



International Maternal Pediatric AIDS Clinical Trials (IMPAACT) Network

Update on IMPAACT Research Agenda: Scientific Committee's Priorities & Accomplishments

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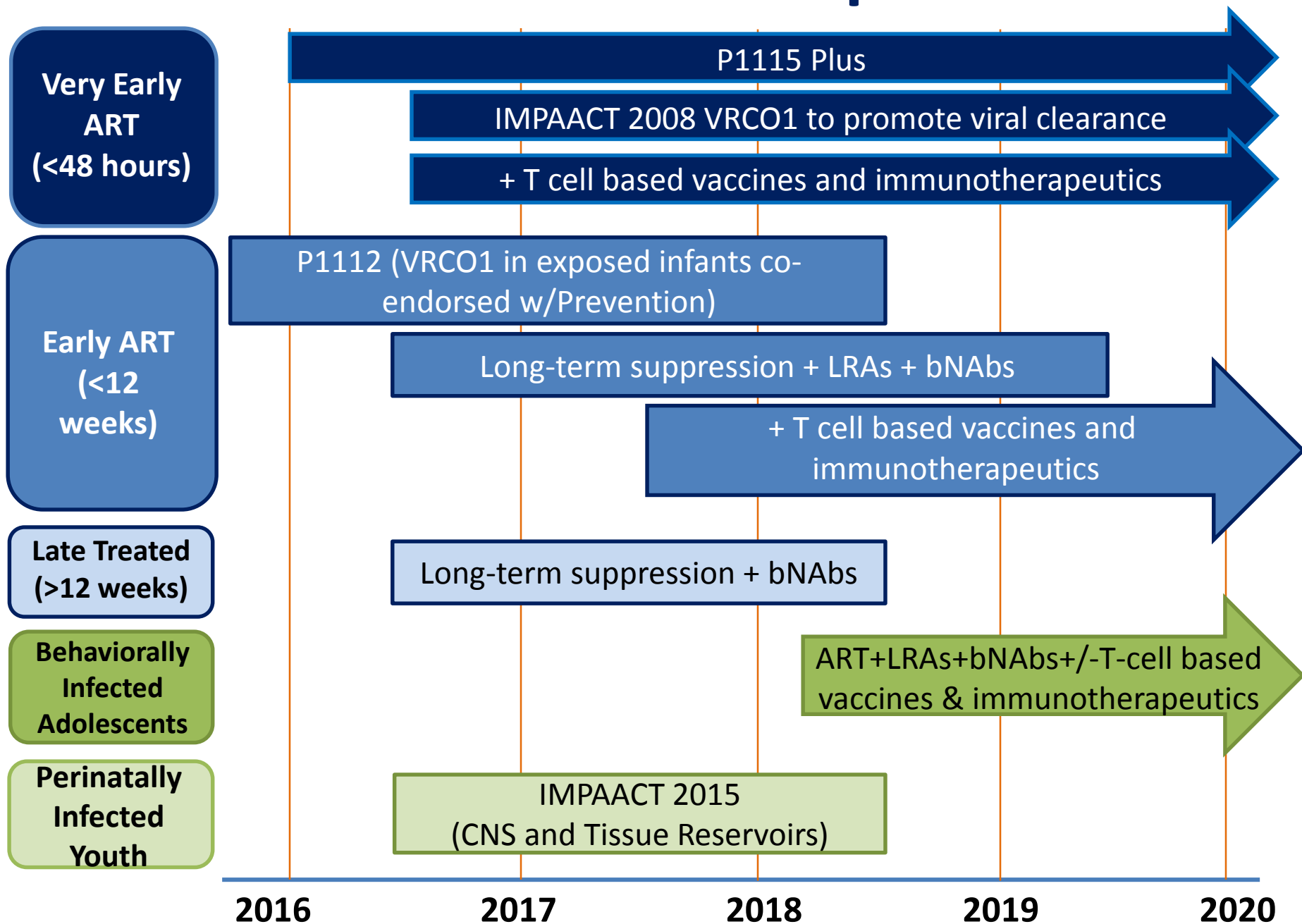
Overview

- Scientific Committee Updates
 - Drivers of each scientific agenda
 - What are the gaps in our current SC portfolios
 - Data to support studies in these cohorts
 - What studies are we planning to develop
- Lab Updates
- Early Career Investigator Program



**What is driving
the Cure agenda?**

Cure Roadmap



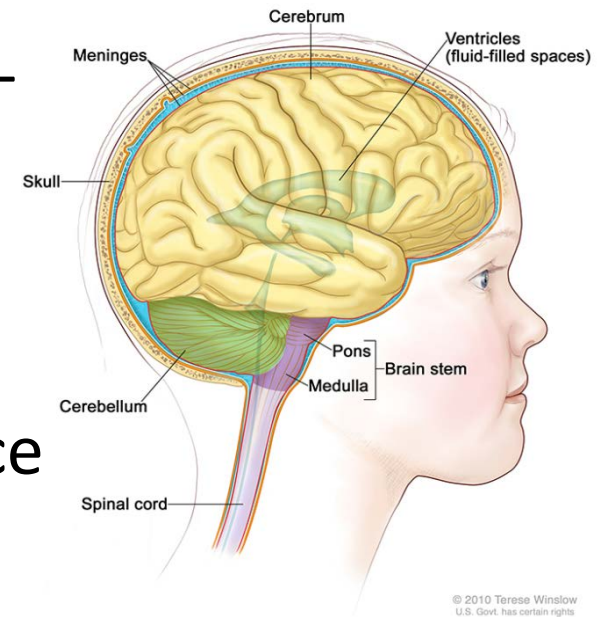
Plans for the Cure Agenda

- Optimizing HIV-1 remission and cure strategies for:
 - Older **infants** with immunotherapeutic agents (for example, IMPAACT 2008 or potential therapeutic vaccine study)
 - Older **children and youth** to reduce residual viremia (for example, characterize anatomic reservoirs and adaptive and innate immune responses)

Study Highlight: IMPAACT 2015

Evaluating the HIV Reservoir in the CNS in Perinatally-Infected Individuals on ART

