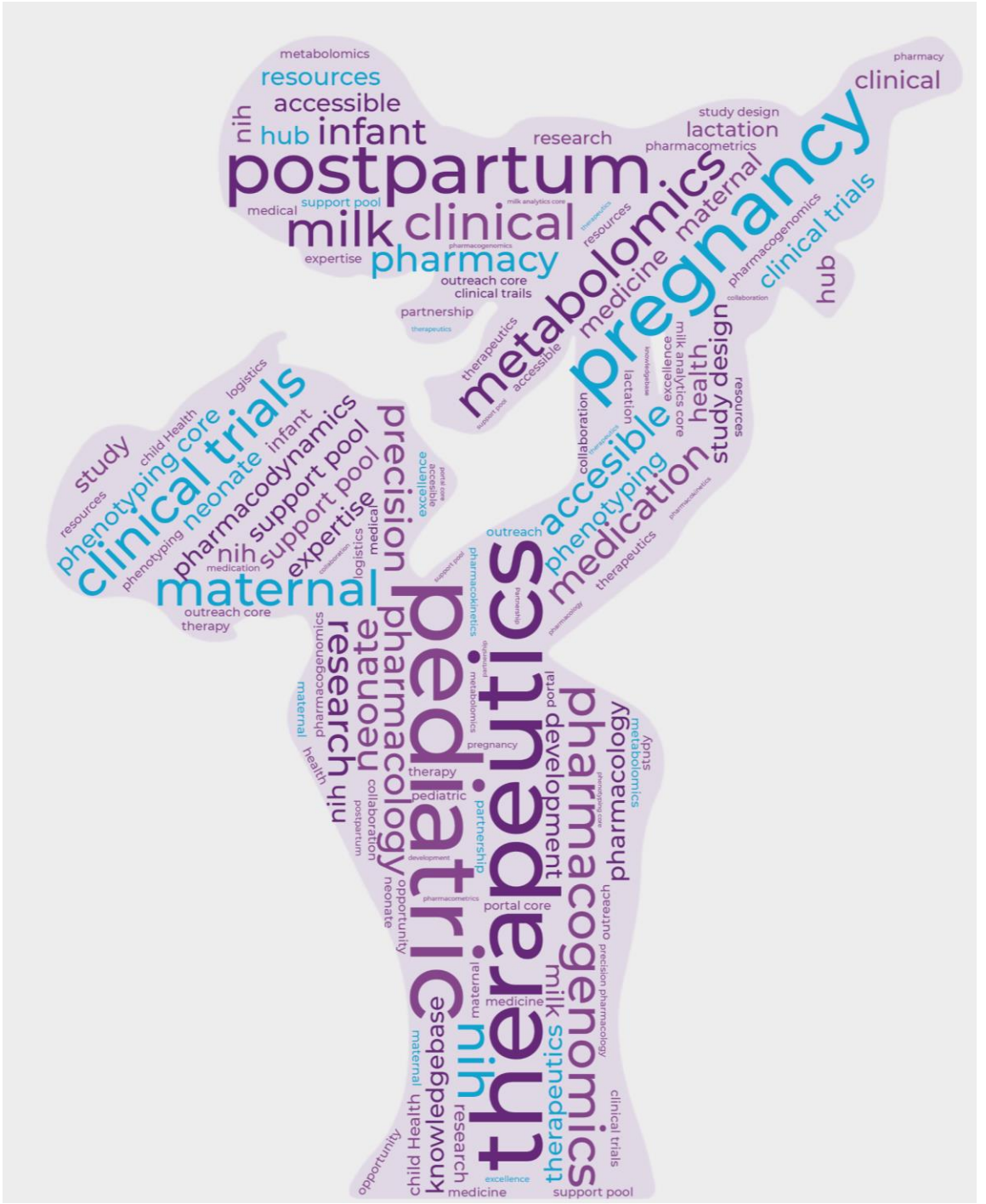
Drug Development Considerations for Pregnant and Lactating Individuals

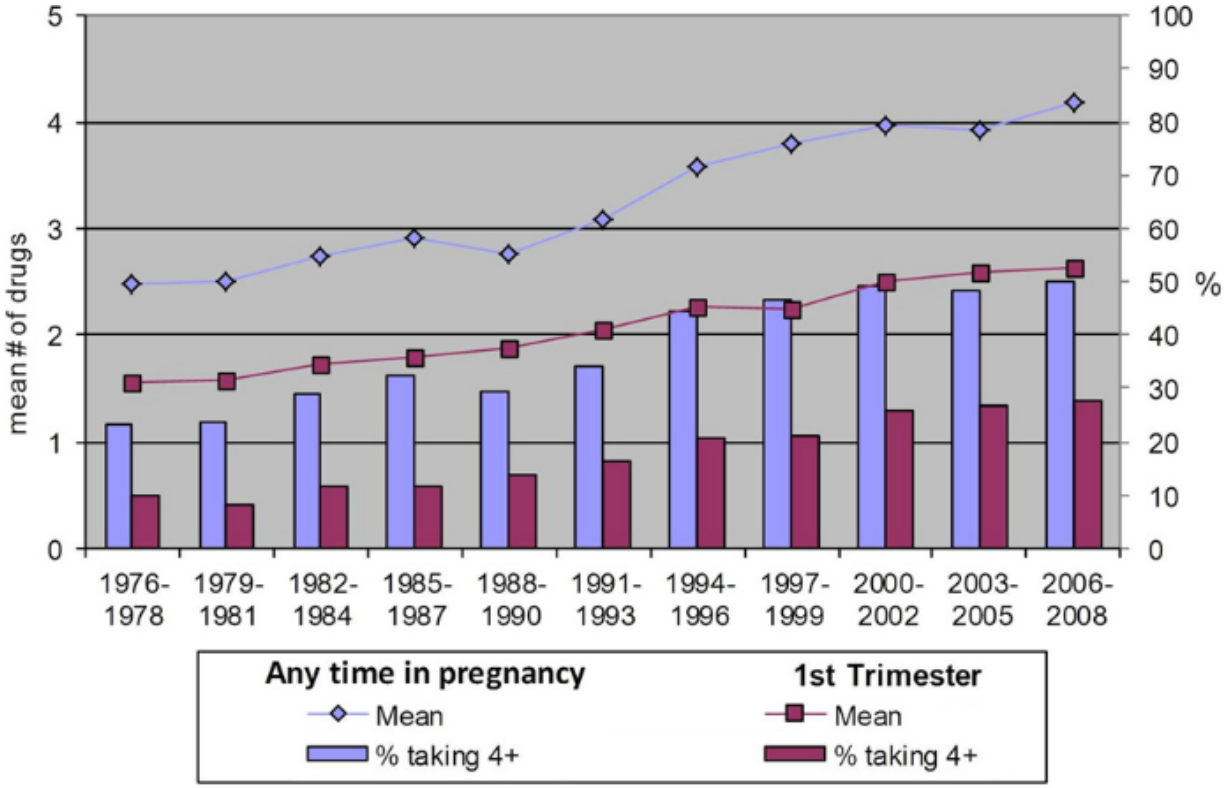
Sara Quinney, PharmD, PhD
Indiana University School of Medicine
May 8, 2024



