Society for Birth Defects Research & Prevention
EST. 1960 AS THE TERATOLOGY SOCIETY

DNTS DEVELOPMENTAL NEUROTOXICOLOGY SOCIETY

OTIS Organization of Teratology Information Specialists

DENVER COLORADO

Dr. Robert L. Brent Lecture

Accelerating Clinical Development for Maternal-Fetal Health: Ensuring Access to Safe and Effective Medicines for All

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VP, Global Head of Epidemiology & Real World Evidence

ViiV Healthcare

Accelerating Clinical Development for Maternal-Fetal Health: Ensuring Access to Safe and Effective Medicines for All

Outline

- Dr. Robert Brent
- Challenges in Clinical Research for Pregnant Women
  - Importance
  - Implications
- Recommendations from PRGLAC (Pregnancy and Lactation Task Force)
- Update on ICH E21 Guidelines
- Accelerating Clinical Data Generation for Antiretroviral (ARV) use in Pregnancy: A Roadmap
- Call to Action for Stakeholders in Maternal-Fetal Health

Dr. Robert L. Brent Lecture

Reaching New Heights in Birth Defects Research: Fundamentals to Cutting-Edge Research

Dr Brent said that one of the most important papers he has ever written was **“Saving lives and changing family histories: appropriate counseling of pregnant women and men and women of reproductive age, concerning the risk of diagnostic radiation exposures during and before pregnancy”**

Polifka, J.E. and Greenspan, J. (2023), Bob Brent: Scientist, physician, scholar, teacher, mentor, and mensch. Birth Defects Research, 115: 1227-1242. https://doi.org/10.1002/bdr2.2162

Society for Birth Defects Research & Prevention

DNTS Developmental Neurotoxicology Society

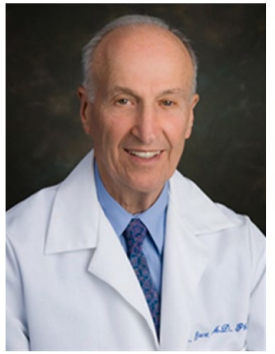
OTIS Organization of Teratology Information Specialists

Dr. Robert L. Brent, M.D., Ph.D., DSc. (1927-2021): Scientist, Physician, Scholar, Teacher, Mentor, and Mensch

Birth Defects Research: Volume 115, Issue 14

Special Issue dedicated to Dr. Robert L. Brent, M.D., Ph.D., DSc. (1927-2021): Physician, Scholar, and Teacher

- World renowned expert on embryonal and fetal radiation exposure
- National and international awards for contributions to the field
- Chairman, Department of Pediatrics at Nemours, Thomas Jefferson Medical College >30 years
- “…one of the greatest perinatologists of all time



Pregnant Individuals as Special Population in Clinical Research

- **People with child-bearing potential (PCBP) are generally excluded from clinical trials if planning a pregnancy & removed from clinical trial if they become pregnant**
- Negative pregnancy test at entry
- Highly effective method to prevent pregnancies is required throughout the study

- **Physiological changes potentially altering the pharmacokinetics and pharmacodynamics**
- Absorption, distribution, metabolism and elimination of drugs
- Increasing drug clearance and decreasing exposure, affecting efficacy
- Changes to all organ systems –CVD/Circulatory, Renal, Respiration, GI, Hepatic
- May require dose adjustment

- **Cross-placental transfer of drug molecules and their metabolites and toxicity**
- Especially during perinatal and 1st trimester the critical period for embryogenesis leading to birth defects

Roadblocks to Data Generation in Pregnant Women

- **Ethical Concerns: Risks, benefits and a “Catch-22” problem**
- Challenges in weighing potential risks and benefits of the research for the woman and the fetus, especially when the interests of one seemingly do not align with the other

- **Legal Concerns: Implications of confusing and complex regulations**
- The HHS regulations for the protection of human subjects in research: Subpart B — Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research
- Cautious interpretations by IRBs and investigators of “minimal risk” for studies holding no prospect of direct benefit to the woman or her fetus

- **Financial and professional disincentives**
- Studies can cost more to conduct, requiring longer-term follow-up, provision of ancillary antenatal care, and potential legal costs linked to liability concerns
- No exclusivity incentive

- **Analytical and logistical complexities**

Task Force on Research Specific to Pregnant Women and Lactating women (PRGLAC)

Task Force on Research Specific to Pregnant Women and lactating women (PRGLAC)