- Study in development within the **Cure** Research Agenda
- Cross-sectional study of perinatally-infected youth and young adults on ART with neurocognitive impairment (n=30)
- Primary objective: assess prevalence of detectable HIV RNA and DNA in cerebrospinal fluid (CSF)

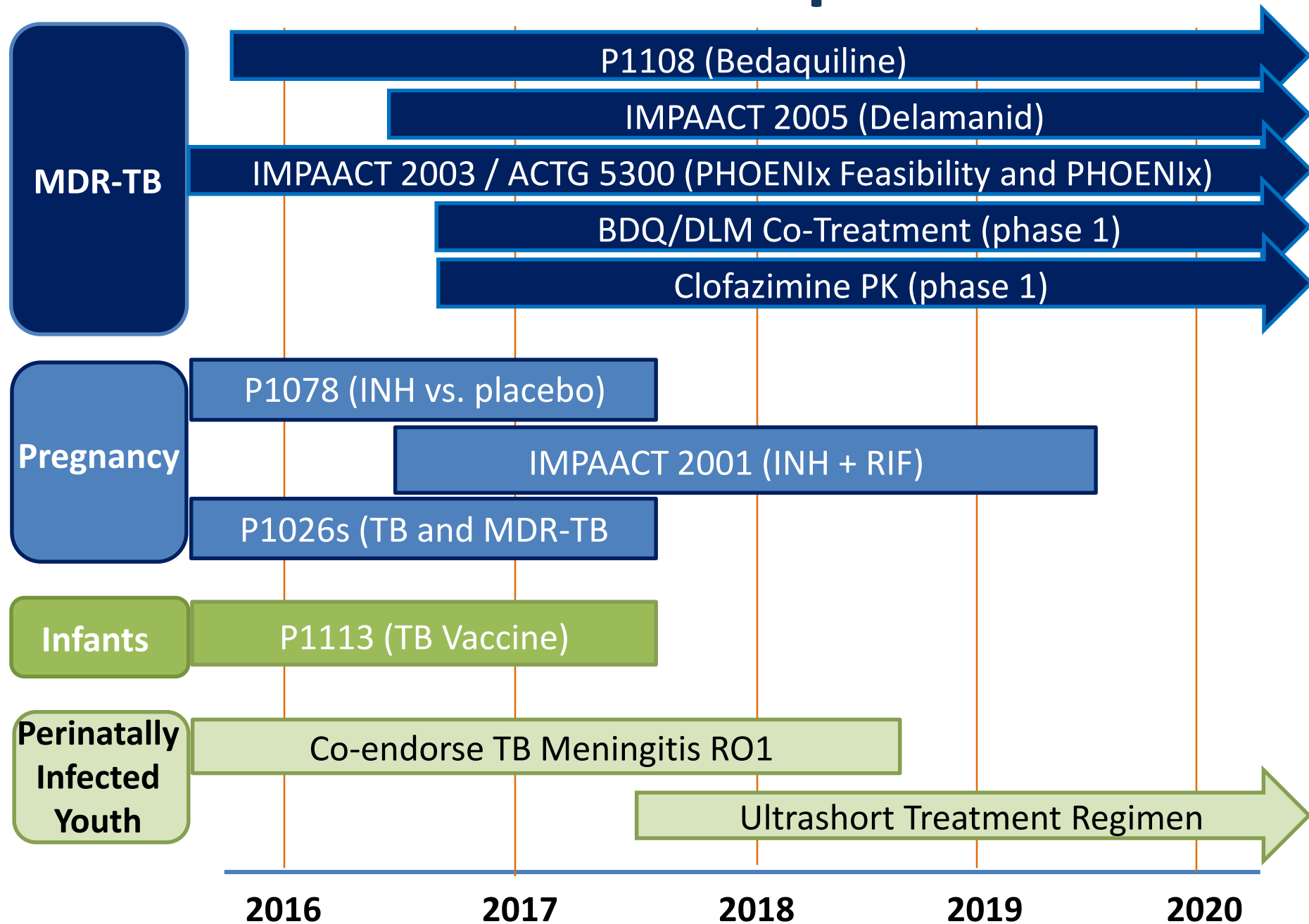




**What is driving
the Tuberculosis agenda?**

Estimated total cases in children	1,000,000 (10% global burden)
Childhood cases notified	360,000
TB deaths	136,000 (81,000 HIV-) 13.6% case fatality rate
Pediatric MDR TB cases	32,000 (underestimate)
TB infections	6.6 million

