Maternal plasma inflammatory markers as biomarkers for adverse pregnancy outcomes in women on antiretroviral therapy

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International Maternal Pediatric Adolescent AIDS Clinical Trials Network

ANNUAL MEETING
2024

Key Messages

- Even with sustained viral suppression, pregnant people living with HIV are more likely to experience adverse pregnancy outcomes (APOs)
- Systemic inflammation has been identified as a factor contributing to APOs
- Technologically advanced profiling of circulating inflammatory proteins permits further investigation into the role of inflammation in APOs
- Plasma Inflammatory proteins from pregnant women living with HIV randomized to 3 ARV regimens in IMPAACT 2010 will be measured

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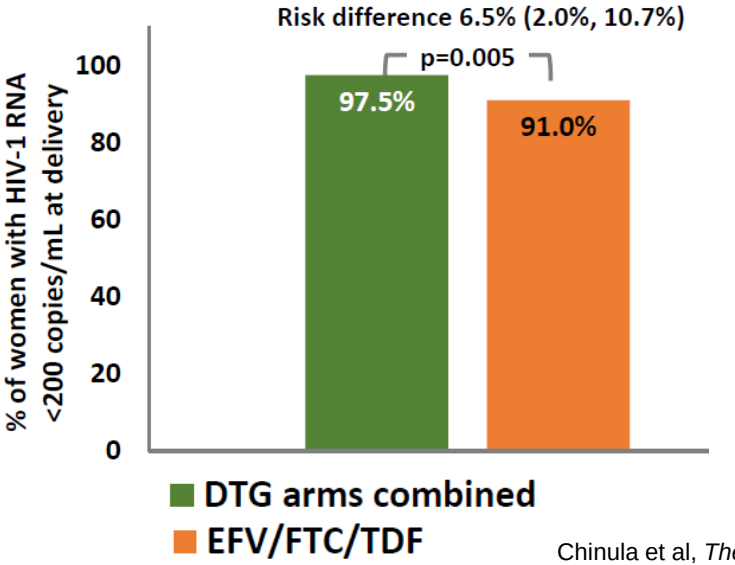
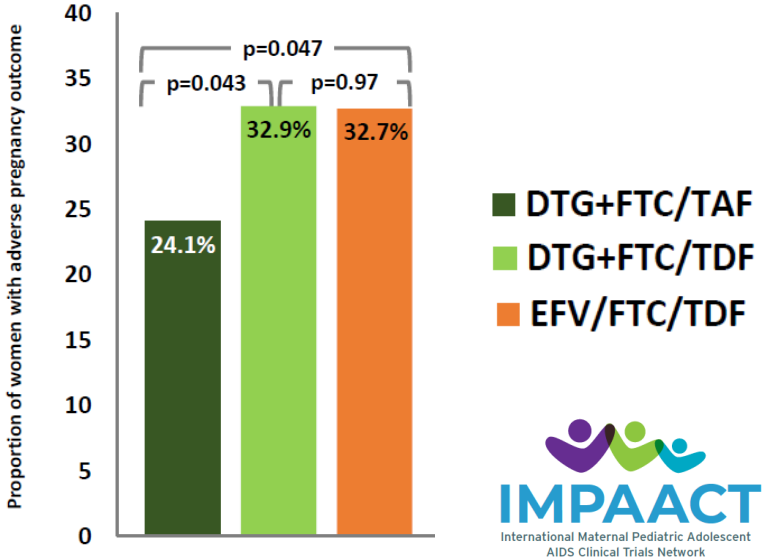
Despite >90% of IMPAACT 2010 mothers achieving viral suppression by delivery, more than 1 in 4 had an adverse pregnancy outcome