1P30HD106451

Medication use in Pregnancy

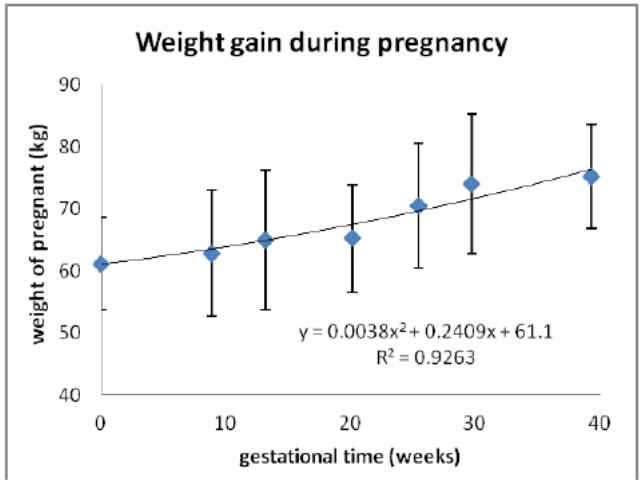
- 97.1% of 9,546 pregnant individuals took at least 1 medication or supplement during pregnancy
- 30.5% took at least 5 medications during pregnancy
- Most common:
  - Antiemetic (34.3%)
  - Antibiotics (25.5%)
  - Analgesics (23.7%)