- **1985:** HHS report of the Public Health Service Task Force on Women's Health Issues
  - **Focused broadly on women's issues and included "requirements of postmarket surveillance" and that "adequate numbers of women be included in clinical trials of drugs that will be used by women, and of all new drugs that are to be recommended for use by women.**
- **1993:** The Institute of Medicine and the National Institutes of Health (NIH) Revitalization Act emphasizing the importance of including women in clinical studies
- **1994:** The Institute of Medicine's report, reviewed the importance of including pregnant women in research
  - **"It is critical to note that the committee is not advocating active recruitment of pregnant women into each and every clinical study. Rather, it is urging that the prevailing presumption regarding the participation of pregnant women in clinical trials and other intervention studies be shifted from one of exclusion to one of inclusion. The committee believes that a strengthened informed consent process can address specific concerns regarding the inclusion of pregnant women in clinical studies."**
- **2000-2016:** FDA draft Guidance for industry pharmacokinetics in pregnancy studies, clinical lactation studies etc., various branches of NIH, professional organizations like ACOG came out with Ethical considerations, responsible inclusion of pregnant individuals in clinical studies etc.
- **In 2017, the 21st Century Cures Act included the establishment of a Task Force on Research Specific to Pregnant Women and Lactating Women**
  - Charged with providing advice and guidance to the Secretary of HHS on activities related to identifying and addressing gaps in knowledge and research on safe and effective therapies for pregnant women and lactating women, including the development of, collaboration on, and coordination of such activities.

PRAGLAC Recommendations

1. **Include and integrate pregnant women and lactation women in clinical research agenda**
   - Remove pregnant women as an example of a vulnerable population in the Common Rule

2. **Increase the quantity, quality and timeliness of research on safety and efficacy of therapeutic products used by pregnant women and lactating women**
   - Expand basic science research to inform drug development

3. **Expand the workforce of clinicians and research investigators with expertise in obstetric and lactation pharmacology and therapeutics**
   - Develop and support training and career development opportunities in obstetric and lactation pharmacology and therapeutics for both clinical and basic science

4. **Remove regulatory barriers to research in pregnant women**
   - Modify subpart B of the Common rule to maternal consent alone

5. **Create a public awareness campaign to engage the public and health care providers in research on pregnant women and lactating women**
   - Engage stakeholders such as Department of Health and Human Services (HHS), professional societies, industry, advocacy groups, and public and global partners

PRAGLAC Recommendations

6. **Develop and implement evidence-based communication strategies with health care providers on information relevant to research on pregnant women and lactating women**
   - Increase the engagement of health care providers to discuss participation in clinical trials, research, and Registries
7. **Reduce liability to facilitate an evidence base for new therapeutic products that may be used by women who are or may become pregnant and by lactating women**
   - Implement a liability-mitigation strategy for conducting research and evaluating new therapeutic products in pregnant women and lactating women
8. **Develop separate programs to study therapeutic products used off-patent in pregnant women and lactating women using the National Institute of Health (NIH) Best Pharmaceuticals for Children Act (BPCA) as a model**
   - Develop separate prioritization processes for therapies and/or conditions in pregnant women and lactating women
9. **Develop programs to drive discovery and development of therapeutics and new therapeutic products for conditions specific to pregnant women and lactating women**
   - Consider a Biomedical Advanced Research and Development Authority (BARDA)-like model and the NIH vaccine model that takes clinical development up to phase II
10. **Implement a proactive approach to protocol development and study design to include pregnant women and lactating women in clinical research**
    - Investigators/sponsors must specifically justify exclusion in study design
    - Develop guidance for institutional review boards and investigators about the inclusion of pregnant women and lactating women in research

PRAGLAC Recommendations

11. **Leverage established and support new infrastructures/collaborations to perform research in pregnant women and lactating women**
    - Encourage networks/collaborations to engage in public-private partnerships to facilitate research
12. **Utilize and improve existing resources for data to inform the evidence and provide a foundation for research on pregnant women and lactating women**
    - Leverage large studies and databases including health systems, health plans, surveillance systems, electronic medical records, registries
13. **Optimize registries for pregnancy and lactation**
    - Develop disease/condition-focused registries; Move toward a single registry for all therapeutic products with input from stakeholders
14. **The Department of Health and Human Services Secretary should consider exercising the authority provided in law to extend the PRGLAC Task Force when its charter expires in March 2019**

11. **Establish an Advisory Committee to monitor and report on implementation of recommendations, updating regulations, and guidance, as applicable, regarding the inclusion of pregnant women and lactating women in clinical research**

ICH E21:
Inclusion of Pregnant and Breastfeeding Individuals in Clinical Trials

INTERNATIONAL COUNCIL FOR HARMONISATION OF TECHNICAL REQUIREMENTS FOR PHARMACEUTICALS FOR HUMAN USE

https://www.ema.europa.eu/en/ich-e21-guideline-inclusion-pregnant-breastfeeding-individuals-clinical-trials-scientific-guideline

ICH E21 – Overview

- ICH Expert Working Group started in 2022, with a guideline expected in 2028

- Plans to provide a framework to conduct trials in pregnant and breastfeeding individuals in a data driven manner
  - Guidance on when contraception requirements can be more flexible, and when pregnant individuals could be included in a trial

- ICH Expert Working Group has submitted the draft guideline (May, 2025), to the regulatory authorities of the ICH regions for internal and external consultation.