- HIV-1 RNA PCR <200c/mL



- Frequent APOs
  - Preterm delivery
  - SGA
  - Stillbirth



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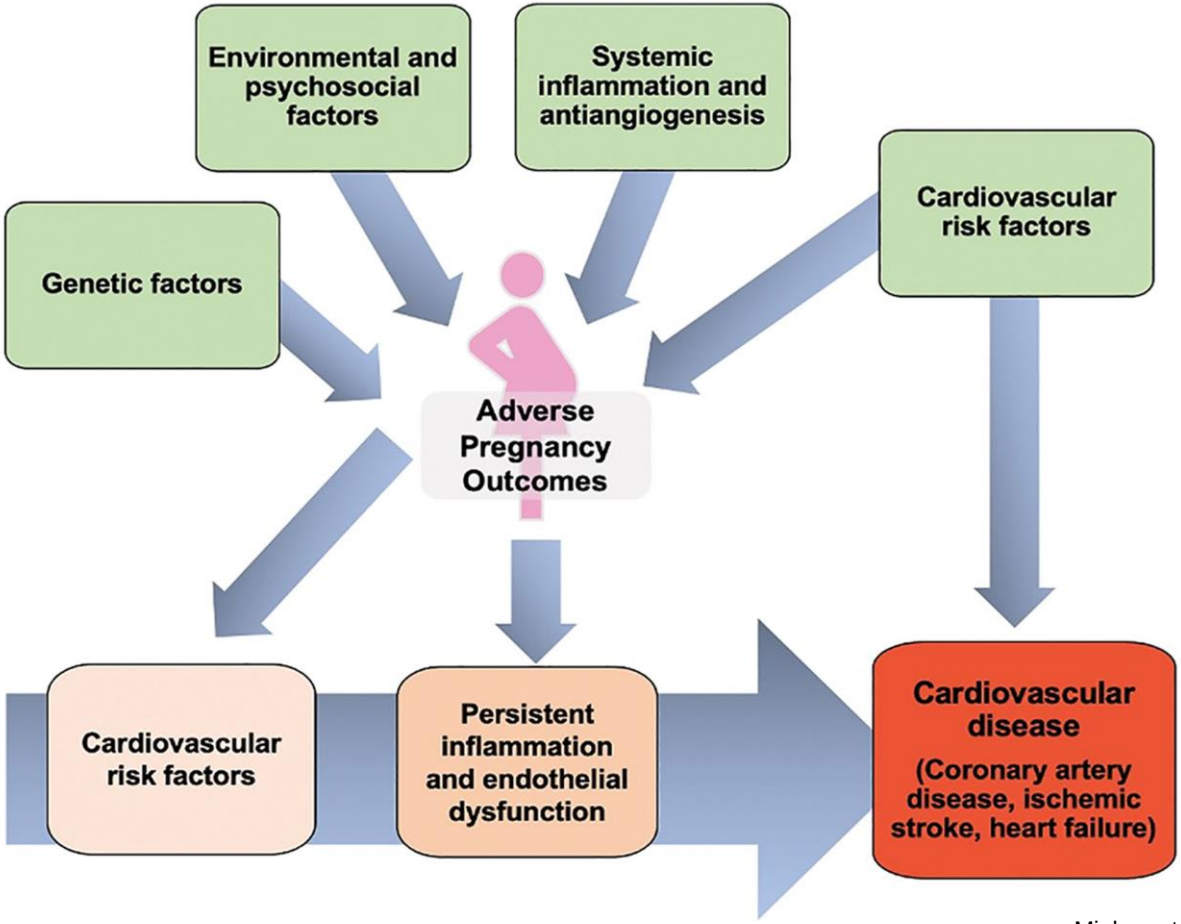
Chinula et al, *The Lancet* 2021

Systemic inflammation contributes to APOs



Minhas et al, 2023

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Study Overview

The proposed study will utilize stored plasma samples from IMPAACT 2010 study to:

- Profile maternal inflammatory proteins longitudinally in pregnant women randomized to 1 of 3 ART regimens
- Compare inflammatory protein profiles between ART regimens
- Delineate the association of inflammatory proteins with APOs
- Identify the association of inflammatory proteins with maternal medical conditions and sociodemographic characteristics

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Study Objectives

- **Primary objectives:**
  - To characterize inflammatory proteomic profiles from pregnant women on DTG and EFV-based ART.
  - To compare inflammatory proteomic profiles among women on DTG and EFV-based ART.

- **Secondary objectives:**
  - To determine association between of inflammatory proteins with APOs.
  - To seek correlation between inflammatory proteins and maternal sociodemographic and clinical characteristics.

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Study Hypothesis

Inflammatory proteomic profiles in maternal plasma measured between 14-28 weeks gestation are differentially expressed between DTG and EFV based ART regimens and are associated with APO events.