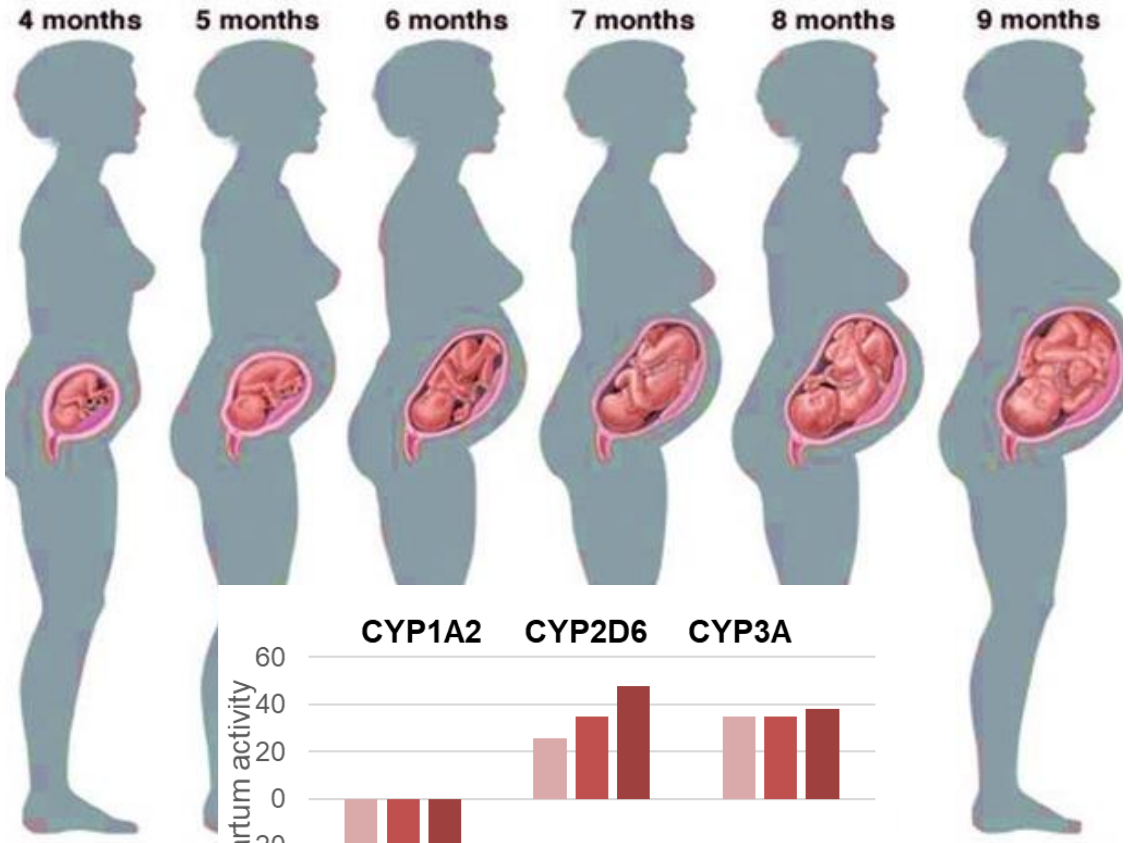


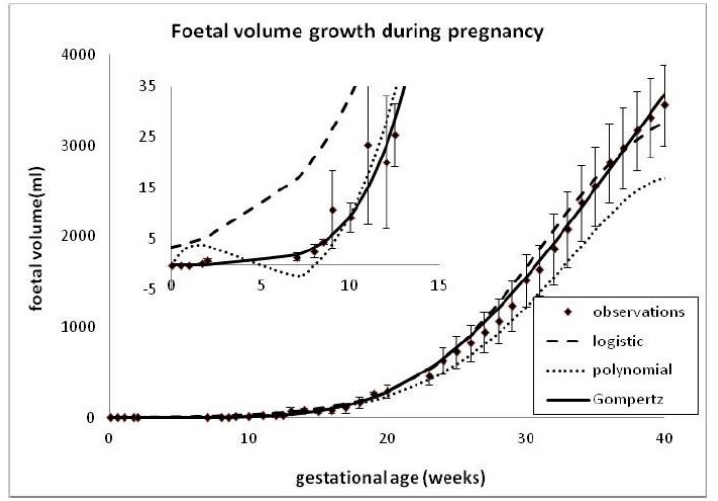
Haas, Obstet Gynecol 2018

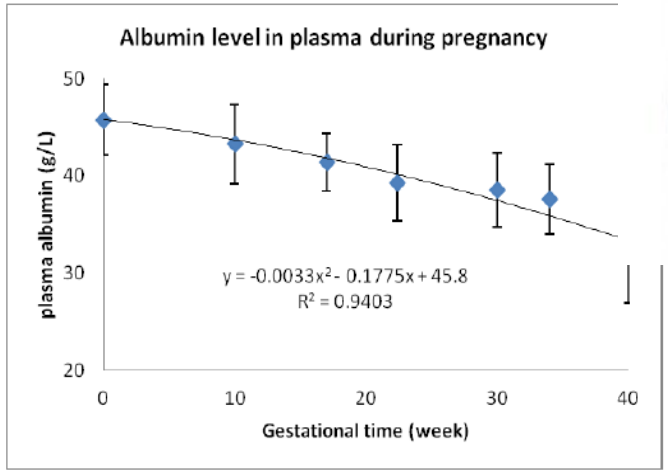
Mitchell, AJOG, 2011

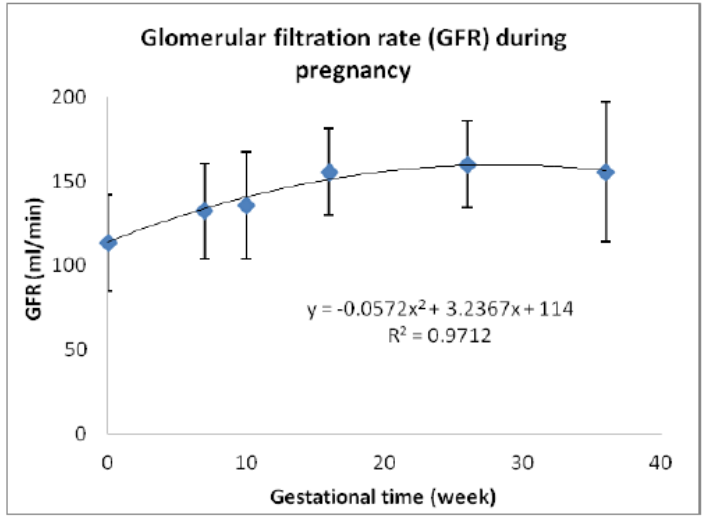
Physiologic Changes in Pregnancy







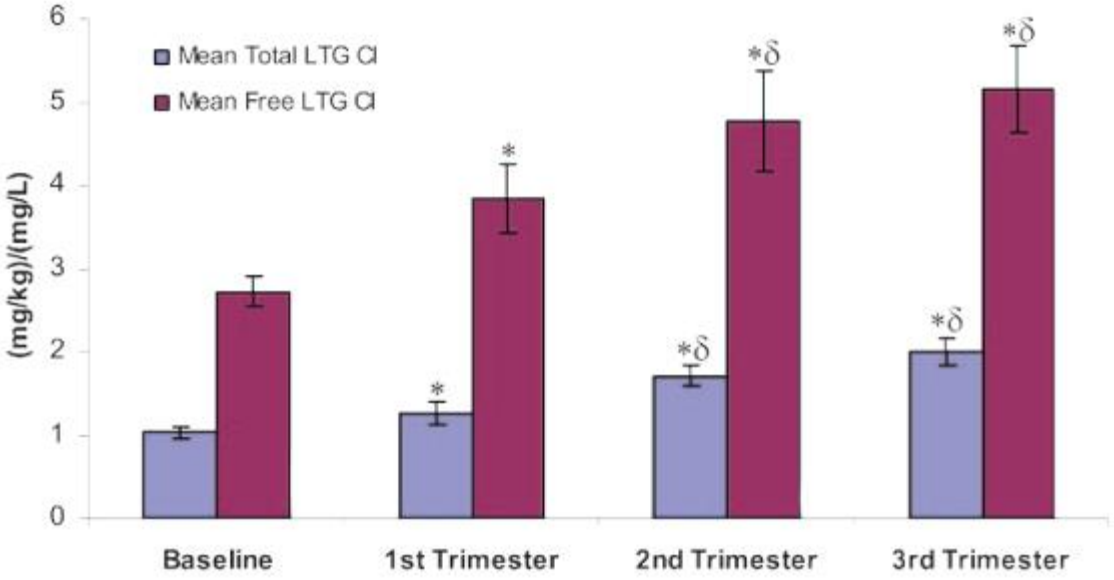


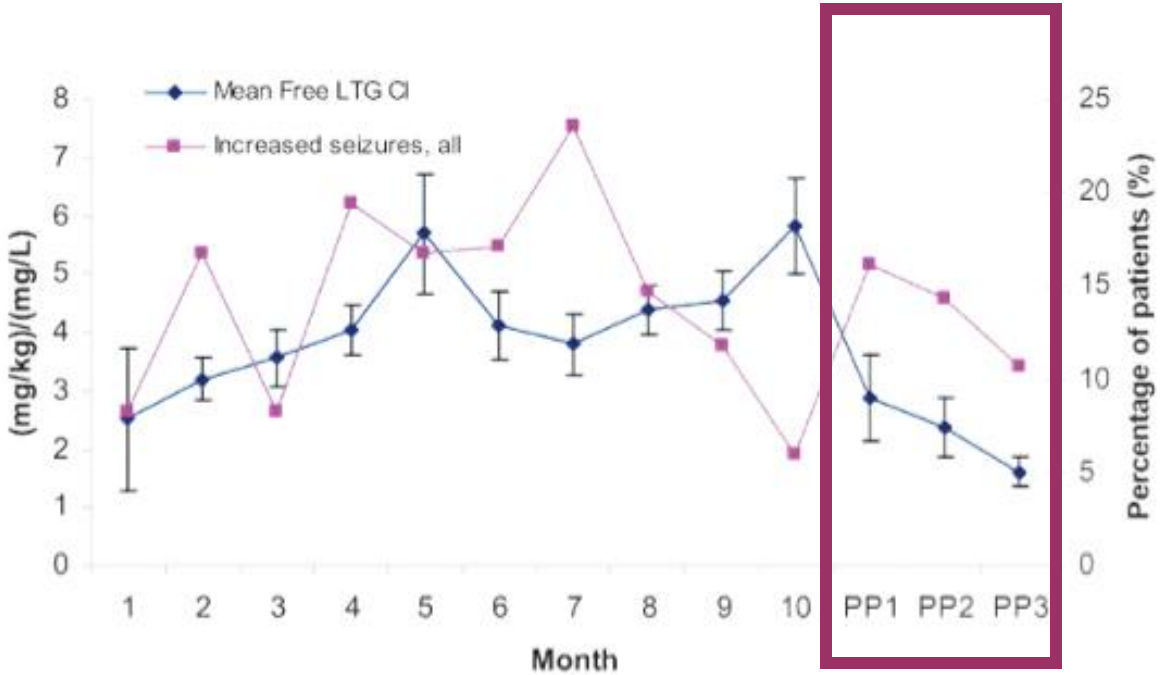


Abduljalil, Clinical Pharmacokinetics 2012; Tracy, Am J Obstet Gynecol 192:633-9, 2005

http://anatomysystem.com/diagram-of-the-stages-of-pregnancy-month-by-month/

Increased Lamotrigine CL/F across pregnancy is associated with increase seizure activity





Pennell, Neurology 2008 PMID 18046009