ICH E21 Framework & Principles

- **Considerations regarding data collection on dosing, clinical efficacy & safety**
  - Development Strategy
  - Study Design, Endpoints and Outcomes to be collected
  - Recruitment and Retention Strategies
  - Ethical Considerations
  - Regulatory Considerations

- **Bridging principles to other ICH guidelines e.g.**
  - E6 & E8 Good Clinical Practice
  - S5 Detection of reproductive and developmental toxicity
  - M3 Non-clinical safety studies
  - E11 Clinical investigations in the pediatric population

Key Points on Development Strategy

- **Factors to consider**
  - Principles related to prioritization
  - Early considerations to include women
  - Regular review of emergent data
- **Types of data needed to include pregnant women in trials**.
  - Generate nonclinical and clinical data needed to make a decision on favorable benefit/risk for inclusion of pregnant women

- **When all the data is not available to make a decision on benefit/risk**
  - Individual benefit/risk assessment
- **When existing data suggest a safety concern**
  - Understanding the risk

Antiretroviral Drugs and Pregnancy

Epidemiology of Pregnancy, and Individuals of Childbearing Potential With HIV

- 53 % (20.67mil) of the 39 million people living with HIV are women and girls
- Among the 1.3 million people newly diagnosed with HIV in 2022, 46% (598,000) are women and girls[2]
- ~1.5 million women living with HIV give birth each year[1]
- Accumulating evidence indicates that women face an increased risk of HIV acquisition during pregnancy[3]
- ~40% to 60% of pregnancies are unplanned[4]

Current guidelines recommend that women with HIV who are already pregnant or planning to become pregnant should maintain their current ART regimen, unless taking a contra-indicated regimen during pregnancy[5]

1. UNICEF. http://www.childrenandaids.org/sites/default/files/2020-12/2020%20World%20AIDS%20Day%20Report.pdf. Accessed May 17, 2022. **2.** UNAIDS. https://www.unaids.org/en/resources/documents/2023/core-epidemiology-slides. **3.** Drake et al. *PLoS Med*. 2014;11:e1001608. **4.** Bearak et al. *Lancet Glob Health*. 2020;8:e1152-e1161. **5.** World Health Organization. Consolidated Guidelines on HIV Prevention, Testing, Treatment, Service Delivery and Monitoring: Recommendations for a Public Health Approach. 2021.

New HIV infections in children and adolescents are still a global concern

1.4 Million
children (0 -14 yrs)

~120K* new HIV infections among children in 2023

*Estimates from 83,000 to 170,000

90% of infants with HIV acquired HIV from their mothers

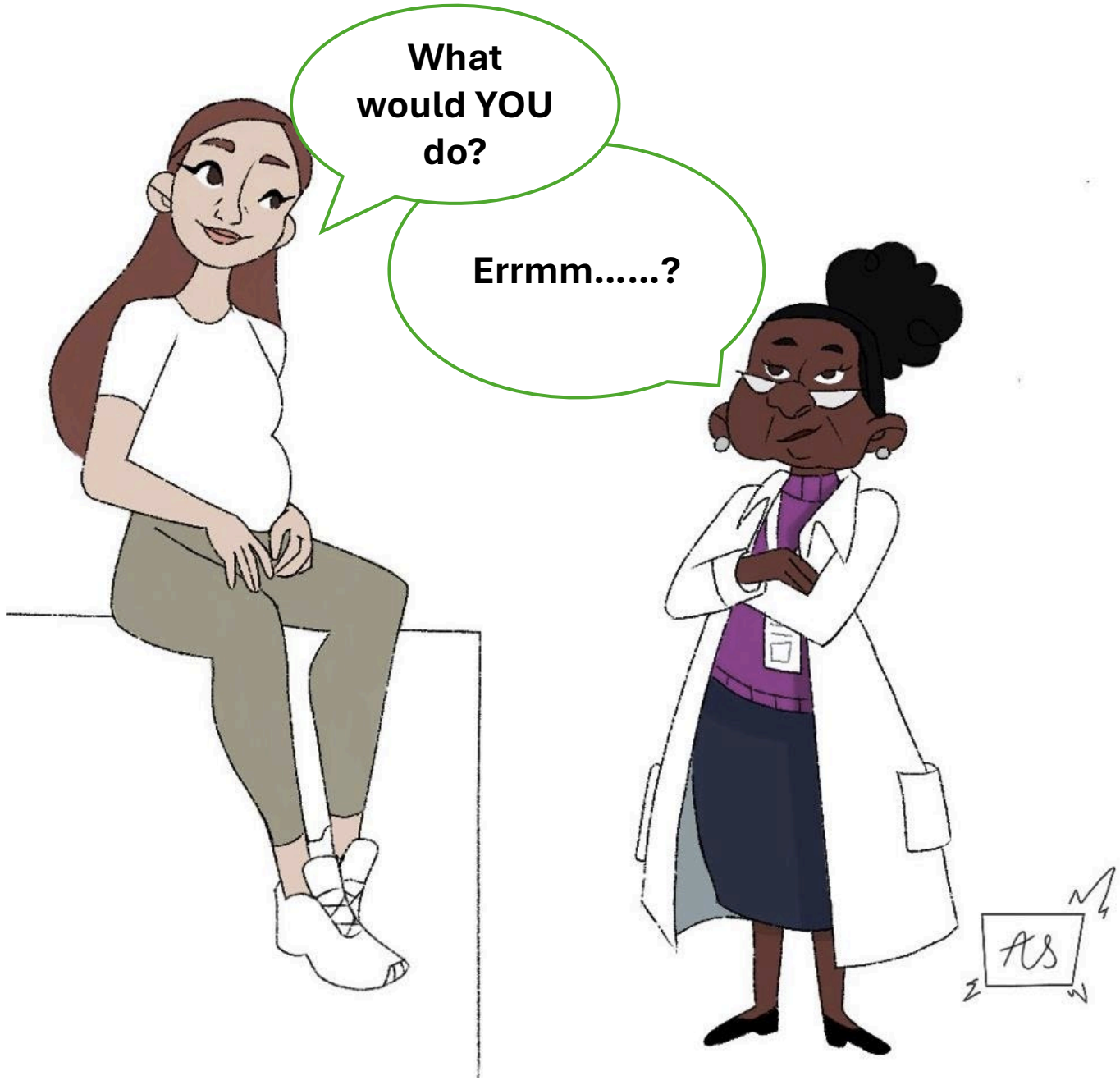
~140K* new HIV infections among adolescents (15–19 years) in 2023