TB Roadmap



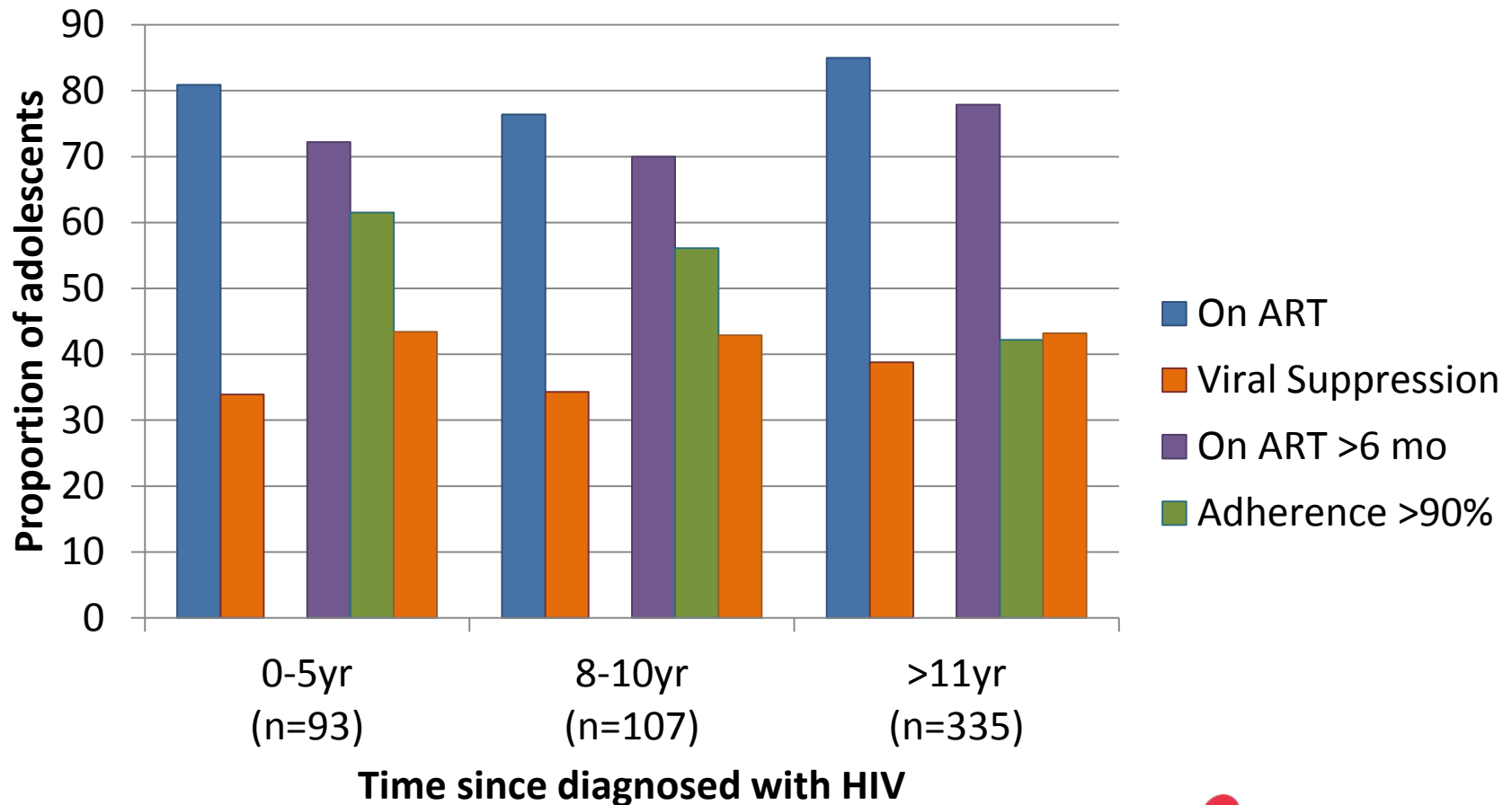
Plans for the TB Agenda

- MDR-TB
 - Injectable sparing short-course MDR-TB treatment for children
 - PK of clofazimine
- DS TB
 - Treatment shortening with rifampin dose optimization
 - Use of novel drugs
- Nest multiomic and imaging biomarker studies for treatment response
- Understand and expand site capacity for TB and MDR TB studies