Design and Methods

- Retrospective laboratory-based study utilizing frozen plasma samples collected from maternal participants enrolled in IMPAACT 2010 who provided informed consent for future use of stored laboratory specimens
- 476 maternal samples (96 APOs) collected at Visit 0 = entry and Visit 8 = 8wks after entry
- Demographic and study outcome data will be obtained from the main study database hosted at FSTRF
- Inflammatory proteins will be profiled using the Olink® Target 96 proteomic platform

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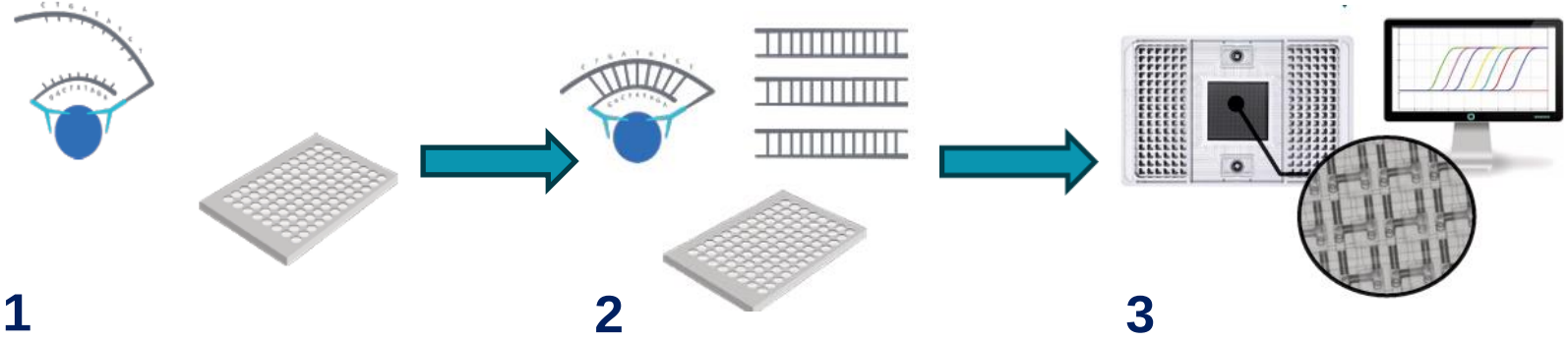
High-throughput proteomic technology: Olink



Incubation

Antibody pairs, labelled with DNA oligonucleotides, bind to their respective protein in the samples –

16-22hrs

Extension and Amplification

Hybridization and extension of oligonucleotides using a DNA polymerase. This newly created piece of DNA barcode is amplified by PCR – 2hrs

Detection

The amount of each DNA barcode is quantified by microfluidic qPCR – 4.5hrs

https://olink.com/products/olink-target-96

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Statistical Analysis

To characterize inflammatory proteomic profiles from pregnant women on DTG and EFV-based ART	• Heat maps of spearman's coefficient correlation
To compare inflammatory proteomic profiles among women on DTG and EFV-based ART	• Compare group means using t-tests
To determine association between of inflammatory proteins with APOs	• Compare the risk of APOs using risk ratios
To seek associations between inflammatory proteins and maternal sociodemographic and clinical characteristics.	• Estimate beta coefficient using linear regression

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Challenges

- Significant delays in establishing specimen transfer agreements with USA collaborating lab

- Identifying a US laboratory ready to perform RNA extractions on HIV plasma samples
- Unclear costs for laboratory processing at the planning stage
- VISA processing for a learning visit to the USA
- Coordinating a team with competing schedules