*Estimates from 39,000 to 240,000

1 million adolescents (15–19 years) were living with HIV in 2023

Nearly 9 out of 10 children and adolescents living with HIV AND new infections in children are in sub-Saharan Africa

UNAIDS. Global HIV & AIDS Statistics Fact Sheet. Global HIV & AIDS statistics — Fact sheet | UNAIDS
UNICEF. Paediatric Care and Treatment. Paediatric care and treatment - UNICEF DATA
UNICEF. Adolescent HIV Prevention. Adolescent HIV prevention - UNICEF DATA


What would YOU do?
Errmm.....?

Healthcare Providers Need to Know

- **Drug Dosage during pregnancy:** Clinical interpretation of PK and dose adjustment

- **Drug safety in pregnancy**
- Maternal
- Fetal/neonatal: Spontaneous loss, still birth, preterm birth, IUGR & Birth defects

- **Drug Efficacy**
- Maternal: Disease control/remission/cure (e.g. Maternal Viral suppression, no seizures, MS remission)
- Infant: Prevent effects of disease on infant (e.g. Perinatal transmission of infections)

Clinical Trials and Pregnant & Women of Childbearing Potential

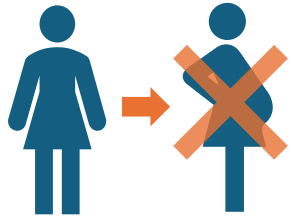
- **1.** UNAIDS. https://www.unaids.org/en/resources/documents/2021/core-epidemiology-slides. Accessed May 17, 2022. **2.** UNAIDS. https://www.unaids.org/en/resources/documents/2021/core-epidemiology-slides. Accessed May 17, 2022. **3.** Curno et al. *J Acquir Immune Defic Syndr*. 2016;71:181-188.

Women represent **~50%** of the **global population living with HIV**[1]

However, **data** on the use of individual ARVs during pregnancy have traditionally been **sparse in clinical programs** for **3 reasons**:

Underrepresentation of women in HIV drug development programs[3]

Participation of pregnant women **prohibited**



Women who **become pregnant** must **discontinue study drug/trial**

Challenges For Women Who Are or Who May Become Pregnant

PK Data availability

6 years

Median time from US Food and Drug Administration approval to first published PK data in pregnancy[1]

Challenges

1. HCPs and WOCBP have **little or no safety information** for commonly prescribed antiretroviral drugs when used in pregnancy

