



Guidance for the Future: Toward an Ethics of Including Pregnant Adolescents in Research

Anne Drapkin Lyerly, MD, MA
University of North Carolina at Chapel Hill



THE UNIVERSITY
of NORTH CAROLINA
at CHAPEL HILL

HIVR4P
October 6, 2024



Toward a Paradigm of Inclusion



2009



Second Wave Initiative

Toward the Responsible Inclusion of Pregnant Women in Medical Research

2013



PHASES

Pregnancy + HIV/AIDS: Seeking Equitable Study

Guidance launched July 2020
AVAC/PHASES Action Plan 2022

2017



PREVENT

Pregnancy Research Ethics for Vaccines, Epidemics, and New Technologies

FDA Draft Guidance PRGLAC Report 2018

2021



PREPARE

PRomoting Equity for Pregnant Adolescents in REsearch

Ethical Foundations



The PHASES Project



- **Pregnancy and HIV/AIDS: Seeking Equitable Study**
- Funded 2013(R56)/2015(R01)
- US, Botswana, Malawi, South Africa
- Developed frameworks to advance research at intersection of pregnancy and treatment and prevention of HIV and co-Infections
- Advocated for **earlier, better and more evidence** on medications of potential (or current) use in pregnancy

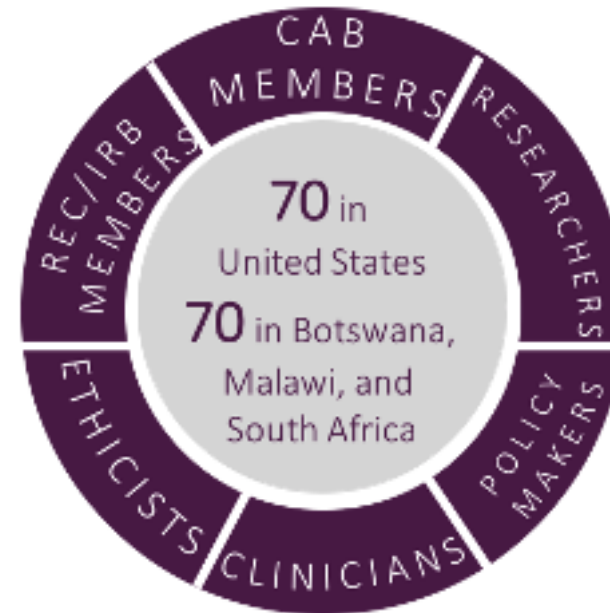
All people deserve safe and effective medication over the course of their lifespan, including during pregnancy, and deserve an evidence base adequate to that fact

