On the importance of including pregnant women in clinical trials: A Q&A

As a research scientist, I've negotiated the complex nature of getting approval to image human subjects. So I know firsthand that it is common to exclude pregnant women from clinical trials. Although this practice is well-intentioned, it is also misguided – according to an opinion piece recently published in *JAMA*. To learn more, I spoke with one of the authors, Heather Byers, MD, a clinical assistant professor in pediatrics at Stanford.

Why are pregnant women excluded from clinical trials?

> *Historically, women in general were excluded from clinical trials because men were thought to be a more homogenous group without hormonal cycles and other sex-based variables that might impact the medical conditions under study.*
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> *In addition, pregnant women are still classified as a 'vulnerable' population for all research studies, so investigators must take additional steps to enroll them to ensure minimum risk. Also, the lack of data about what pregnant women can safely be exposed to leads to more uncertainty. So many investigators choose to exclude them, even if they might benefit from the study intervention.*

Why is this a problem?

> *Excluding them is a problem because women don't stop getting sick or stop having chronic medical conditions just because they are pregnant. The average woman is exposed to four medications during her pregnancy and over 80 percent of medications haven't been studied in a like population. This*

forces pregnant women to take medications on an "off-label" basis – meaning, the medications weren't studied or approved for use in pregnant women – because there's no other option. Pregnant women deserve better. It's a matter of justice.

What are the barriers and how do we overcome them?

First, we advocate reclassifying pregnant women from 'vulnerable' to 'scientifically complex.' Pregnancy doesn't alter a woman's capacity for autonomous decision-making. Indeed, a pregnant woman frequently makes complex medical decisions for herself and her fetus that reflect her family's values.

Another barrier for medical investigators is the perceived legal risk regarding a potential adverse outcome in the fetus or mother. As we discuss in the JAMA Viewpoint, this barrier could be addressed by standardizing the informed consent process.

Finally, federal regulations don't define 'acceptable risk' to the woman or fetus and this uncertainty is perceived as a risk in itself. But in some cases, pregnant women may accept the uncertainty and risk.

For example, it was imperative to reduce mother-to-child transmission of HIV. So obstetricians reluctantly included pregnant women with HIV in their study of antiretroviral treatments, since the risk of the drugs were thought to be low and the potential benefit high. And the effectiveness of this study helped transform the AIDS epidemic.

Is progress being made?

Although progress has been slow, there has been an increased effort to enroll pregnant women. Several high-profile clinical trials involving pregnant women recently completed and institutions like the National Institutes of Health are

working to change their polices. For example, the NIH Task Force on Research Specific to Pregnant Women and Lactating Women recently issued a report that summarizes the current gaps in knowledge and provides recommendations for continued progress.

How did you become involved?

I first became interested in this subject as a medical student during my rotation at NIH with Pamela Stratton, MD, one of the obstetricians involved in the study of antiretrovirals to prevent vertical transmission of HIV.

Later, as an obstetrics resident, I was frustrated by the lack of information to share with my patients regarding the risk and clinical impact of various medications, vaccines and medical conditions in pregnancy. Every anecdotal story – such as my patient who was hospitalized in intensive care for months with influenza because she'd been too afraid to get the flu vaccine earlier in her pregnancy – is one too many. There should be a better way.

One thing that has changed is the rise of social media and patient support group accessibility. Although this should not replace the controlled setting of a clinical trial, partnerships between motivated patient advocacy groups and medical investigators can be a powerful tool for obtaining information about risk and benefits going forward.

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