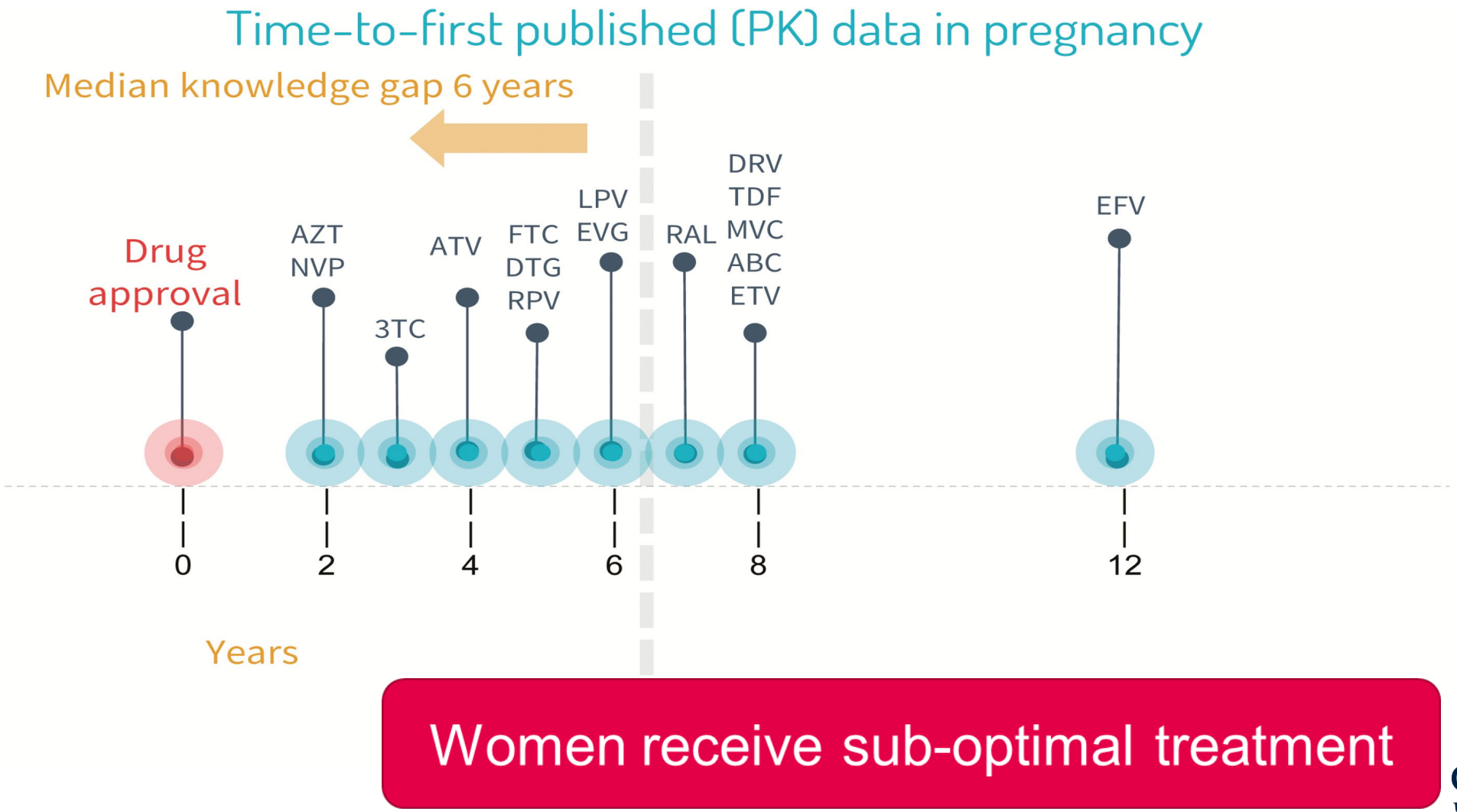
2. Women who become pregnant while on stable ART may be switched to another regimen with **potential loss of virological suppression** or with new undesirable side effects

3. **Risk of incorrect dosing** since the PK of the drug may vary across the different stages of pregnancy, which may result in inadequate viral suppression or new safety/tolerability issues

4. **Drug-drug interactions** between ART and other drugs commonly used in pregnancy may impact either the co-administered medicine or the ART

1. Colbers et al. *Clin Infect Dis*. 2019;69:1254-1258.

Figure 1. Years between US Food and Drug Administration approval and publication of pregnancy data for different antiretroviral drugs



Dolutegravir – Cluster of Neural Tube Defects 2018

- Very little data on DTG in pregnancy
- Unplanned interim analysis of Tsepamo study
  - Botswana
- Cluster of 4 cases of NTD
- ~ 10 x higher than comparator group Efavirenz
- Global change in guidelines
- WOCBP taken off DTG & not prescribed DTG
- Global protest by women

Signal resolved; DTG is Back in the guidelines

ViiV Healthcare's previous approach

- Encourage clinical development teams to enroll women of childbearing potential in Phase 3 clinical trials so that some data are available
- Permit participants who become pregnant the option to continue their participation, once a reasonable safety and benefit-risk profile is established after completing Phase 3 data (as done with the CAB + RPV treatment program)
- Collaborate with organizations (e.g., WHO, IMPAACT, CIPHER/IAS) to explore innovative ways to accelerate the study of new drugs for HIV in pregnant and lactating individuals
- Conduct passive accrual of data on pregnancies through registries and Non-Interventional studies –The Antiretroviral Pregnancy Registry (APR)

Call to Action

World Health Organization (WHO) and the International Maternal Pediatric Adolescent AIDS Clinical Trials Network (IMPAACT) –Dec 2021

