



# IMPAACT Prevention Science Working Group :

PROMISE Update  
June 14, 2016



Promoting Maternal and Infant Survival Everywhere

# PROMISE : Past, Present and Future

## Its been a long Journey!



# The Beginnings, 2009-2011

- 2009--Jerry Coovadia and Lynne Mofenson propose a comprehensive concept to address all remaining major PTMCT questions!
- 2009-2011 The PROMISE name is born over a glass of wine at the Double Tree Rockville.
  - Many meetings, Many hotels,
  - Lynne n wears out at least one computer
  - Protocol trainings par excellence per FHI
- March 2011, the first enrollment!

# 1077BF is Launched: 3 Components

**Antepartum**  
(14 wks-term)

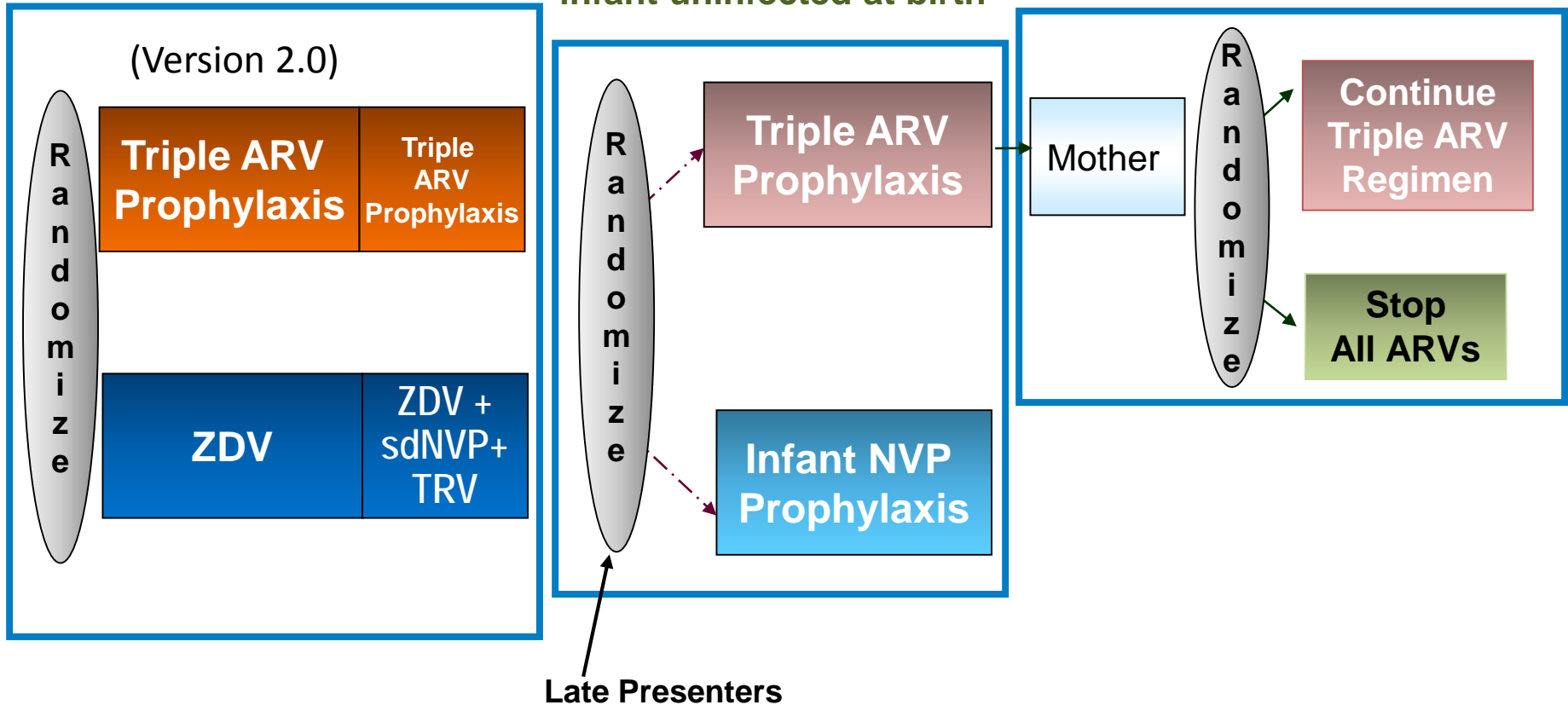
**Labor/  
Delivery**

**Postpartum**  
(for duration of BF)

**Maternal Health**  
(after BF cessation)

Maternal  
CD4 >350

infant uninfected at birth



# 1077FF is Launched: 2 Components

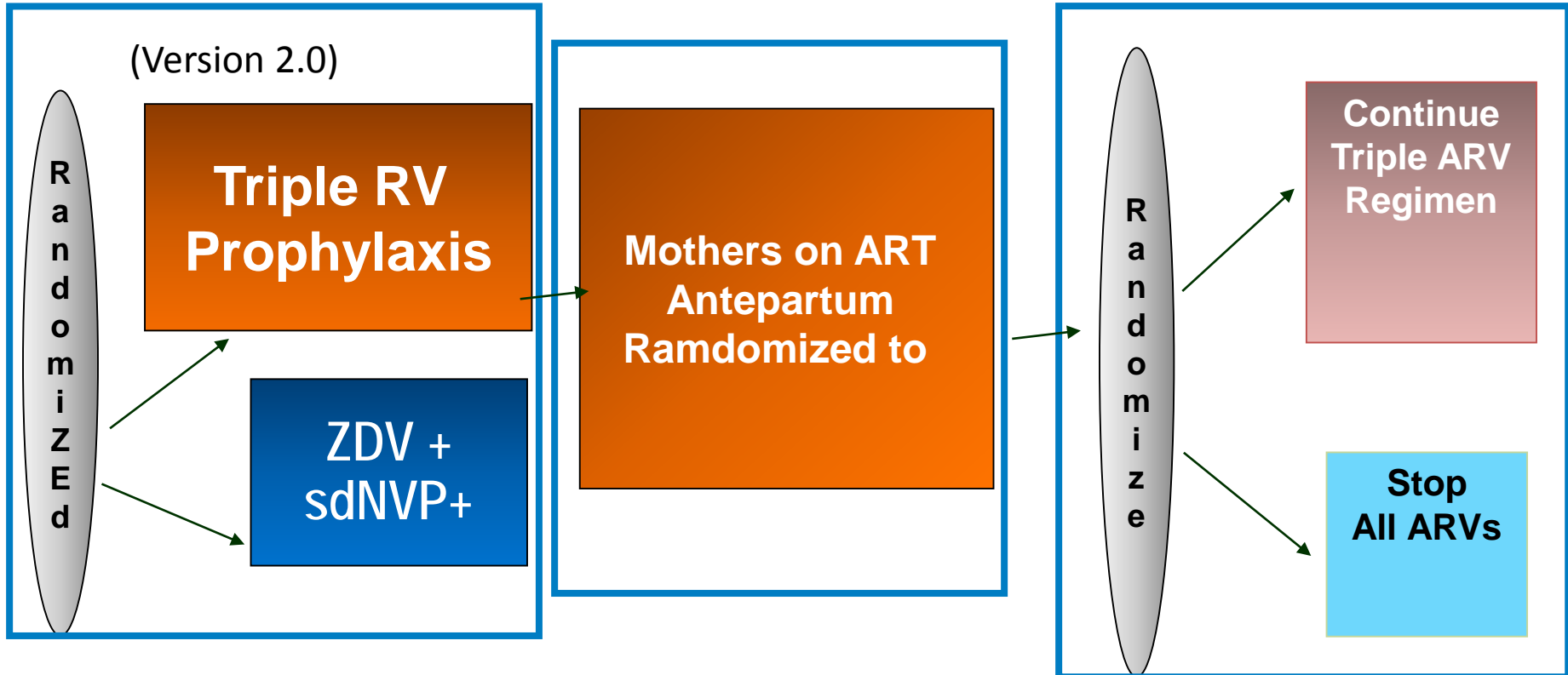
**Antepartum**  
(14 wks-term)

**Labor/  
Delivery**

**Maternal Health**

Maternal  
CD4 > 350

Babies Formula Fed



# IMPAACT 1077BF

Designed for settings in which the standard of care for PMTCT involves maternal use of zidovudine (ZDV) or other non-triple antiretroviral (ARV) regimens during pregnancy and the standard method of infant feeding is breastfeeding



## **Sites in:**

- *India\**
- *Malawi*
- *South Africa\**
- *Tanzania*
- *Uganda*
- *Zambia*
- *Zimbabwe*

*\* Also FF sites*

# PROMISE 2011-2015

- 2011-2014 Ongoing Enrollment
- Semi Annual DSMB meetings
- NIAID Convened Ethics meeting May 2012
- **HPTN 052 results IAS Vienna 2012**
- 2013 WHO Harmonized Guidelines Announced
- 2014 PROMISE Enrollment Halts—
  - July Late presenters and 1077FF
  - Oct 1, Antepartum, Post partum, Mat Health
- March 2015, last PROMISE baby is born!
- **June 2015, START results announced;**
- **PROMISE randomized data ends July, 2015**

# PROMISE Substudies

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## Hepatitis B Substudy

- **139** Hepatitis B co-infected mothers enrolled
  - Estimated Hepatitis B prevalence = **3.9%**
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## P1084s Substudy