Guidances Relating to Pregnancy & Lactation

Draft Guidance Oct 2004

Guidance for Industry

Pharmacokinetics in Pregnancy — Study Design, Data Analysis, and Impact on Dosing and Labeling

April 2005

Reviewer Guidance

Evaluating the Risks of Drug Exposure in Human Pregnancies

Draft Guidance May 2019

Postapproval Pregnancy Safety Studies

Guidance for Industry

Draft Guidance April 2018

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

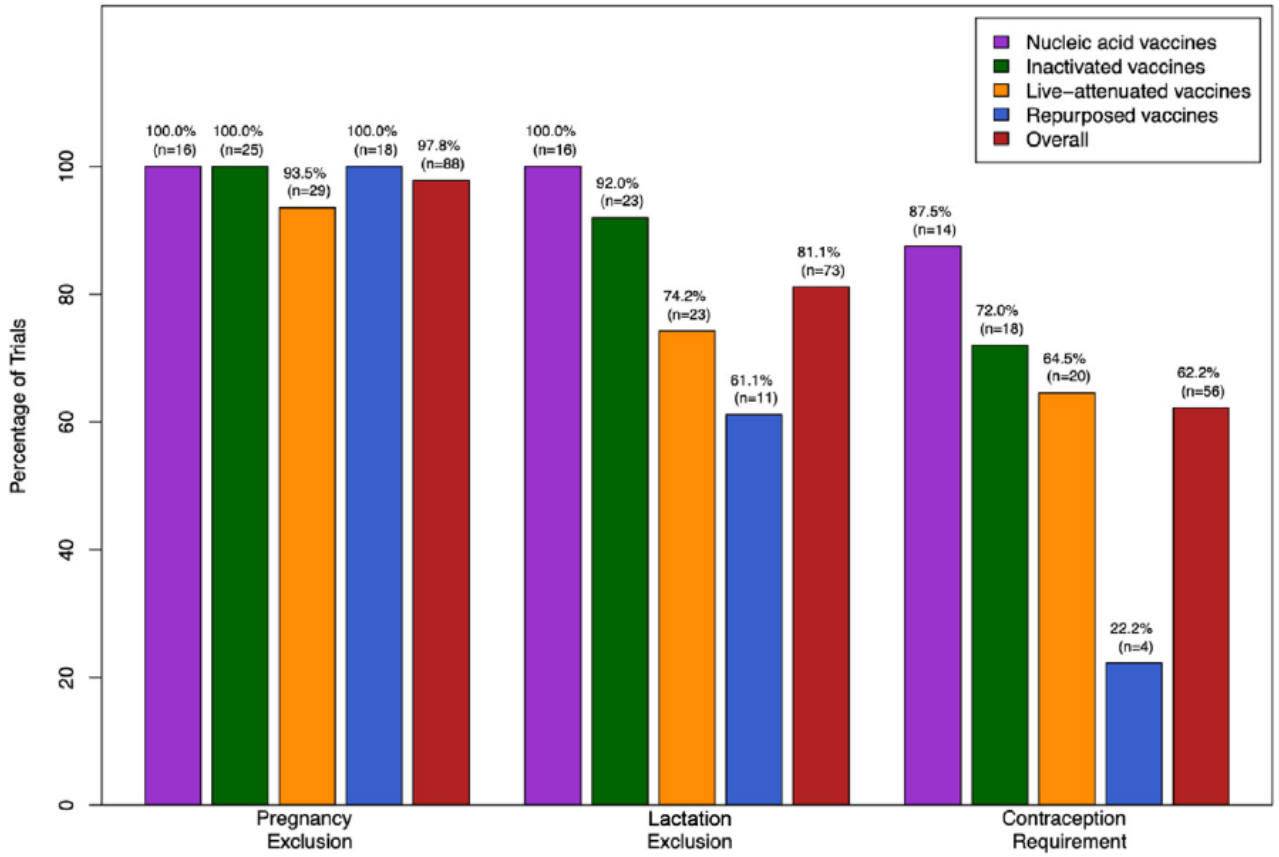
Guidance for Industry

July 2020

Pregnancy, Lactation, and Reproductive Potential: Labeling for Human Prescription Drug and Biological Products — Content and Format