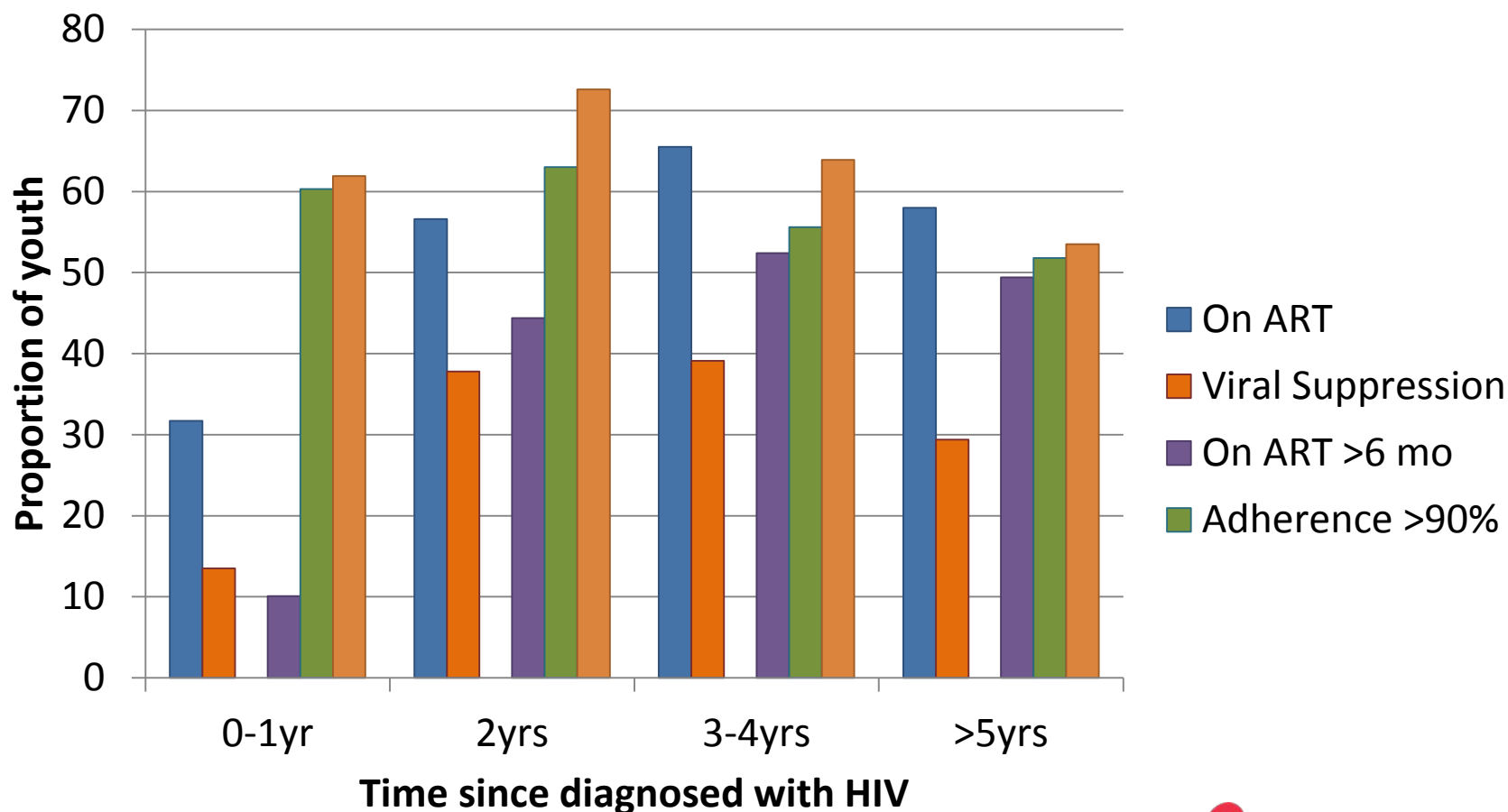


**What is driving
the Treatment agenda?**

Rates of viral suppression among 649 perinatally-infected youth, US



Rates of viral suppression among 1,547 youth with behaviorally acquired HIV, US



ARVs for Neonates and Infants

WHO ARV Dosing Annex, 2015

Table 4 (C). Drug dosing of liquid formulations for twice-daily dosing in infants less than 4 weeks of age*

NOTE: LPV/r not recommended for use in infants less than 2 weeks of age

Drug	Strength of liquid (mg/mL)	2-3 kg	3-4 kg	4-5 kg
AZT	10 mg/mL	1 mL	1.5 mL	2 mL
NVP	10 mg/mL	1.5 mL	2 mL	3 mL
3TC	10 mg/mL	0.5 mL	0.8 mL	1 mL
LPV/r****	80/20 mg/mL	0.6 mL	0.8 mL	1 mL

**** Do not use LPV/r solution in infants <2 weeks of age

~1.5 million Pregnant HIV-Infected Women Globally

Considerations for evaluating new drugs during pregnancy

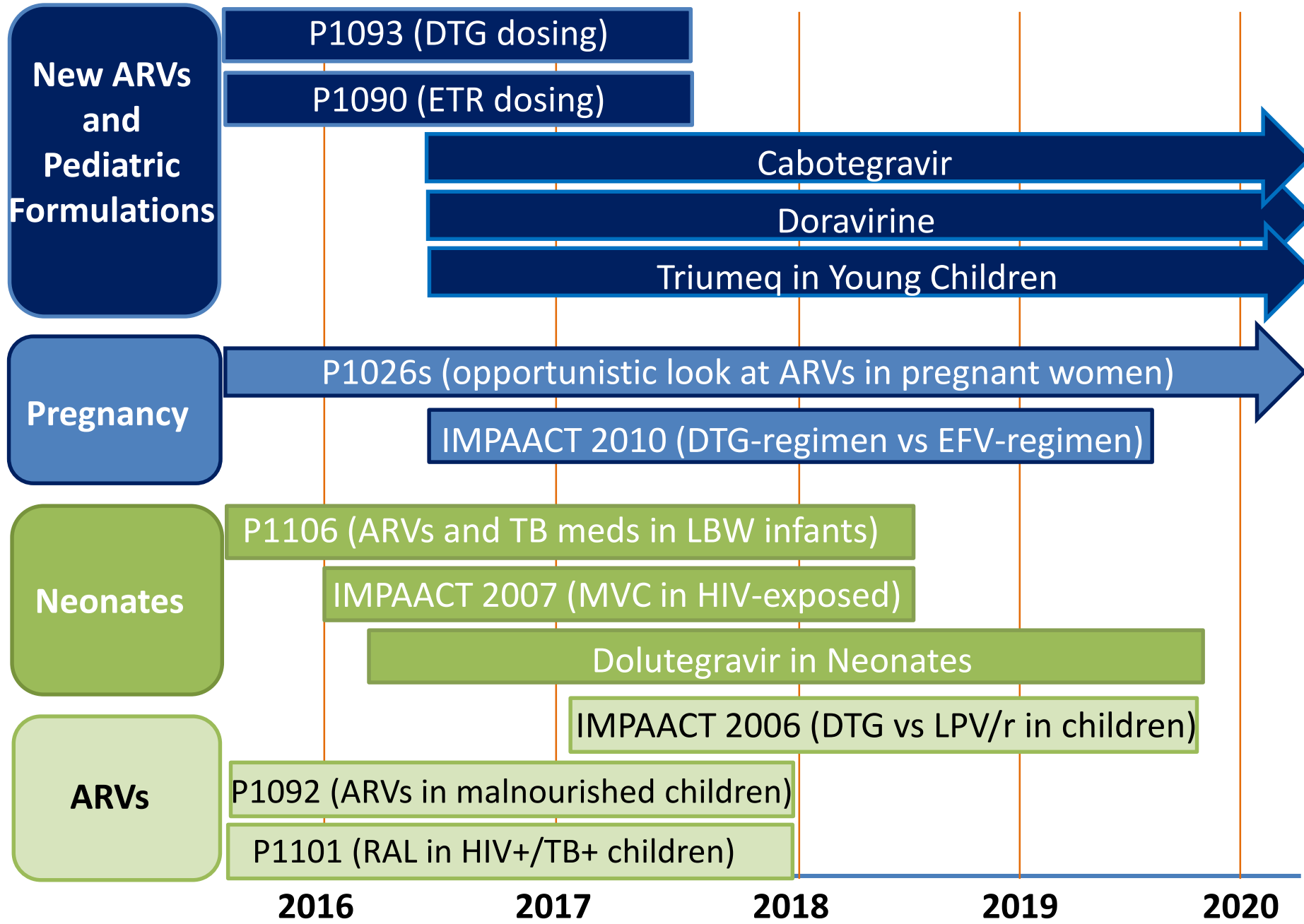
Pregnant Women

- **PK** – ensure proper dosing
- **Safety** – identify safety concerns of drug or drug combinations
- **Efficacy** – viral suppression

Children

- **Safety** – teratogenicity, birth outcomes, life course impact (short and long term effects)
- **Efficacy** – perinatal transmission, maternal viral suppression