The PHASES Project – Built on Engagement

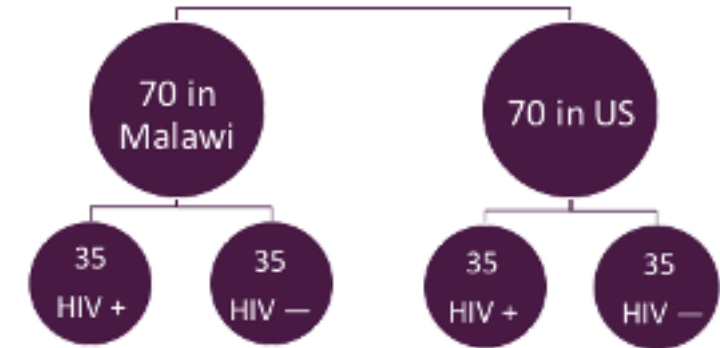


Engagement
Consultations
Empirical Research

140 Interviews with stakeholders



140 Interviews with pregnant/recently pregnant women



Legal & Ethical Analysis

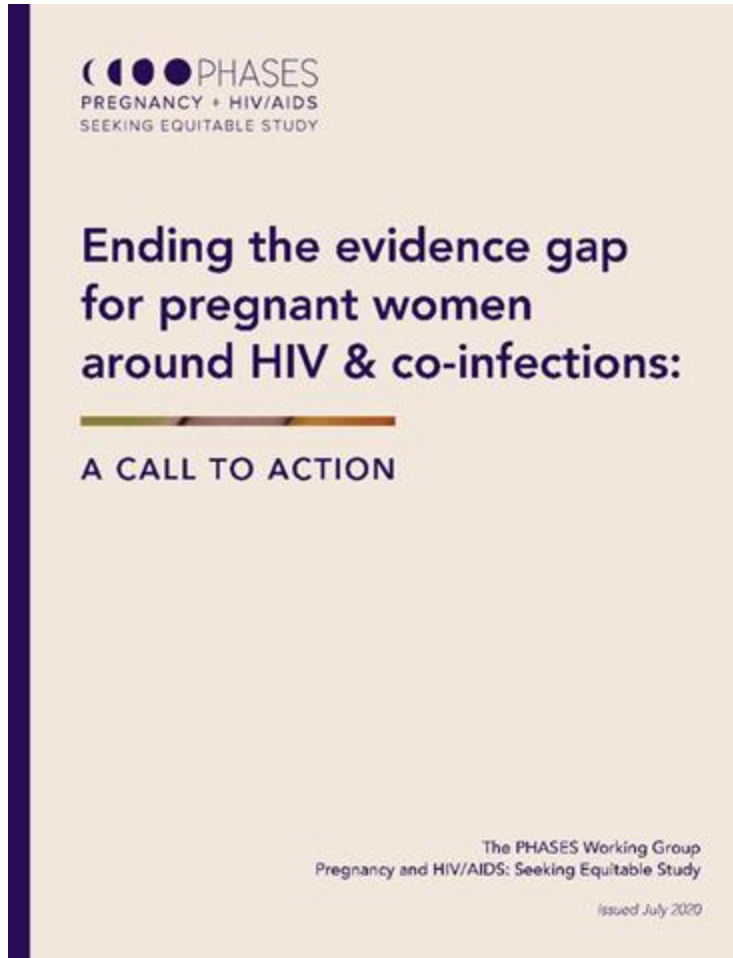


Guidance Development

PHASES Working Group

- 26 members
- Expertise in bioethics, public health, law, obstetrics and maternal-fetal medicine, pediatrics, HIV research, infectious disease, pharmacology and community advocates for women living with HIV
- From Botswana, Kenya, Malawi, South Africa, Switzerland, Uganda, the United Kingdom and the United States.
- Feedback on drafts from subject area experts

PHASES Guidance, 2020



- 12 recommendations, four themes
- PDF available online (scan for website)



Conceptual Shifts

Vulnerable population → *Complex population*

Protection from research → *Protection through research*

Presumptive exclusion → *Fair inclusion*

Evidence of a shifting paradigm



“ [A] **cultural shift is necessary** to emphasize the importance and public health significance of building a knowledge base to inform medical decision-making for [pregnant and lactating women]. **Research on therapies for these populations must be facilitated and greatly augmented.**”

“Filling the knowledge gaps regarding safe and effective use of drugs is **a critical public health need**, but one that raises complex issues”

PRGLAC Task Force on Research Specific to Pregnant and Lactating Women



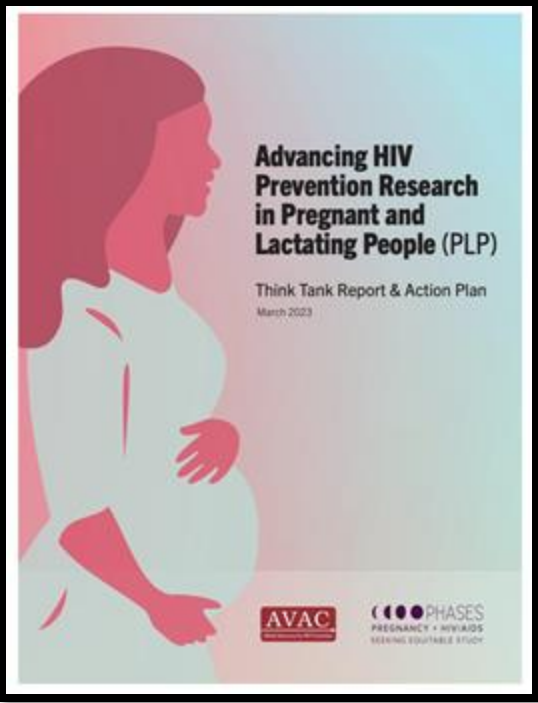
Eunice Kennedy Shriver National Institute of Child Health and Human Development

Healthy pregnancies. Healthy children. Healthy and optimal lives.