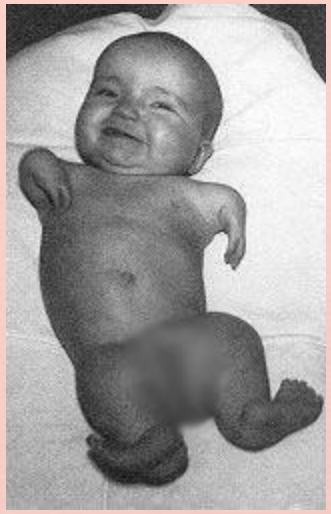
Guidance for Industry

Majority of COVID-19 Studies Excluded Pregnant and Lactating Individuals



K.M. Kons Women's Health Issues 32:557–563 (2022)

When Pregnant People are Left Out of Research



Terminology Matters

Vulnerable Special		Complex Understudied
Protected **from** research		Protected **through** research
Prioritizes Fetal Safety		Balances Fetal and Maternal Safety
Presumes Exclusion		Fair Inclusion

Lyerly et al., J Int AIDS Soc. (2021)
Catriona Waitt

NATIONAL ACADEMIES Sciences Engineering Medicine

Advancing Clinical Research with Pregnant and Lactating Populations: Overcoming Real and Perceived Liability Risks

Role of the Food and Drug Administration

- Early inclusion of pregnant and lactating persons in studies
- Safety, efficacy, and dosage studies in pregnancy & lactation initiated no later than the end of Phase III studies in the general population.
- Diversity action plans required by the Food and Drug Omnibus Reform Act (FDORA) should include pregnant and lactating persons
- Harmonization of FDA and HHS OHRP Guidances
- Improvements in real-world data capture & centralized repository for post-marketing registries & other RWE resources

Approach to Barriers

Preclinical

Optimize Interpretation of preclinical animal data

Accelerate Completion of preclinical animal studies

Timing of clinical studies - when to move forward

Translational studies

Clinical

Drug Prioritization (among existing drugs)

Framework for including Pregnant Women in Trials

Risk & Liability: IRB capacitation & Trial Insurance

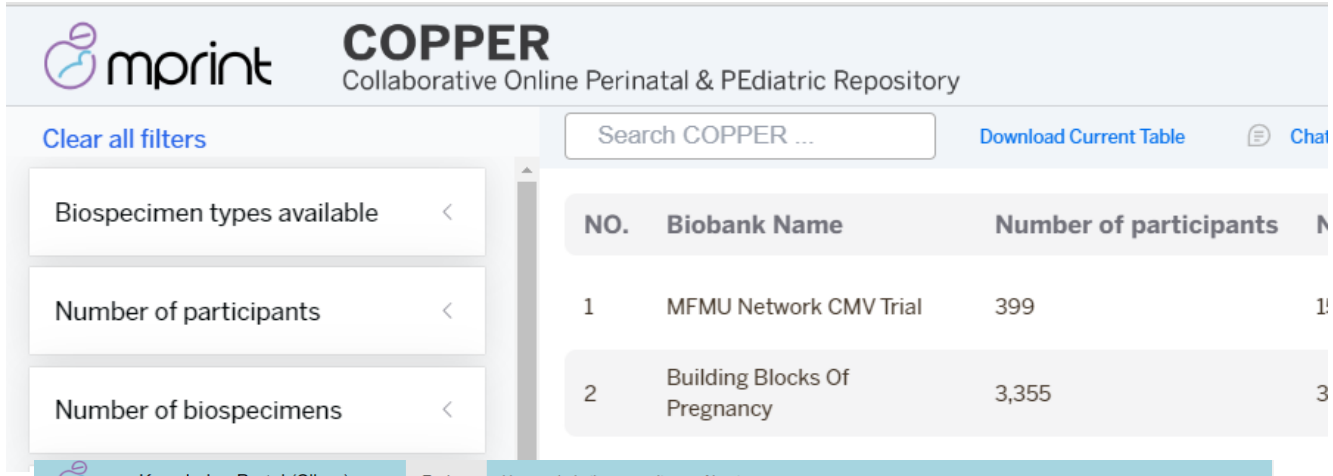
Standardization of **Maternal**, **Infant** and **Pregnancy** Outcomes