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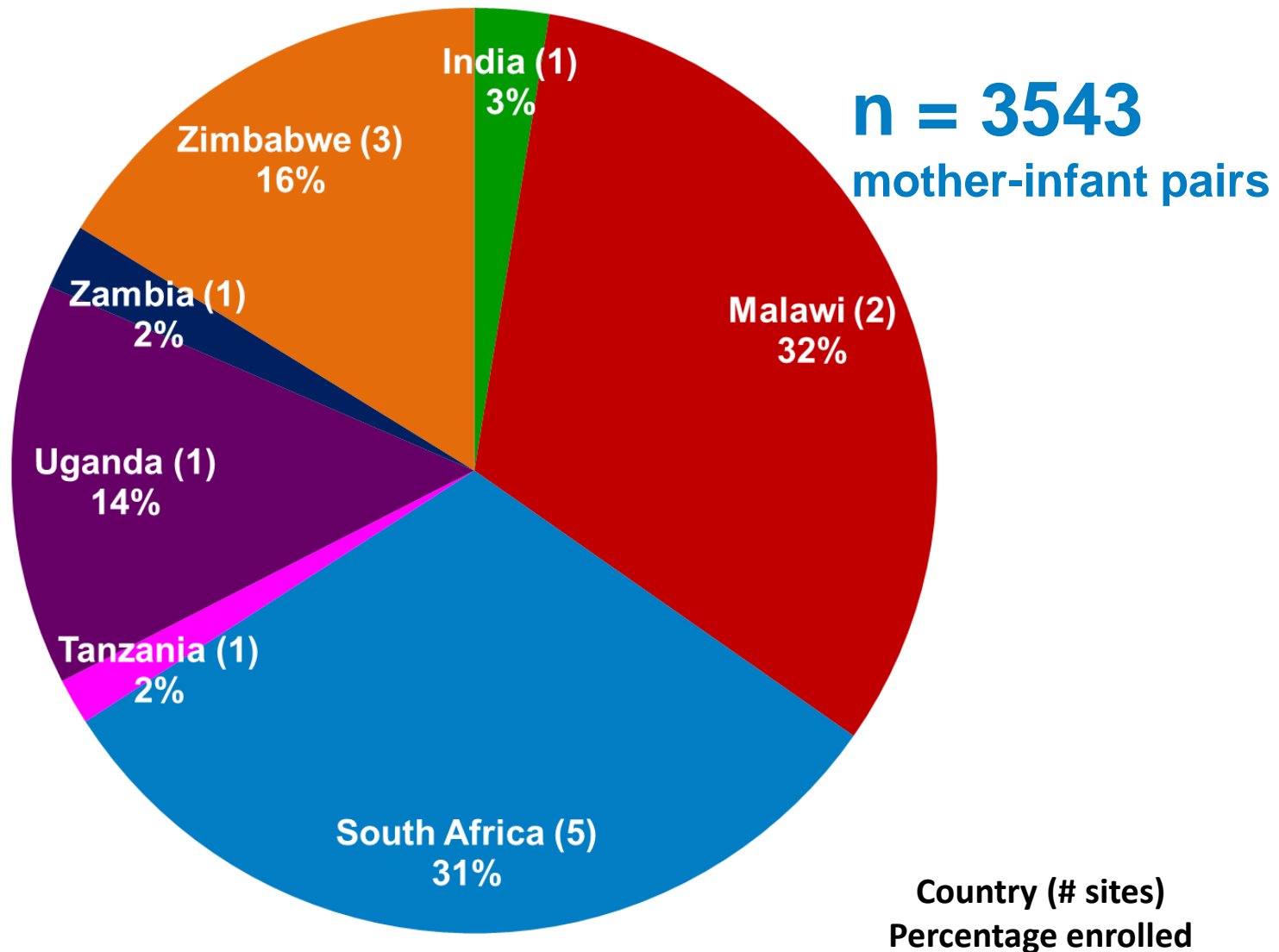
- **400** pairs enrolled in the Postpartum Part **479** pairs enrolled in Antepartum Part
  - Antepartum analyses presented CROI
  - Postpartum analyses to be presented Durban
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## Oher Substudies:

**Resistance, Inflammatory Markers, Hair ARV levels, Adherence and other planned Studies**



# 1077BA and 1077FA Final Accrual by Country



# Data and Safety Monitoring Board (DSMB) Reviews and Recommendations

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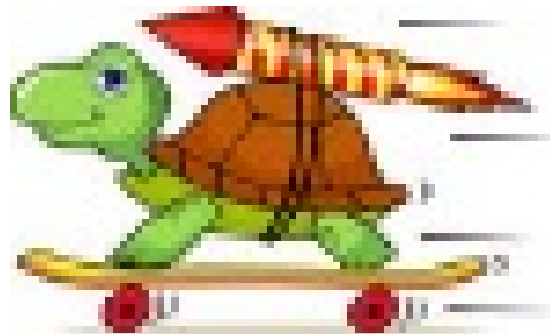
- Nov 2014 interim review, DSMB reported pre-specified efficacy boundary for 1077 **Antepartum Component** was crossed and safety differences by arm. Disseminate
- **START results announced June 2015**
- Offering of ART to all women in PROMISE begins July 2015.
- **Continue Safety Follow up in 1077HS thru Aug 2016; and 1077BF/FF through Sept 2016**
- **Nov 2015: Disseminate PROMISE Postpartum and Maternal Health**