Treatment Roadmap



Plans for the Treatment Agenda

- Safety and pharmacokinetics of ARVs in infants, children, and adolescents
 - ✓ Doravirine in HIV-Infected Adolescents (IMPAACT 2014)
 - ✓ Triumeq® in HIV-Infected Children (Capsule 525)
 - ✓ Oral & Injectable Cabotegravir in HIV-Infected Children & Adolescents (Capsule 524)
 - ✓ Dolutegravir in HIV-Exposed Neonates (Capsule 521)

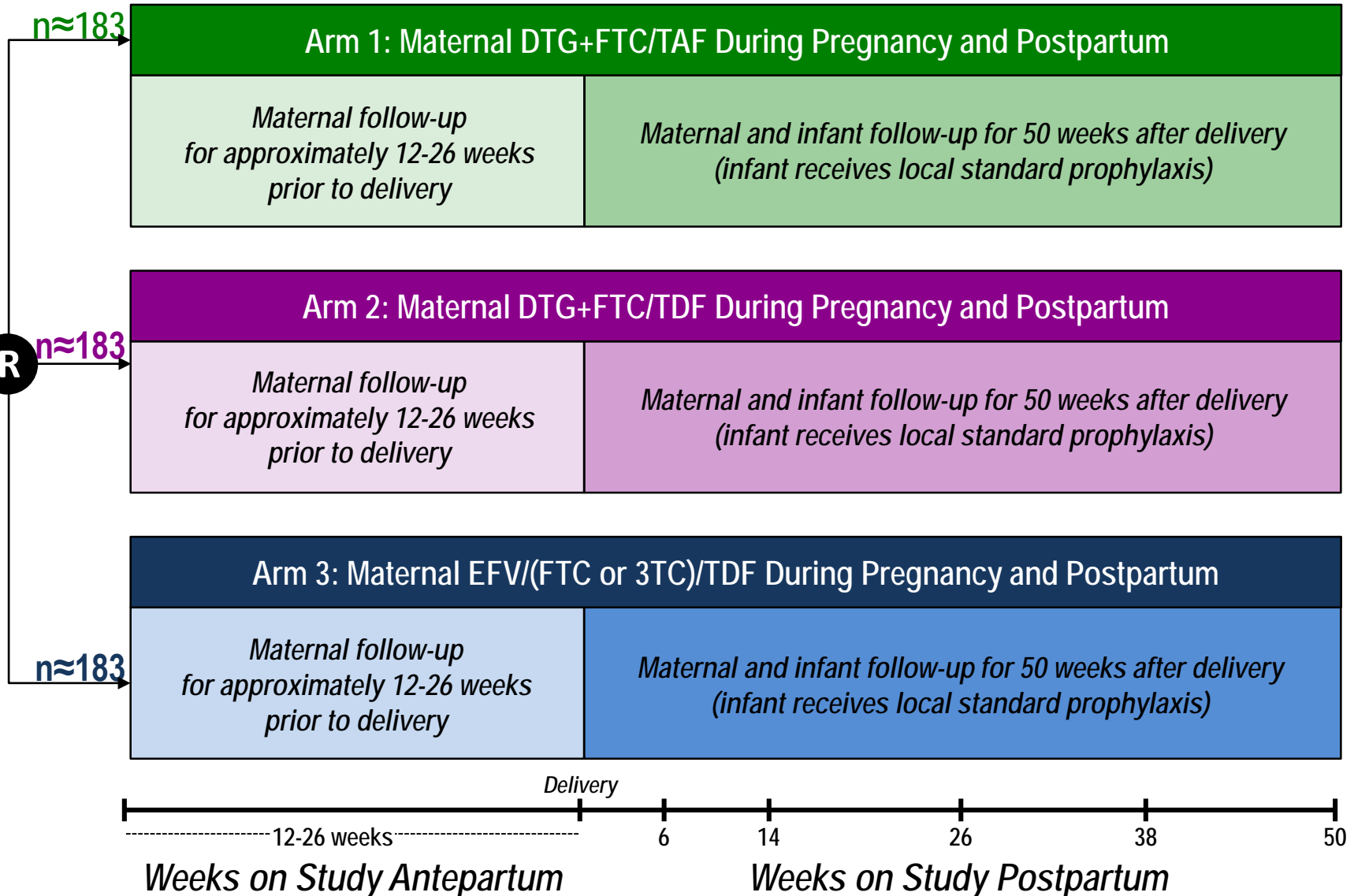
Study Highlight: IMPAACT 2010

Efficacy & Safety of DTG-Containing Vs. EFV-containing ART Regimens in HIV-Infected Pregnant Women & Their Infants

- Study in development within the **Treatment** Research Agenda
- Phase III study among HIV-infected pregnant women and their infants
- Purpose: compare virologic efficacy and safety of three ARV regimens



IMPAACT 2010



It's not just about the ARVs

- Where does adherence fit in?
- What about the different populations?
 - Pregnant women
 - Infants
 - Adolescents

Adherence Working Group

- Established in June 2015 with 14 members from IMPAACT, NIH, and external experts
- Purpose to review and provide guidance on IMPAACT studies
 - IMPAACT 2009
 - IMPAACT 2010
 - PHOENIX



