggoner is supported by the Greenwall Foundation Faculty Scholars Program and the National Science Foundation (Award 1945448). Lyerly is supported by a grant from the National Institutes of Health (Award 2 R01 AI108368-05). The content of the article is solely the responsibility of the authors and does not necessarily represent the official views of the sponsors.

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