Pregnant Women:
Scientific and Ethical Considerations
for Inclusion in Clinical Trials
Draft Guidance for Industry

PHASES – Impact and Engagement



<https://www.who.int/tools/antiretrovirals-in-pregnancy-research-toolkit>

- Ethical considerations
- Community engagement and communication
- Pharmacokinetics and dosing
- Clinical trials and observational studies
- Surveillance studies and registries
- Data harmonization
- Key background references

Ethical considerations

Resources in this section

- Ethical guidelines for research in pregnancy >
- Affirming statements, guidance and reports >
- Tools for research design and evaluation >
- Advocacy and training resources >

Conceptual shifts that support inclusion

The increasing consensus on the ethical imperative to conduct research with pregnant people reflects a trio of conceptual shifts in how we think about research with this population. These include a shift from understanding pregnant people as a vulnerable population to understanding them as a complex population; from the idea that pregnant persons and fetuses should be protected from research to the recognition that they are best protected through research; and from the general practice of summarily excluding pregnant persons from research, without justification (presumed exclusion) to a model in which they have equitable access to both the direct benefits of research and the benefits of a robust evidence base that would result from their fair inclusion in the biomedical research agenda. Further discussion of each conceptual shift can be found below.

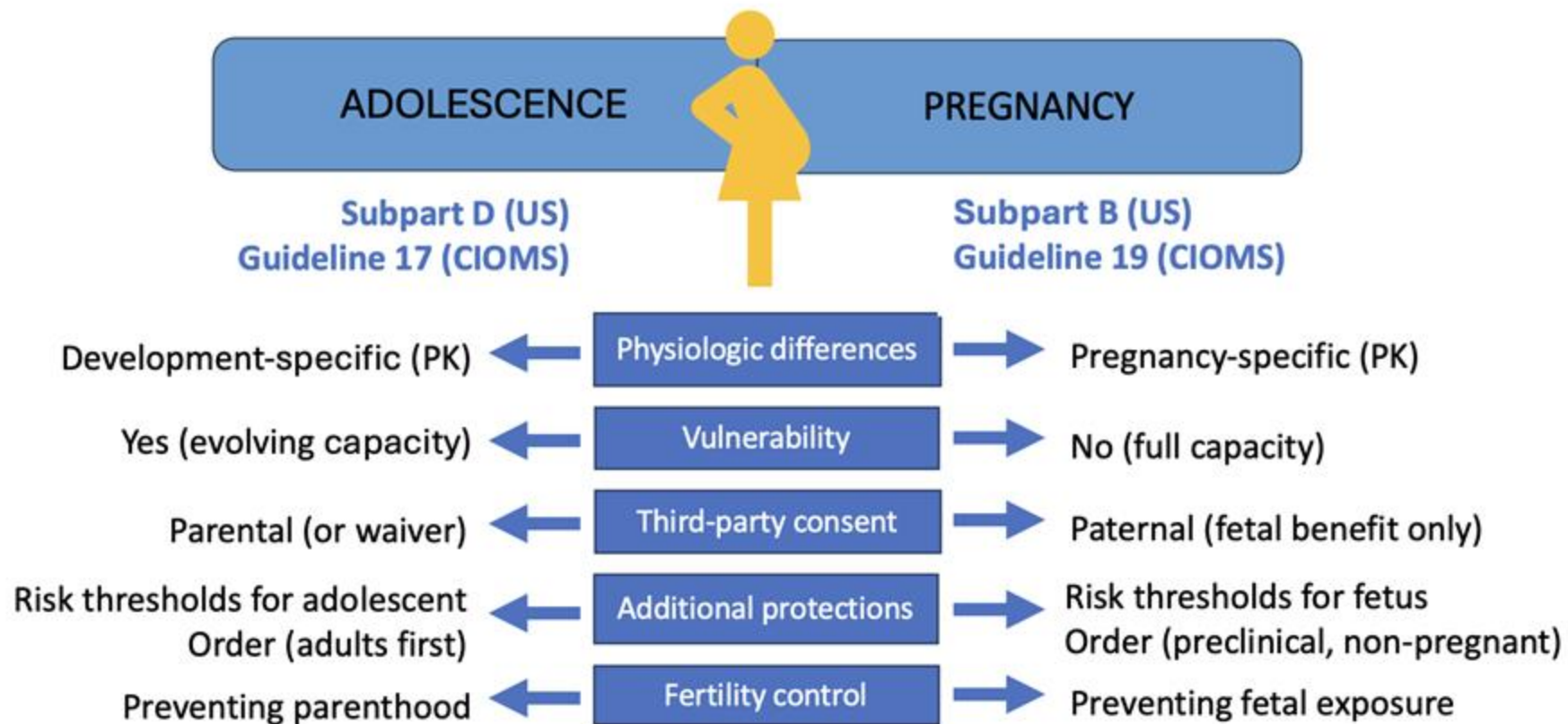