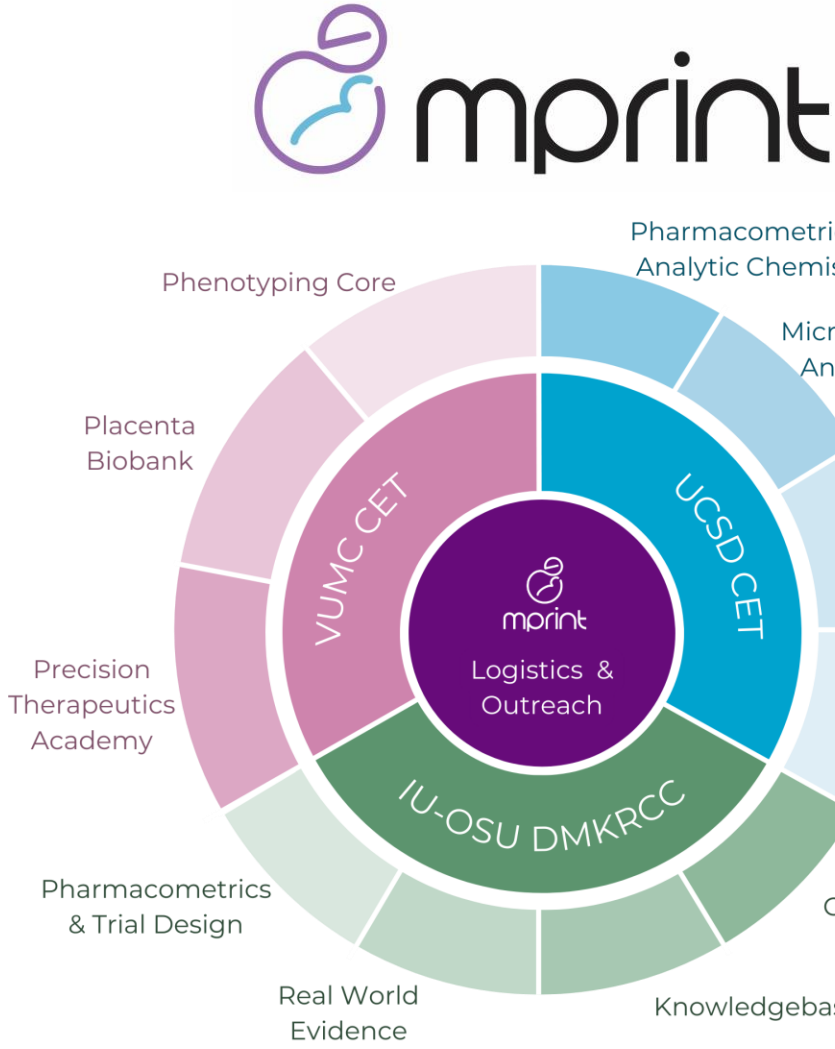
Study Design Considerations

Toolkit for researchers

A Collaborative Effort is Needed to Accelerate Optimal and Ethical Inclusion of Pregnant Women and Persons in Research

Slides Adapted from Presentation by Nicole Salazar-Austin, MD ScM
Slide Courtesy of Kelly Dooley





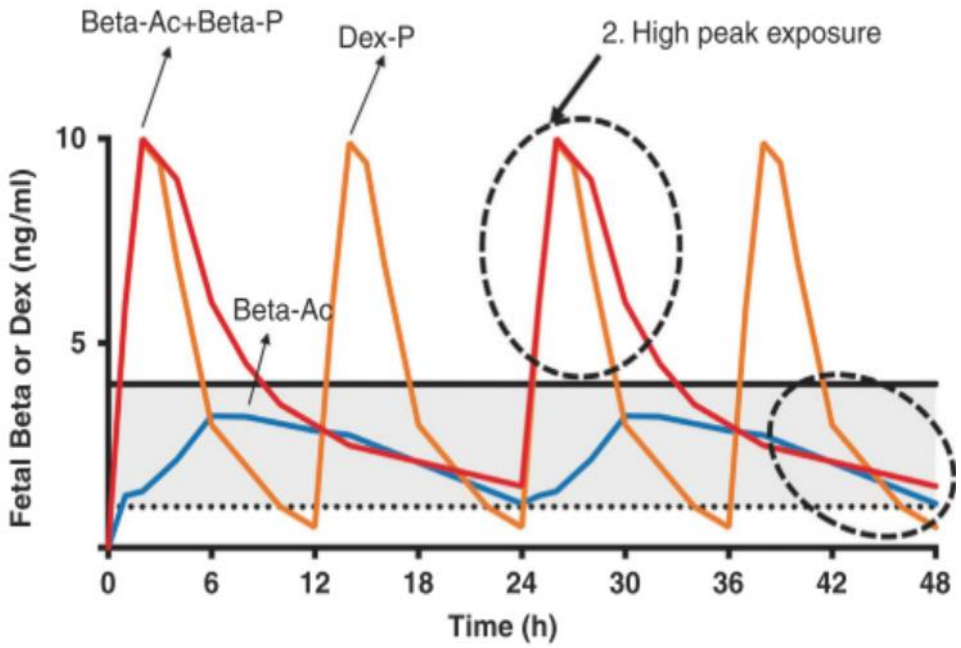
VANDERBILT UNIVERSITY MEDICAL CENTER

Department of Pediatrics

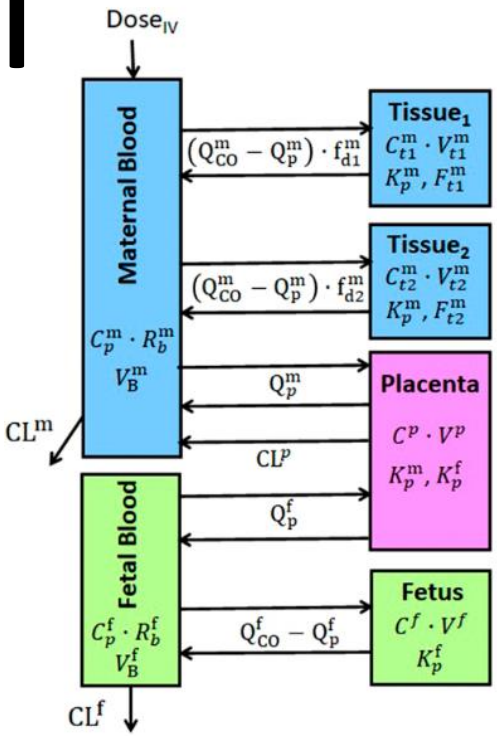
About | Divisions | Centers/Institutes | Research | Patient Care | Diversity