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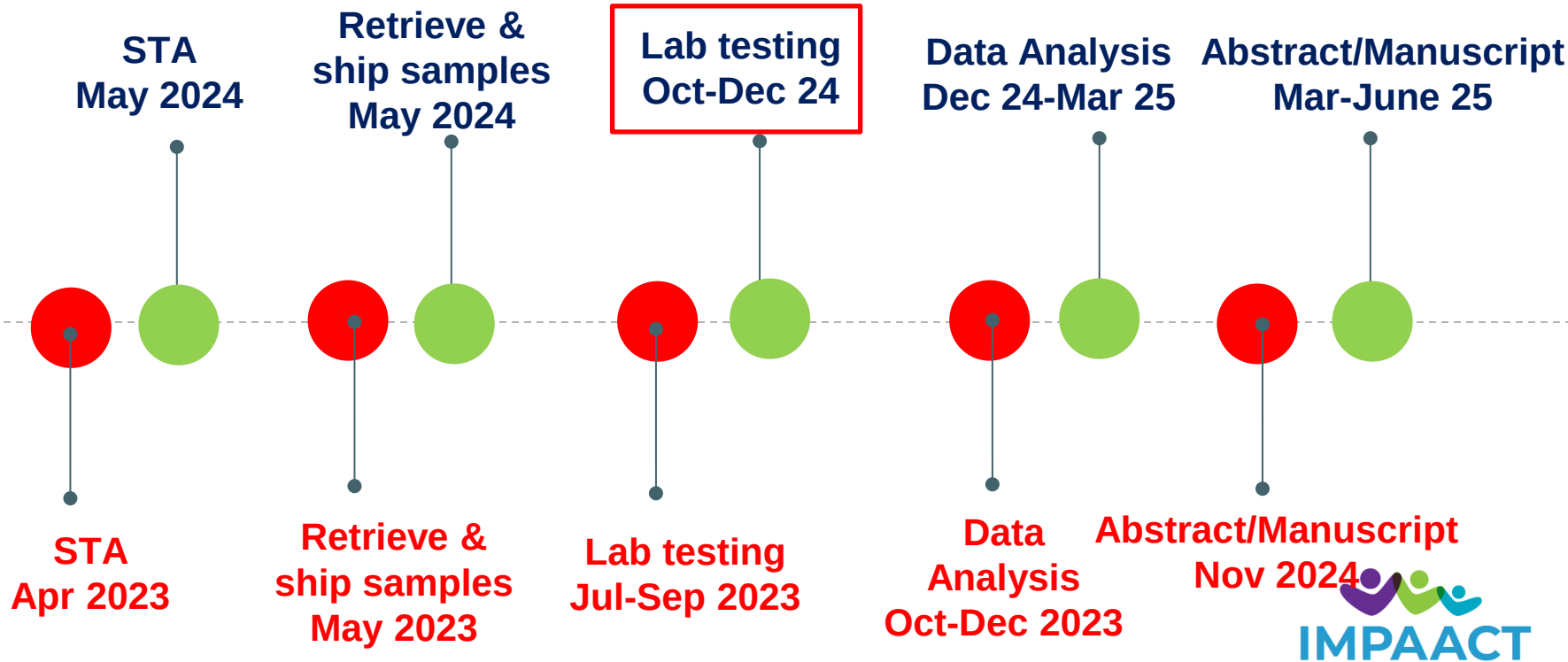
Study Timelines



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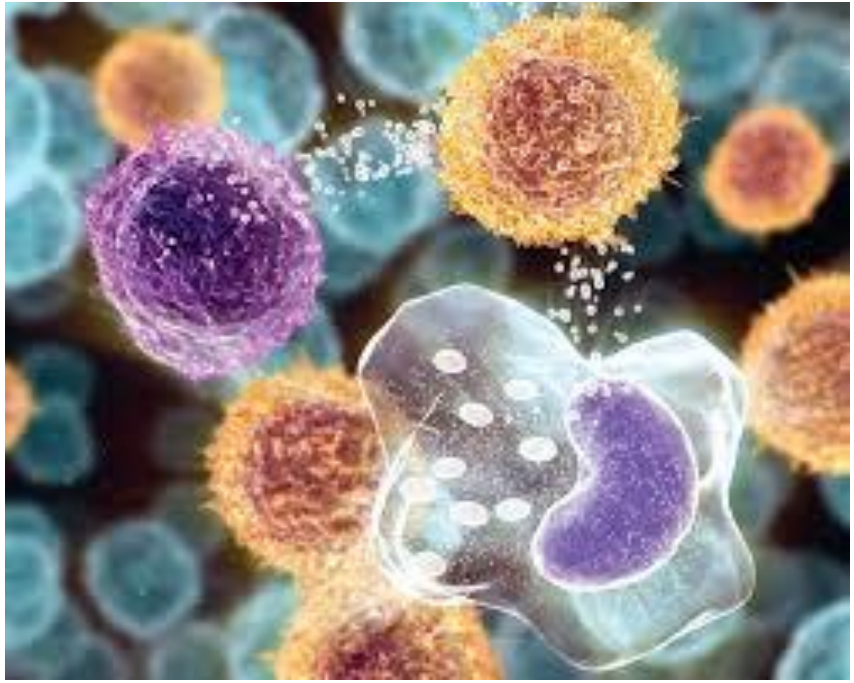

Thank You!

Any questions?

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