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# PROMISE 1077

## Durban Presentations



# 2016 Durban Abstracts

- Pediatric International Workshop
  - Post partum efficacy/safety results
  - 1084s Maternal DXA results
  - 1084s Growth results
  - Maternal Uptake post START Results
  - Neurodevelopmental and Growth results, Malawi and Uganda compared to controls
- IAS
  - 1077BP Post Partum Results
  - 1077HS results
  - Maternal Uptake ART post START results—HS and BF



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# PROMISE 1077 Publication Updates



# PROMISE Publications

- Antepartum
  - Efficacy and Safety— submitted NEJM
  - Risk Factors for LBW and PTD—in prep
  - Risk Factors for Transmission
  - 1084s newborn growth results—presented CROI—manuscript in prep
- Cross Cutting
  - Hepatitis B
  - Resistance

# PROMISE Publications: Primary and Secondary Objectives

- Post Partum
  - Efficacy and Safety— in prep
  - Risk Factors for Transmission
  - 1084s postnatal growth results—
  - Maternal DXA results by treatment arm
  - Infant infection –RF
  - Late Presenters
- Maternal Health
  - Efficacy and safety—in prep
  - Maternal adherence—in prep
- DACS and investigator initiated using PROMISE data and specimens

## PROMISE Grants: Submitted and Planned

- Resistance –Lisa Frenkel/Susan Fiscus
- Inflammatory Markers – Risa Hoffman/Judy Currier, Adrianna Weinberg
- Hair ARV measures—Monica Gandhi
- Breast Milk antibody responses – Sallie Permar



# Life after PROMISE

What's next ?

# Extended Follow up of Safety at High Enrolling PROMISE Sites: PROMOTE

- PEPFAR funded
- 7 sites in Zimbabwe, S. Africa, Uganda and Malawi
- Focus on follow up of safety including
  - Repeat pregnancy outcomes
  - Safety outcomes by specific regimens
  - Maternal DXA follow up
  - Long term maternal adherence
  - Development of resistance over time
  - Child growth and Developmental Follow up
- Mentor/Mentee implementation science

# Summary and Conclusions

- PROMISE has achieved many of its goals in providing important safety and efficacy
- All ART regimens appear effective as do simpler regimens
- Longer Term Follow up for Safety of ART will be important for maternal complications including resistance, child growth and development
- PK and safety of new drugs is needed in pregnancy and neonates
- Maternal lifetime adherence remains a major challenge for HIV infected mothers

# PROMISE Team

## Acknowledgements

- All the Women and their Children who gave their time and participated in the PROMISE study
- The investigators and PROMISE staff at all the PROMISE sites
- IMPAACT Leadership
- FSTRF –Michal Basar/ FSTRF PROMISE staff
- SDAC—David Shapior, Terry Fenton, Min Qin, Nadia Konstantia, Mae Casseday/SDAC staff
- FHI 360—Anne Coletti, Katie McCarthy, Megan Valentine
- NIH staff –Lynne Mofenson, Devasena G, Karin Klingman, Renee Browning, George Siberry

# Acknowledgements

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The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

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# 1077HS is Launched: 1 Component

Antepartum (14 wks-term) Labor/Delivery)

Maternal Health

Maternal  
CD4  $\geq$  400

Babies Formula Fed

Mothers on Triple  
ARVs  
Antepartum as SOC  
Randomized  
at Delivery to

R  
a  
n  
d  
o  
m  
i  
z  
e

Continue  
Triple  
ARV  
Regimen

Stop  
All ARVs

# IMPAACT 1077HS

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*Conducted in settings where the standard of care for PMTCT involves use of triple antiretroviral regimens throughout pregnancy and the standard method of infant feeding is formula feeding*



## **Sites in:**

- Argentina
- Botswana
- Brazil
- China
- Haiti
- Peru
- Thailand
- US



# PROMISE Enrollments

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## *Accrual into all components closed on or before 1 October 2014*

- 3259 mother-infant pairs 1077BA
- 284 pairs in 1077FA  
(**3543** pairs in Antepartum total)
- 204 pairs in 1077BL
- 2431 pairs in 1077BP
- 799 women in 1077BM
- 76 women in 1077FM (875 in MH total)



National Institutes  
of Health



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Thanks to everyone for all the hard work  
and dedication to carry out PROMISE!