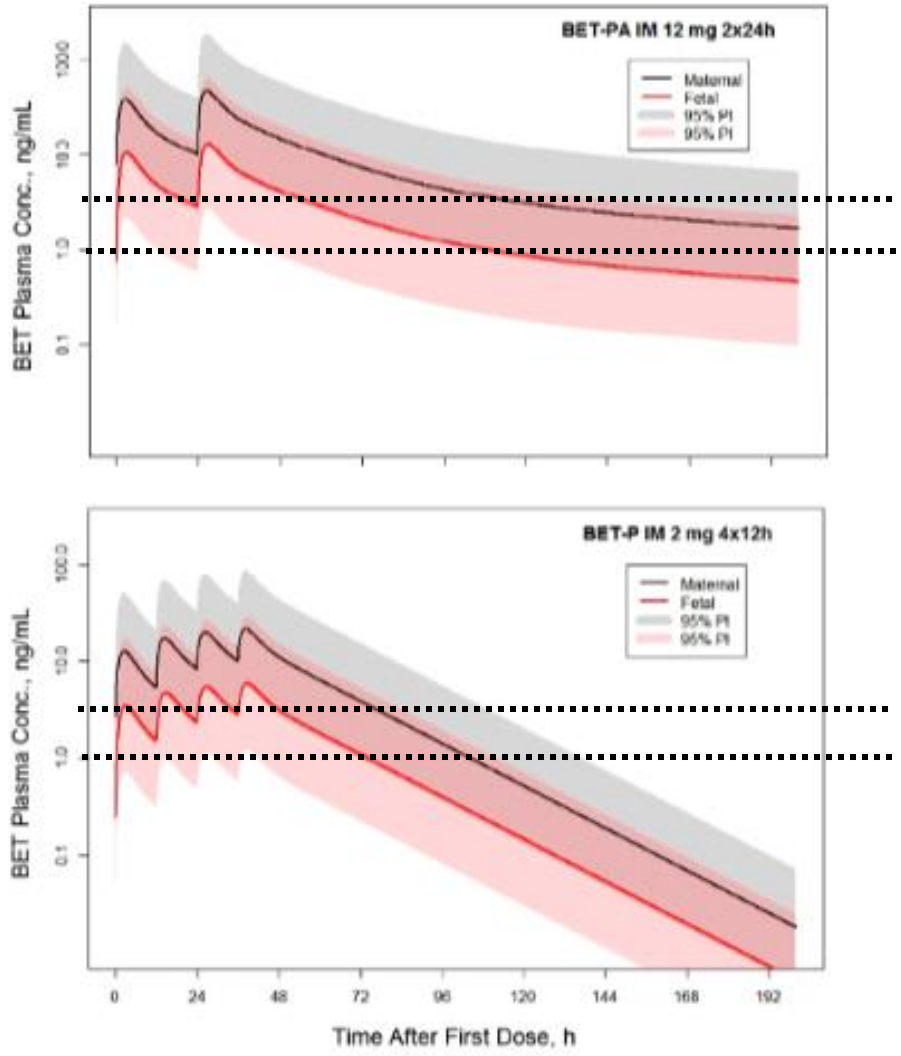
Vanderbilt MPRINT Precision Therapeutics Academy

