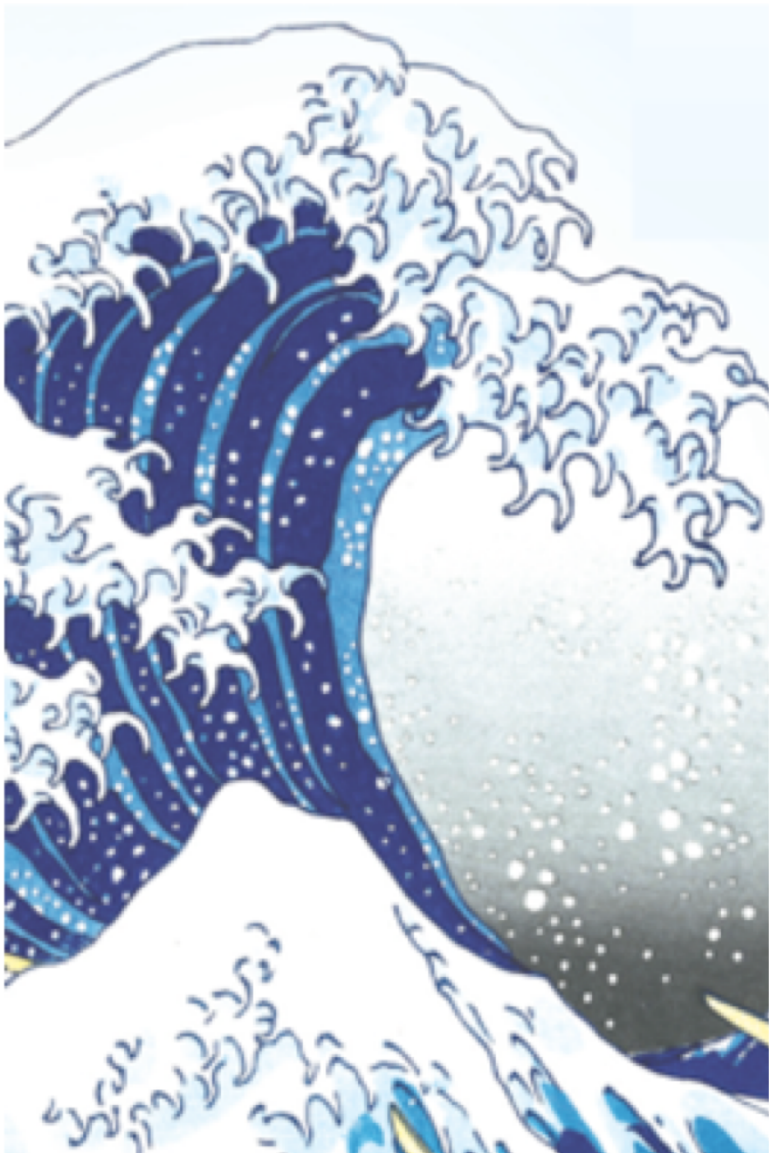




# Clinical research with pregnant women: historical context & ethical considerations

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Maggie Little, BPhil, PhD  
Director, Kennedy Institute of Ethics



Toward the Responsible Inclusion of  
Pregnant Women in Medical Research

THE SECOND WAVE INITIATIVE

PHASES  
PREGNANCY + HIV/AIDS  
SEEKING EQUITABLE STUDY



Pregnancy Research Ethics  
for Vaccines, Epidemics,  
and New Technologies

PREVENT



# Background

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- Women in general underrepresented in research studies in the early 1990s
- 1993 NIH Revitalization Act
- Women are now more than half of all research participants (though sex-specific outcomes still need more attention)
- But research with pregnant women still lags far behind

# Disease burden in pregnancy

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In the US, approximately 4 million women give birth each year

Many face medical conditions:

- Hypertension (5%; 190,000)
- Diabetes (4%; 150,000)
- Psychiatric disorders (~15%; 500,000)
- Lupus, cancer, et cetera

Globally, approximately 130 million women give birth each year

Many face medication conditions:

- HIV (~16% in Southern Africa)
- Malaria (30 million at risk globally)
- Active TB (216,500 globally)
- Emerging epidemics, et cetera

# “Pregnant women as drug orphans”

(Scaffidi, Mol, and Keelan, 2017)

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- 98% of drug treatments approved by the U.S. FDA since 2000 have insufficient data to determine teratogenic risk
- 75% of drugs approved since 2000 do not have human pregnancy data

Why is this evidence gap a problem?

# 1. Efficacy

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Pregnant women need effective prevention and treatment

Pregnancy can change PK/PD and dosing

Example: glyburide

## 2. Fetal safety

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Pregnant women need preventives and treatments that are safe for use during pregnancy

Some drugs are problematic for fetal health: teratogens, low birthweight, et cetera

Example: ACE inhibitors during first trimester of pregnancy



# 3. Reticence

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The absence of evidence can lead to:

- Reluctance to use needed medication
- Reliance on older or less effective treatments

# 4. Justice

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Justice for the class of pregnant women and their offspring



# 4. Justice

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Justice for individuals

Fair access to trials involving the “prospect of direct benefit”

Example: Zika



N Doce / Reuters 2016

# Endorsement for responsible research with pregnant women

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- Pan American Health Organization
- American College of Obstetricians and Gynecologists
- Council for international Organizations of Medical Sciences
- 21<sup>st</sup> Century Cures Act

Research with pregnant women: allowed?

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YES!

# Subpart B

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2001 revision of HHS 45 CFR 46:

- “Pregnant women or fetuses may be involved in research if all of the following conditions are met”:
  - Background evidence on risks
  - If prospect of direct benefit, reasonable ratio of risks to benefits
  - If no prospect of direct benefit to either woman or fetus, risks to fetus capped at “minimal”



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