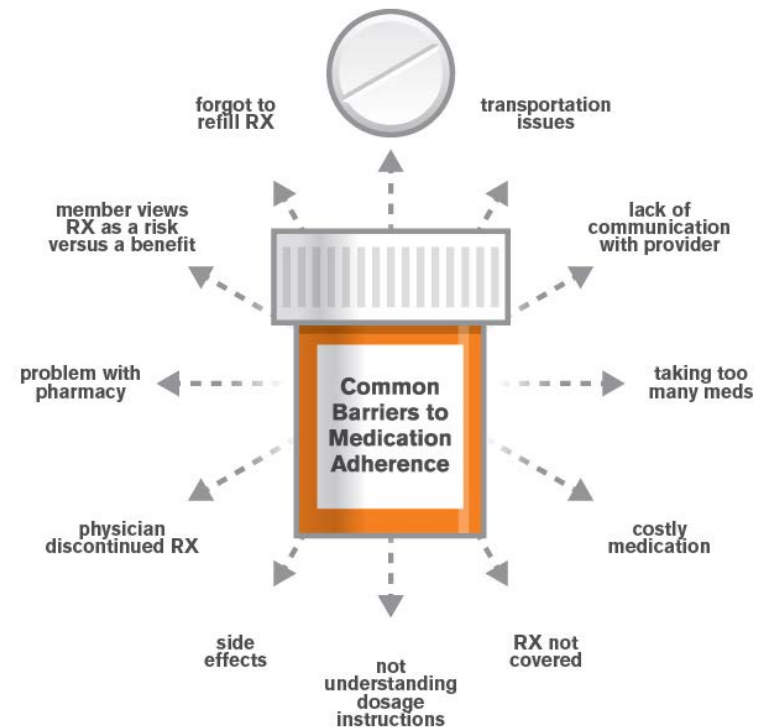
Adherence Working Group

- Collaborative projects

- IMPAACT 2010: capsule proposed to explore adherence post-delivery
- PROMISE: data sharing to evaluate adherence data over time to model adherence over the course of pregnancy and post-delivery

- Independent projects

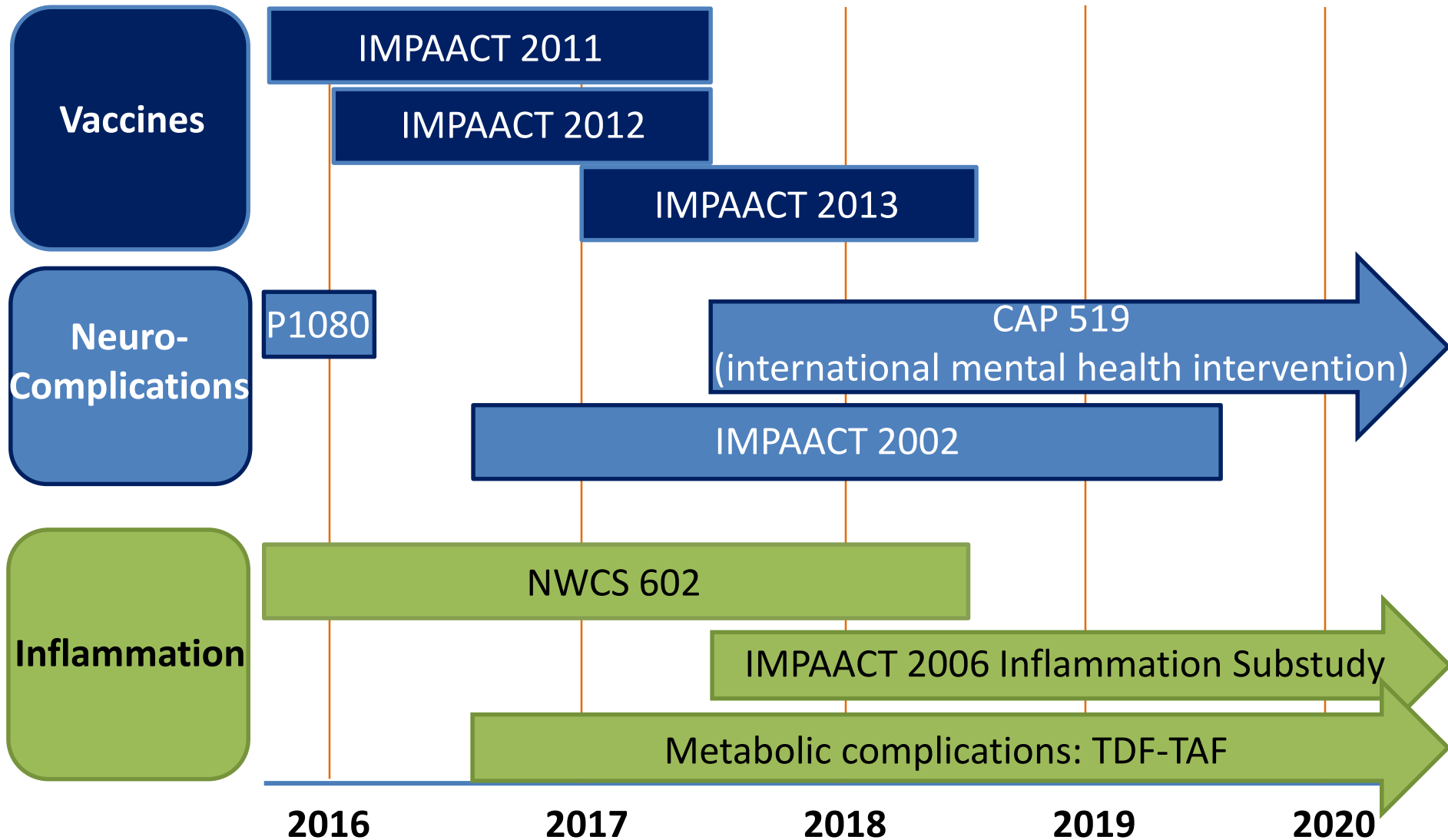
- Intervention to promote adherence post-delivery
- Intervention to promote adherence in youth





**What is driving
the Complications &
Comorbidities agenda?**

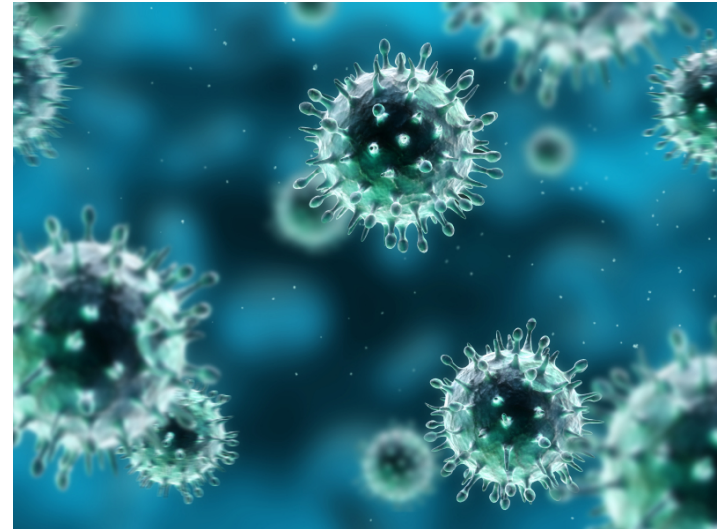
Complications & Comorbidities Roadmap



Study Highlight: IMPAACT 2011

RSV Candidate Vaccine Study

- Study OPEN TO ACCRUAL within the **Complications** Research Agenda
- Phase I placebo-controlled study among healthy RSV-seronegative children 6-24 months of age
- Purpose: determine whether the LID Δ M2-2 1030s vaccine candidate is attenuated and immunogenic