The Role of Pharmacometrics: Rethinking Antenatal Corticosteroids



Jobe, Pediatric Research, 2021





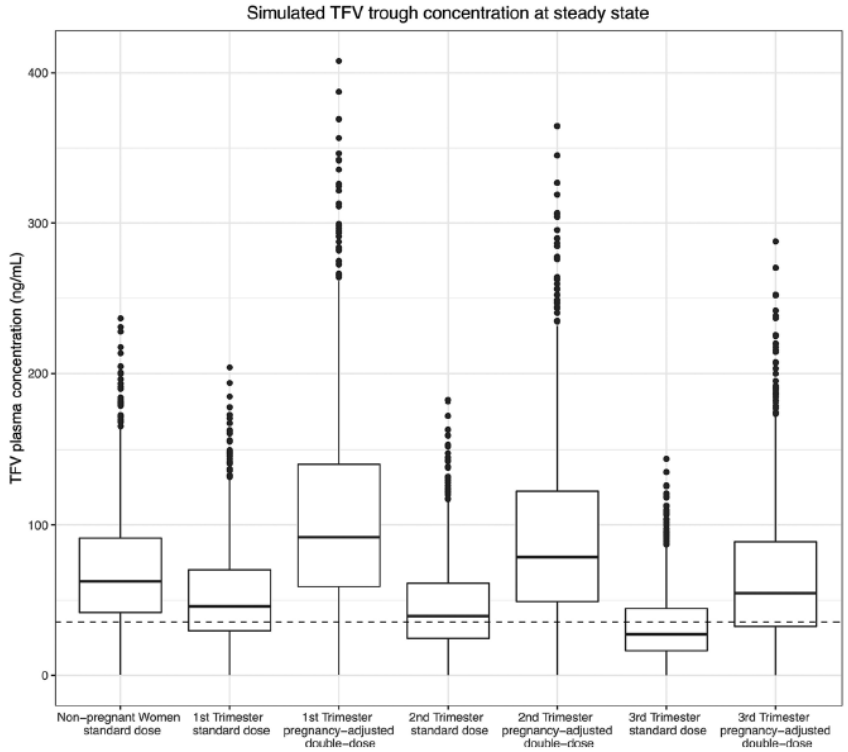
Krzyzanski, CPT:PSP, 2023

The Role of Pharmacometrics: Clinical Study Design in Pregnancy

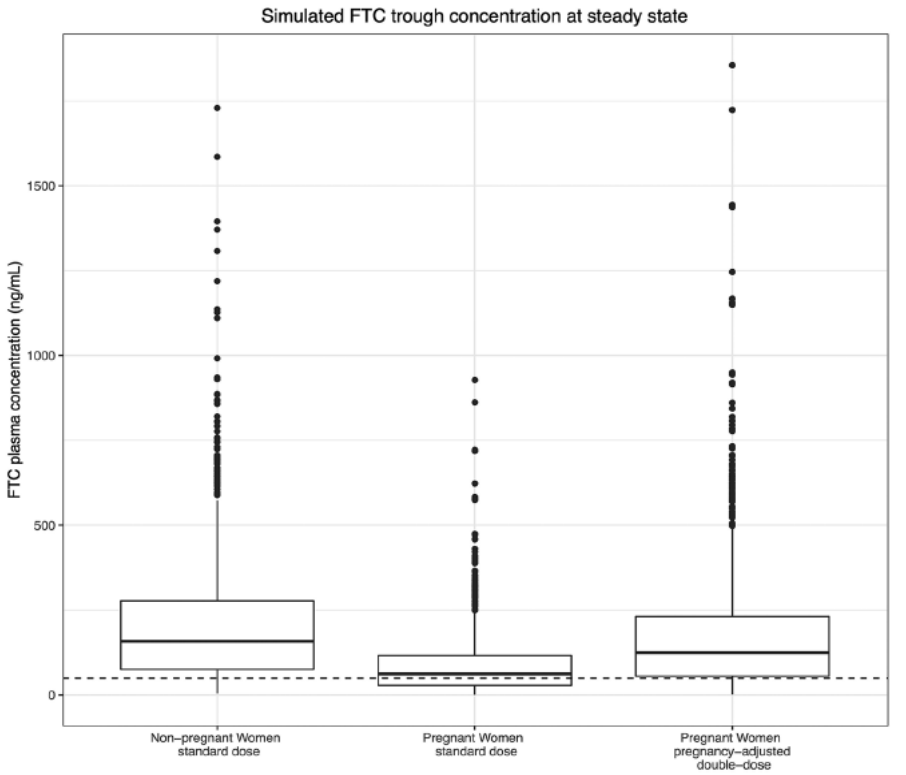
Population PK Model Developed using data from
95 non-pregnant & 33 pregnant individuals

	CL/F Increase	RSE %
TFV, 1st Trimester	21.4%	55
TFV, 2nd Trimester	33.9%	34
TFV, 3rd Trimester	63.9%	29
FTC, pregnancy	63.1%	23

Tenofivir (TFV)

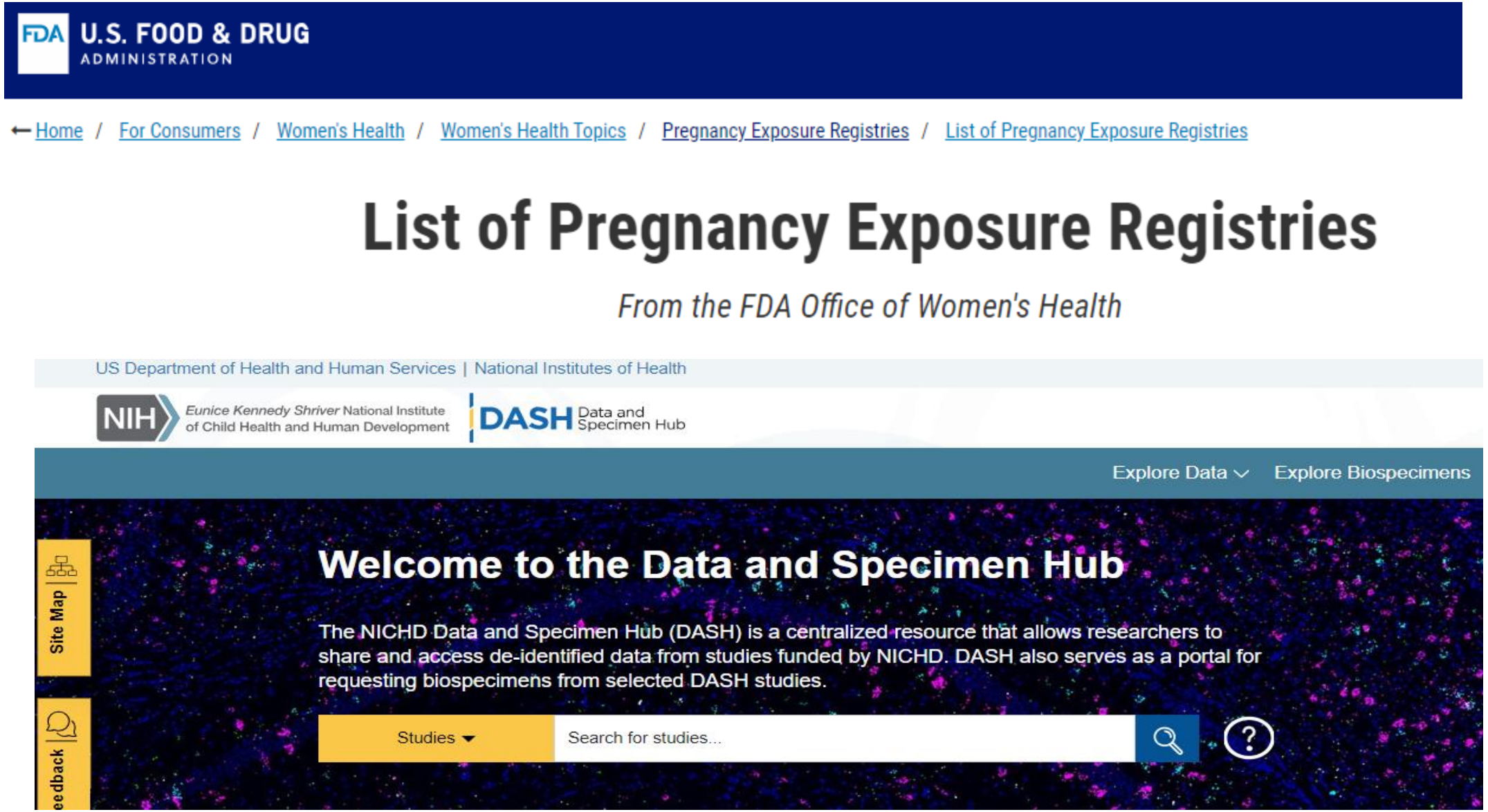


Emtricitabine (FTC)



Scott, Frontiers Reprod Health 2023

Real-World Evidence Resources



Take-Home Messages

- Not “vulnerable” or “special” but “complex” and “understudied”
- Protection **through** research not **from** research
- Maternal populations should be studied earlier in drug development
- Preclinical, clinical, and real-world data can be integrated through pharmacometric modeling to support study design
- Regulatory Support
  - Reduce regulatory barriers to enrolling pregnant & lactating individuals
  - Justify exclusion
  - Preclinical and translational studies in pregnancy earlier in development
  - Encourage use of quantitative modeling to guide dosing