Until recently, pregnant persons were categorized alongside children, prisoners, and individuals with intellectual disabilities as a vulnerable population. Yet unlike these populations there is nothing about pregnancy per se that constrains a person’s ability to provide valid consent or makes them particularly susceptible to exploitation. This designation is therefore inaccurate, and had a chilling effect on research in pregnancy. Ethical and regulatory guidance no longer uses the term vulnerable to describe pregnant people; some instead designate them as a complex population to capture the scientific and ethical complexities that research in pregnancy can bring up.





- Pregnant adolescents face **compounded challenges** in the HIV context: heightened risk of infection and vertical transmission and maternal and fetal morbidity/mortality.
- Remain **broadly excluded** from HIV/co-infections research, resulting in a poor evidence base and unjust research practices



Reproductive Justice

Right to
have children

Right not to have
children

Right to parent in
a safe and healthy
environment

§ **Recognizes** the right to reproduce or not as a **foundational human right**

§ **Corrective** to the reproductive rights-based approach which failed to address systemic inequalities

§ **Elevates and centers** the needs, voices, lived experiences, and leadership of African and other Black and Brown women, transgender and gender diverse people, **and youth**



HIVR4P 2024

The PREPARE Project: Approach



**Engagement/
Empirical Research**



**Conceptual-Analytic
Research**



**Guidance
Development**

The PREPARE Working Group

- 44 members
- Includes researchers, ethicists, policy & legal experts, community-based organizations/advocates, ethics review board members
- Based in/working in US, EU & African countries

Goal: To develop concrete and actionable guidance for advancing timely, ethically responsible HIV/co-infections research with adolescents who are pregnant.