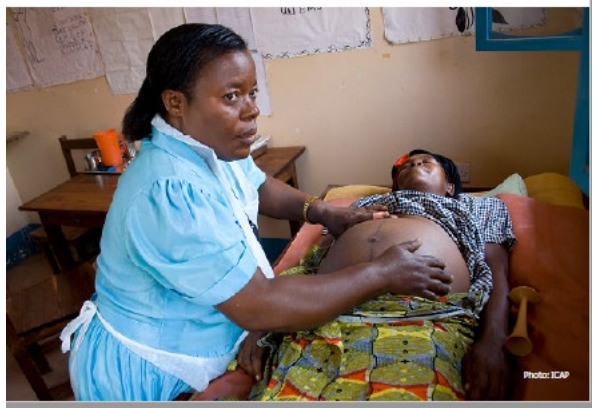
- **Accelerate generation of clinical data on antiretroviral drugs among pregnant women**
- **Consider pregnant individuals as a complex population rather than a vulnerable population**
- **Move away from “protecting from research” to “protecting through research”**
- **Promote fair inclusion in, rather than presumptive exclusion from, clinical drug trials**

ARV use in Pregnancy

World Health Organization · IMPAACT · CIPHER Paediatric HIV Matters · IAS

Research for informed choices: Accelerating the study of new drugs for HIV in pregnant and breastfeeding women

A call to action



2

Equity demands that research is more inclusive of women

More than 19 million women are living with HIV worldwide and the majority are of childbearing potential. There is a public health imperative to ensure that these women can make informed choices about the drugs they take for HIV treatment or prevention. Information to support optimal antiretroviral drug choices in pregnancy

Infect Dis Ther
https://doi.org/10.1007/s40121-024-00993-4

COMMENTARY

Responding to the Call to Action: Framework to Accelerate Clinical Data Generation for Antiretroviral Use in Pregnant Individuals with HIV

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Keywords: ARV; Clinical trial; Drug development; HIV care continuum; HIV prevention; Pregnancy; Treatment

INTRODUCTION

An estimated 1.2 million people living with human immunodeficiency virus (HIV) become pregnant each year, and approximately 300,000 initiate antiretroviral therapy (ART) during pregnancy [1]. Moreover, > 120,000 preventable new HIV transmissions occurred among children in 2022, mostly due to lack of ART during pregnancy or breastfeeding [1]. Clinical data demonstrate that perinatal transmission risk can be reduced to ≤ 1% when effective ART, combined with other prevention strategies, is used during and after pregnancy [2].

Clinical data on individual antiretroviral agent use during pregnancy or lactation have been delayed or sparse, partially because pregnant individuals have long been categorized as a vulnerable population [3], which adds ethical considerations (e.g. challenges in weighing potential risks and benefits to the pregnant individual and foetus) and legal concerns (e.g. cautious interpretation of federal guidance for "not greater than minimal" risk) [4]. Moreover, regulatory authorities do not require clinical pregnancy data for marketing approval, mandating only non-clinical data and descriptions of restricted use in specific populations, such as pregnant individuals, in drug labelling [5]. This

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Roadmap to Accelerating Clinical Data Generation for ARV use in Pregnancy

Taskforce

- Epidemiology
- Non-Clinical Safety and DMPK
- Clinical Pharmacology
- PBPK Modeling
- Safety and PV
- Statistics
- Patient /Community Affairs
- Regulatory Sciences
- Labeling
- PBPK Modeling
- Clinical Development
- Clinicians

Study Design Considerations Specific to Pregnancy

- **For a trial of new drug in pregnancy, usually need:**
  - Preclinical repro-tox data, without safety concerns
  - Drug dose and safety, sufficiently established in non-pregnant population
  - Efficacy in non-pregnant (at least phase 2 data)
  - Pregnancy pk data, before enrolling larger group of pregnant women

- **Multiple pregnancy/fetal/neonatal outcomes:**
  - Maternal toxicity/safety, fetal/infant toxicity/safety (short and longer term), efficacy (likely do not need virological efficacy endpoint if pregnancy PK is reassuring

- **Gestational age:** affects drug PK, potential risk to fetus, and feasibility of enrolment
  - For pre-conception and first trimester exposure (and rare outcomes, post-registrational surveillance and monitoring may be more suited)
  - Maybe easier to enrol and assess pre-conception & 1st trimester exposures, if on long-acting ARV regimen

Framework to Accelerate Clinical Data Generation in Pregnancy

1. Develop a pregnancy data acceleration plan for each early-stage compound

2. Accelerate completion of reproductive toxicology assessments (EFD, PPN, FEED) and accelerate PK and modeling assessments

3. Phase 1b and 2 trials: include more WOCBP (contraception or sterilization required) to allow meaningful data collection – must discontinue if pregnancy occurs

4. Phase 3 trials: once effective dosing in women is established, and sufficient safety data in women are known, allow women to continue treatment if they become pregnant

5. Phase 3 trials: recommend, but do not require, use of contraception by non-sterile women

Roadmap to Accelerate Generation of Clinical Data on Antiretroviral Drugs among Pregnant Women

Framework to Accelerate Clinical Data Generation in Pregnancy

6. Develop a regulatory strategy for each compound, engage relevant health authorities through development (usual process) to align on process for an evidence-based pregnancy data acceleration plan – align early, if possible, on labeling options and requirements

7. Develop a statistical strategy for each compound that allows for early and consistent participation of women in clinical studies, and for data handling options for women who become pregnant in Phase 3 (e.g., sample size adjustments, pre-specified analysis plans, sensitivity analyses for primary or secondary endpoints)

