Exclusion of mothers-to-be from clinical studies unfair and potentially harmful

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The widely accepted principle that mums-to-be are a 'vulnerable' group unfairly excludes them from taking part in clinical studies, and perpetuates the knowledge void around the impact of drugs taken during

pregnancy, conclude researchers online in the *Journal of Medical Ethics*.

There is a pressing need to break this vicious circle to gather hard evidence, because drugs such as antibiotics and treatments for asthma and nausea are increasingly being prescribed to, and taken by, pregnant women, they emphasise.

And despite the use of 'vulnerability' as a reason to routinely exclude pregnant women from clinical studies, there is no universally accepted definition of this term, they argue.

In a bid to try and explore whether, and if so, to what extent, pregnant women really are vulnerable, the researchers looked for published evidence citing reasons for this presumption.

They used the ethical principles for research participants, set out in 2008 by Samia Hurst, as a working definition of vulnerability.

Out of 65 relevant studies, 13 were included in the final analysis. Four main themes emerged: informed consent (9 studies); susceptibility to coercion (7); heightened risk because of lack of scientific knowledge (7); and the vulnerability of the developing fetus (6).

Although informed consent could be compromised because of the need to weigh up the pros and cons not only for themselves, but also for their baby, particularly in the absence of evidence to inform their decision, "there is no immediately obvious reason to assume that pregnant women are incapacitated during pregnancy," insist the authors.

There are other situations where few/no data make it very difficult to give truly informed consent: patients with orphan diseases or elderly patients, they say.

The idea that pregnant women would be subject to coercion because of their own and society's desire to protect the developing fetus is rather paternalistic, and not really warranted, they suggest.

The vulnerability of the fetus may be an issue, primarily because there isn't enough scientific data on the potential impact of drugs taken during pregnancy, particularly new drugs. But the fact the unborn child can't speak for him/herself is no reason for vulnerability; it only means there should be a surrogate decision-maker, which is the pregnant woman, they say.

Therefore, "there is no reason to assume that the vulnerability of the fetus renders pregnant women increasingly vulnerable in comparison with ordinary research subjects," they write.

In fact, pregnant women's vulnerability boils down to the lack of research carried out in this group, and it's a dilemma that can only be overcome by including mums-to-be in clinical studies, they say.

"Our study once and for all demonstrates that there is no indication that pregnant women are vulnerable because of informed consent, susceptibility to coercion, or vulnerability of the fetus," they write.

"The only reason why pregnant women are potentially vulnerable in clinical research is to the extent that they are increasingly exposed to higher risks due to a lack of scientific knowledge which might render them vulnerable as research subjects," they continue.

"Only a joint effort to promote fair inclusion by funding agencies, drug authorities, researchers, methodologists, pharmacologists, guideline committees and [research ethics committees] can successfully reduce pregnant women's vulnerability," they conclude.

In a linked Commentary, Drs Carleigh Krubiner and Ruth Faden, of the Berman Institute for Biothethics at Johns Hopkins University, Baltimore, argue that the designation of pregnant women as 'vulnerable' "is inappropriate and disrespectful."

And rather than protecting them, it has had the opposite effect, and created a great deal of uncertainty and anxiety.

Of the 172 drugs approved by the US regulator, the FDA, between 2000 and 2010, nearly all (97%+) had an "undetermined" risk for pregnancy. And the average length of time to find out how safe drugs are in pregnancy is 27 years, they point out.

"There is a desperate need to shift the paradigm to protect pregnant women through research, not just fromresearch," they write.

The powers that be are starting to take this on board, recognising the scientific and ethical importance of including them in research. And now is the time to move the agenda forward, they suggest.

"With the recent emergence of the Zika crisis and the rapid pace of vaccine development, we have a crucial opportunity to demonstrate what proactive and intentional inclusion of pregnant women's interests in the R&D agenda looks like," they conclude.

More information: Vulnerability of pregnant women in clinical research, *Journal of Medical Ethics* (2017). DOI: 10.1136/medethics-2016-103955

Commentary: Pregnant women should not be categorised as a 'vulnerable population' in biomedical research studies: ending a vicious cycle of 'vulnerability' *Journal of Medical Ethics* (2017). DOI: 10.1136/medethics-2017-104446

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