Next Priorities for Vaccines

- Expanded safety and immunogenicity study of promising RSV vaccine candidate
- Expansion of RSV vaccine studies to HIV+ children
- Explore differences in responses between HIV-exposed/uninfected and HIV-unexposed; characterize underlying mechanisms
- Initiate RSV vaccine efficacy trial with NIH



Next Priorities for Neurodevelopmental Research

- Determine best treatment strategies for [depression, ADHD, anxiety, etc.] in HIV-infected youth
- International interventional study addressing mental health
- Define role of inflammatory and immune activation in neurobehavioral and neuropsychologic outcomes



- Identify anti-inflammatory or other neuroprotective factors that warrant further study
- Reservoirs; including the CNS

Next Priorities for Inflammation and Immune Activation

- Assess correlations of inflamm/immune activation and HIV complications (CNS, CV, renal, metabolic)
 - Neurobehavioral/neuropsych outcomes and inflammation/immune activation (New Works Concept Sheet 602)
 - International settings
- Incorporate markers of inflammation into studies of mental health interventions (e.g., 2002)
- Anti-inflammatory intervention trial?
 - End-organ assessments
 - Neurobehavioral/neuropsych assessments



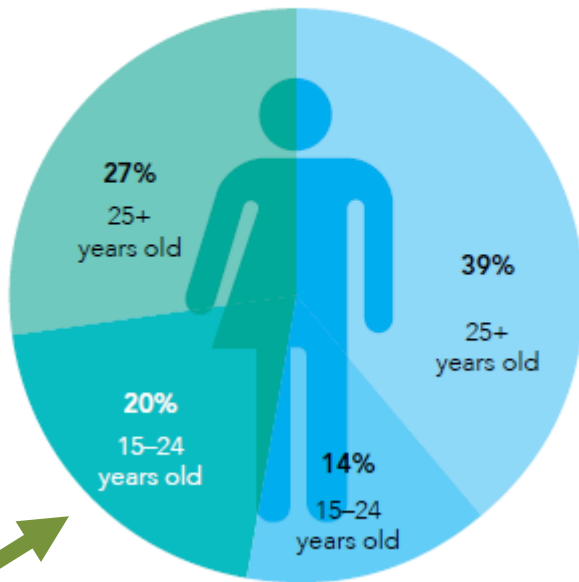


**What is driving
the Prevention agenda?**

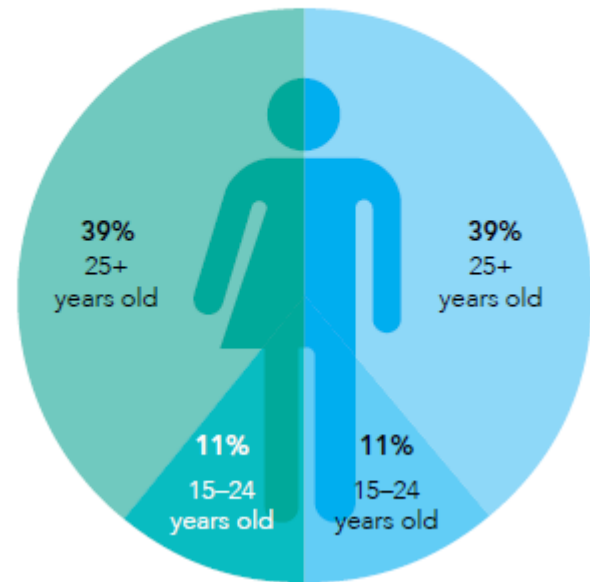
Prevention

Young Women at High Risk for HIV

NEW HIV INFECTIONS AMONG ADULTS, BY
AGE AND SEX, GLOBAL, 2015



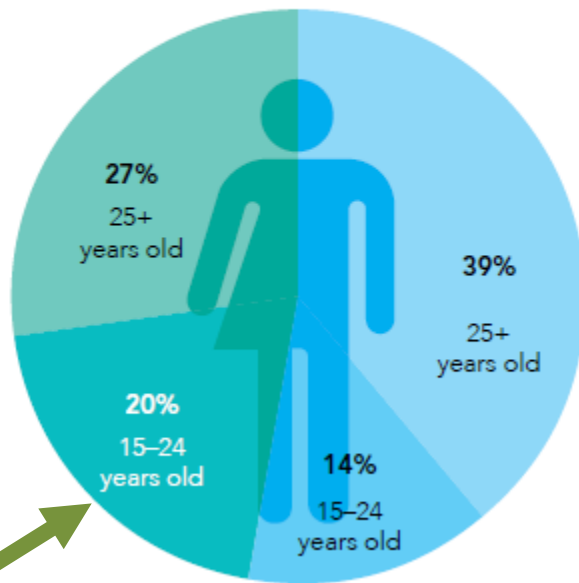
ADULT POPULATION, BY AGE AND SEX,
GLOBAL, 2015



- Pregnancy doubles your risk of acquiring HIV infection
- Seroconversion during pregnancy increases:
 - risk to male partners
 - risk to infant