8. Consider planning a dedicated pregnancy trial to be conducted once sufficient safety data are available from Phase 3 (pre- or post-approval)

9. Engage and consult with community representatives early and consistently

10. Publish available data on use of ARVs in pregnancy, early and frequently

The Framework has been endorsed by ViiV Governance Committee

The product specific data generation plan will be subject to internal governance and dependent on the evolving data and appropriate benefit risk assessment

Pregnancy Data Acceleration Plan (PDAP)

Each Drug Development team to develop their own pregnancy plans

Content

- Details of accelerated toxicology and PK assessments, how women will be included in Phase 1b-2 in line with proposed framework, how pregnant women will be allowed to remain in Phase 3, and how pregnant women may be proactively evaluated once a satisfactory clinical database is established
- Regulatory interaction strategy
- Statistical planning for Phase 3
- Community involvement plans

Timing

- Some elements (tox, PK, Phase 1 plans) should be described prior to IND filing
- Later-phase elements may be described before Phase 2 initiation

Align with organization diversity goals

- Ensure meaningful numbers of women in Phase 1-2 trials to provide data for decision-making to support Phase 3 and beyond
- Consider also race, ethnicity, age, gender issues

Reproductive Toxicology to Support Clinical Studies in Pregnant Women

Study Designs

- **Teratology Studies** (**Embryo Fetal Development or EFD studies**)
  - Evaluate the potential for congenital abnormalities by exposing pregnant animals during organogenesis (typically rabbits and rodents)

- **Reproductive Performance Studies**
  - Assess the effects on fertility, gestation, and lactation by exposing animals before and during mating, as well as during pregnancy and lactation

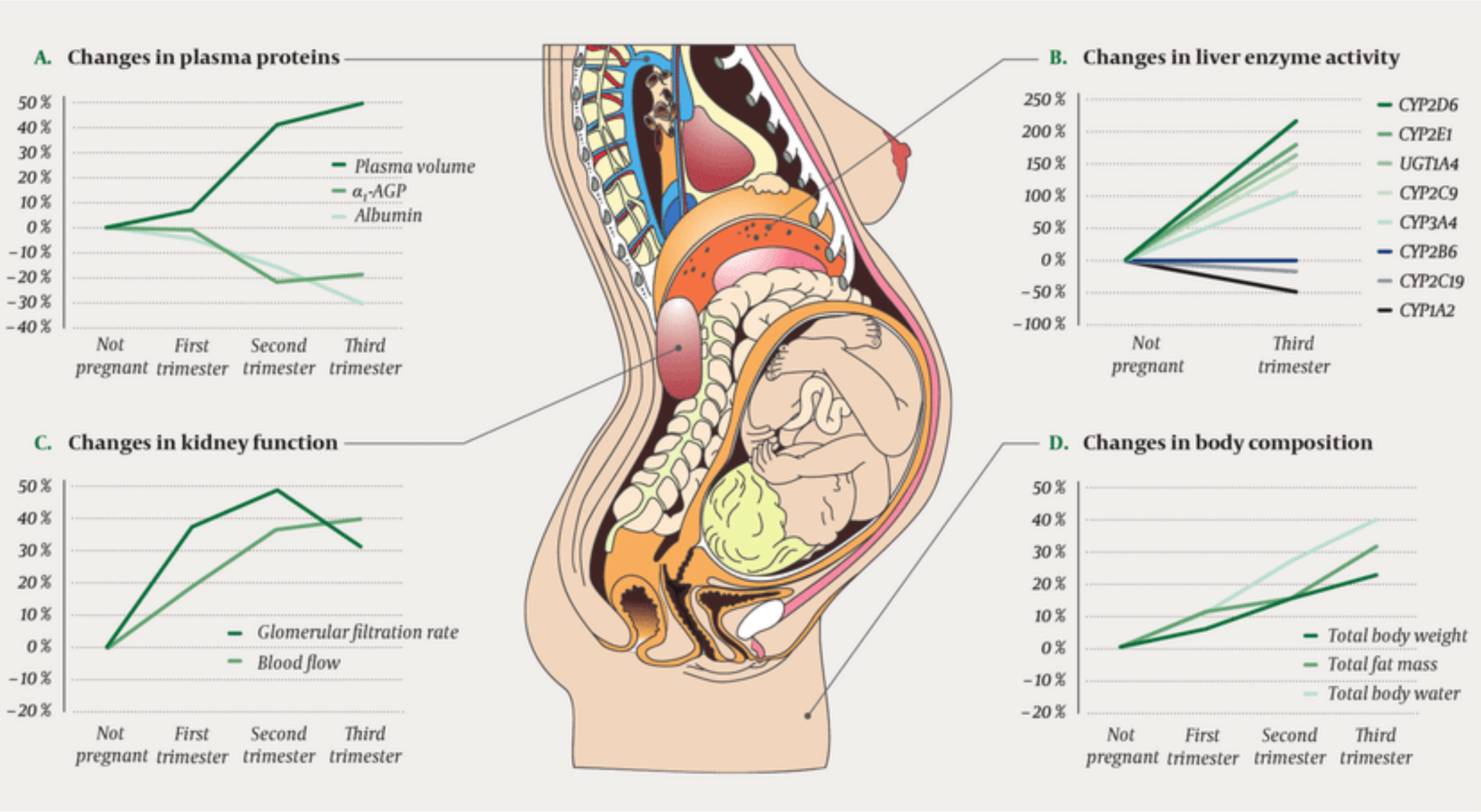
- **Perinatal and Postnatal Studies**
  - Investigate the impact on offspring during late pregnancy and early postnatal development, examines survival, growth and behavioral changes, includes assessment of multigenerational effects