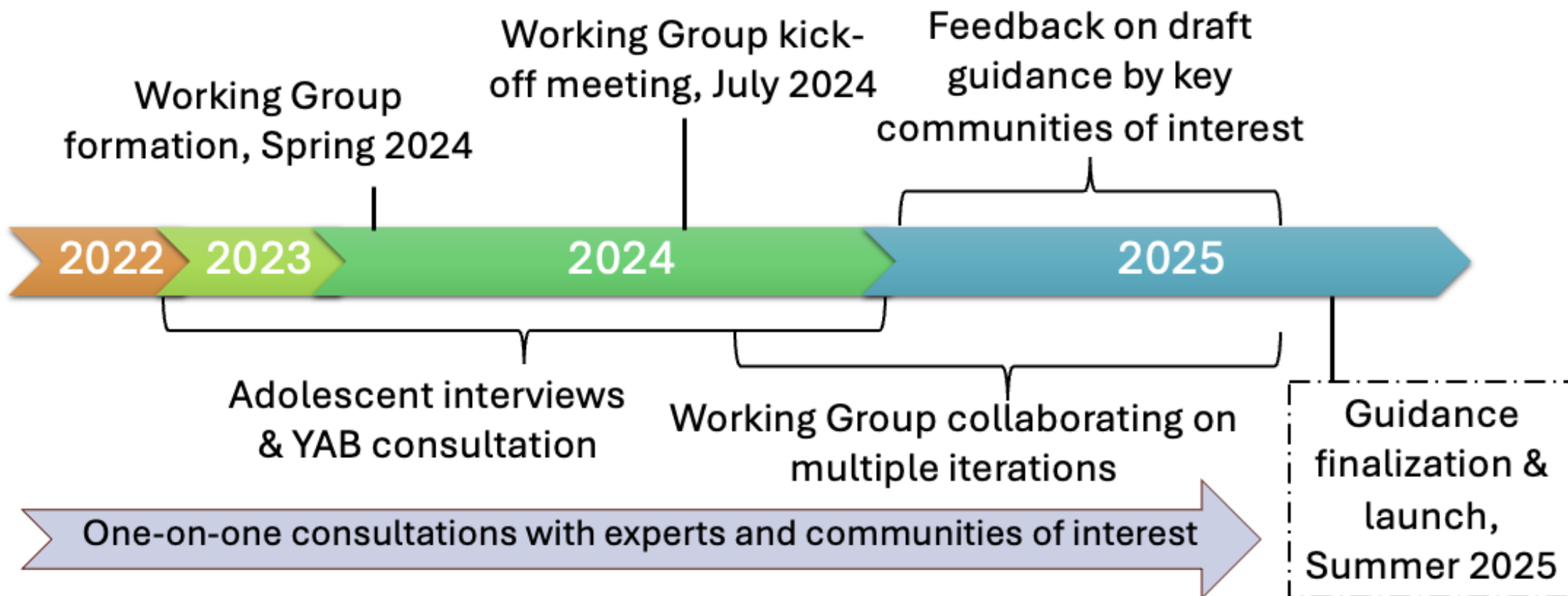
Inclusion of Youth Voices: Youth Advisory Boards (YAB)

'Every child has the right to express their views, feelings and wishes in all matters affecting them, and to have their views considered and taken seriously.'

Article 12 UN Convention Rights of a Child (1989)

- YAB meetings include both instructional activities and guided discussion
- Field notes collected to inform study activities
- YAB members joined the PREPARE Working Group Meeting (Munich, July 2024)

PREPARE Guidance Development Process



Closing thoughts

- Ethics is one of many disciplines needed to advance research in pregnant populations – it is a ***resource, not a barrier.***
- Getting the ethics right requires robust inclusion of voices ***across disciplines and expertise,*** with priority given to those most affected (those living with or at risk for disease and pregnancy).
- Partnerships across projects and organizations can help ensure that guidance is as useful and impactful as possible.



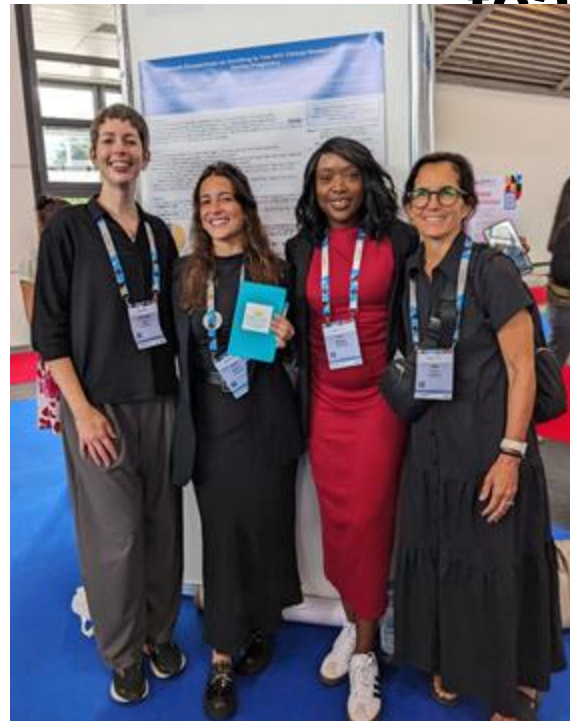
Linda-Gail Bekker



THANK YOU!



To all participants & partners, our YAB, our Working Group, & our study team



PREPARE Website:



Funder:
NIAID

(2R01AI108368)

Contact Info:
alyerly@email.unc.edu