# Ethical issues in therapeutic use and research in pregnant and breastfeeding women

Ethel Weld<sup>1</sup>, Theodore Bailey<sup>2</sup>, and Catrionia Waitt<sup>3</sup>

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#### Abstract

Pregnant, or potentially pregnant women have historically been excluded from clinical trials of new medications. However, it is increasingly recognised that it is imperative to generate evidence from the population in whom the drugs are likely to be used in order to inform safe, evidence-based shared clinical decision making. Reluctance by researchers and regulators to perform such studies often relates to concerns about risk, particularly to the fetus. However, this must be offset against the risk of untreated disease or using a drug in pregnancy where safety, efficacy and dosing information are not known. This review summarises the historical perspective, the ethical and legal frameworks which inform the conduct of such research, then highlights examples of innovative practice which have enabled high quality, ethical research to proceed to inform the evidence-based use of medication in pregnancy.

#### Hosted file

Ethics in Pregnancy Final Draft.pdf available at https://authorea.com/users/403986/articles/515306-ethical-issues-in-therapeutic-use-and-research-in-pregnant-and-breastfeeding-women

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<sup>&</sup>lt;sup>1</sup>Johns Hopkins University School of Medicine

<sup>&</sup>lt;sup>2</sup>Greater Baltimore Medical Center

<sup>&</sup>lt;sup>3</sup>University of Liverpool

## Idea 1: Commensurable with Non-Pregnant Population

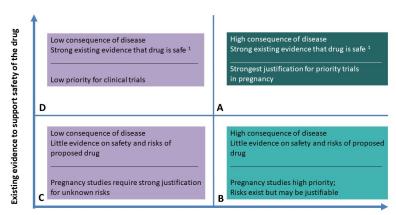
No differences between general population and pregnant population Information from all research participants provides similar data Research question can be addressed without including pregnant women Risks to pregnant woman and fetus cannot be justified

Non-Pregnant Population Pregnant Population

## Idea 2: Incommensurable with Non-Pregnant Population

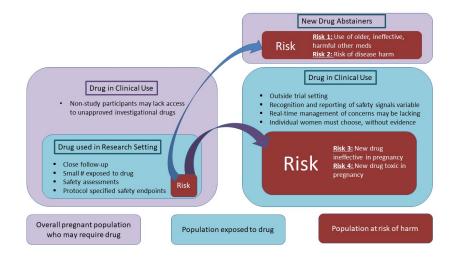
Physiological changes in pregnancy likely to impact disease, drug exposure, or effect Safety, efficacy and dosing from general population cannot be assumed to inform that in pregnancy

Research question can only be addressed by including pregnant women
Potential risk to pregnant women and fetus can be justified
Not to include pregnant women in research brings risk



### Consequence of untreated/ undertreated disease

¹(from trials, pharmacovigilance systems, etc.)



# Scenario 1: Ebola Virus Disease Therapeutics (Urgent Gap-Filling Research)

Risk of death in untreated mother: >80%
Risk of infant death without treatment: 100%
Highly infectious, person to person spread
Outbreaks in regions with poor infrastructure and
access to medical care

Potential benefits of vaccine or therapeutic: Very high Tolerance of potential risks: Even moderate risks likely to be considered acceptable

#### Scenario 2: Alternative formulation of existing safe and effective drug. Example: antiretroviral tenofovir ("Me-Too" Research)

Risk of death with existing regimen: Very low Risk of infant infection with existing drug: Very low Risk of therapeutic failure with existing drug: Same as proposed alternative as same active compound

Potential benefits of new drug: Incremental Tolerance of potential risks: Need to have clear justification for use in pregnancy