Timing Of Reproductive Toxicology Studies

- ICH M3 Guidance is the starting place but to enable women who become pregnant to remain on study or to loosen requirements for contraception during development, studies should be conducted sooner than ICH requirements
  - Complete fertility and EFD studies in 2 species prior to Phase 2B
  - Plan to complete PPN study prior to or early Phase III
  - Successful early planning requires input from multiple disciplines (clinical, CMC, Clin Phar, DMPK, Toxicology)
  - Biologics require a case-by-case approach (depending on target, available animal models, etc)
    - Considered safer based on limited exposure to fetus from large molecules

Clinical Pharmacology Considerations

Physiologic changes in pregnancy



30 October 2018. Tidsskr Nor Legeforen. DOI: 10.4045/tidsskr.18.0065

Studying drugs in Pregnancy: Clinical Pharmacology considerations

- **Dose Selection/Dose adjustment:**
  - Determining the most appropriate initial dose
  - Consider impact of physiologic changes throughout pregnancy which are trimester-specific and drug-specific.
  - Achieve therapeutic exposures that are safe and well-tolerated for mother and fetus throughout pregnancy

- **Drug Interactions:**
  - Many pregnant women require medications for conditions such as gestational diabetes (2 – 10% of pregnancies in US), hypertension (preeclampsia occurs in ~4 % of pregnancies in US), nausea and vomiting (up to 70% of pregnancies), etc.
  - Evaluation should be sufficient to provide guidance on likely drug interactions

- **Fetal/Neonatal exposure:**
  - Transfer of drug from mother to fetus during pregnancy
  - Transfer of drug during breastfeeding
  - Drug exposure in neonate post-delivery

Summary

- **This proposed strategy accelerates non-clinical data, early PK and modeling assessments, and allows for the participation of women who are or who may become pregnant in Phase 3**
  - **Will lead to earlier availability of efficacious, safer, and more convenient ART options for women, and for unborn and newborn children**

- Although the risks of ART drug exposure to the fetus and newborn must be carefully assessed, a proactive and evidenced-based approach will allow women who are or who may become pregnant to participate in clinical trials at an earlier stage

- The data generated through this acceleration will increase options for women of childbearing potential and allow their healthcare providers to provide novel drug options for treatment and prevention

What Next?

- **Stepwise data-driven approach to decide if and how it would be appropriate to advance inclusion of women of child-bearing potential and pregnant individuals in clinical trials**
  - Determine if acceleration is appropriate for the population, asset, and indication
  - Decide when to include in the clinical development plan so that all enabling work (e.g. Nonclinical studies, API estimates, etc.) can be completed

Further Reading

1. Polifka, J.E. and Greenspan, J. (2023), Bob Brent: Scientist, physician, scholar, teacher, mentor, and mensch. Birth Defects Research, 115: 1227-1242. https://doi.org/10.1002/bdr2.2162
2. The PHASES Working Group Pregnancy and HIV/AIDS: Seeking Equitable Study. Ending the evidence gap for pregnant women around HIV & co-infections. 2020.
3. World Health Organization. Research for informed choices: accelerating the study of new drugs for HIV in pregnant and breastfeeding women: a call to action. 2021.
4. Abrams EJ, Calmy A, Fairlie L, et al. Approaches to accelerating the study of new antiretrovirals in pregnancy. J Int AIDS Soc. 2022;25(S2)
5. Vannappagari V, McCallister S, Romach B, et al. Responding to the Call to Action: Framework to Accelerate Clinical Data Generation for Antiretroviral Use in Pregnant Individuals with HIV. *Infect Dis Ther*. Published online 2024. doi:10.1007/s40121-024-00993-4.
6. Riley MF. Including Pregnant and Lactating Women in Clinical Research. Viewpoint: Moving Beyond Legal Liability. JAMA. Published online April 10, 2024. 2024;331(19):1619-1620. doi:10.1001/jama.2024.6874.

Call to Action to Research Community

Reinforce	Encourage	Advocate
• Reinforce the importance of prioritizing clinical research in pregnancy to improve health outcomes for mothers and their babies.	• Encourage stakeholders to adopt the roadmap and collaborate to accelerate progress.	• Advocate for sustained commitment and investment to ensure safe, effective, and evidence-based treatment options for pregnant individuals.