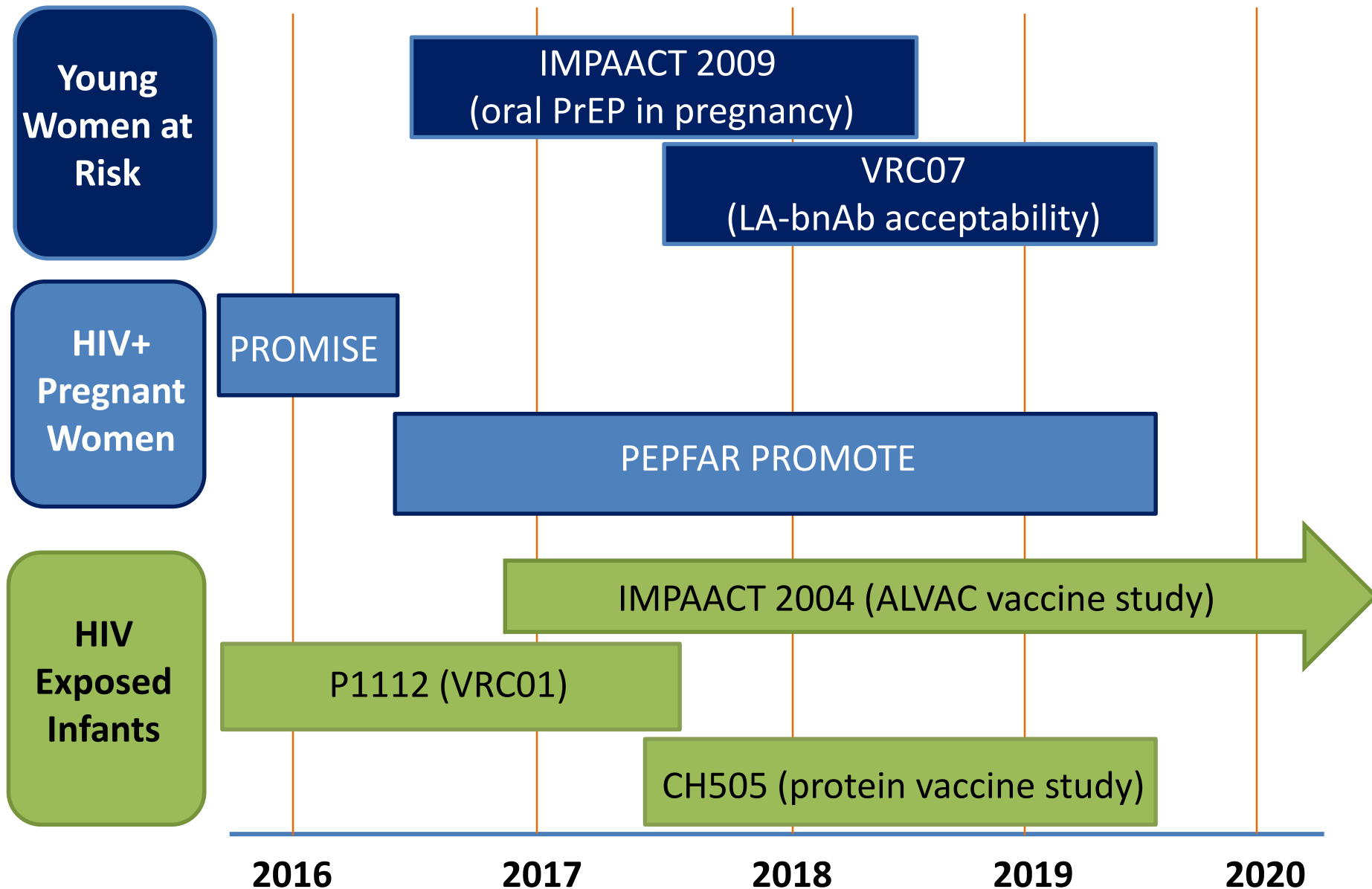
More Pronounced in Sub-Saharan Africa

NEW HIV INFECTIONS AMONG ADULTS, BY
AGE AND SEX, GLOBAL, 2015



- Harmful gender norms and inequalities, insufficient access to education and sexual and reproductive health services, poverty, food insecurity and violence, are at the root of the increased HIV risk of young women and adolescent girls.
- Female centered HIV prevention strategies are needed to protect this vulnerable population, and IMPAACT's agenda is aligned with other networks to address this need (such as HPTN and MTN).

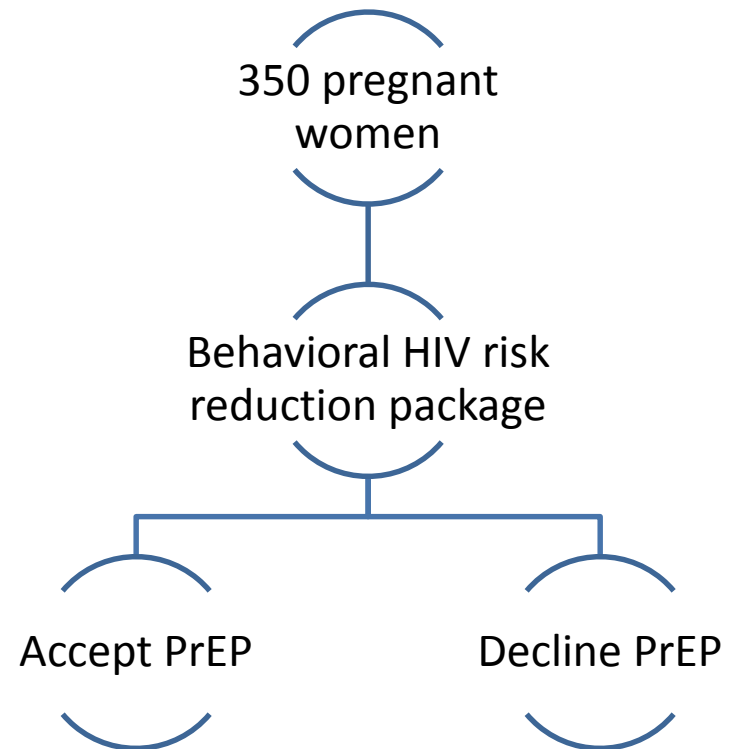
Prevention Roadmap



Study Highlight: IMPAACT 2009

PrEP in Pregnant Women

- Study in development within the **Prevention** Research Agenda
- Purpose: determine feasibility, acceptability, and safety of oral PrEP among HIV-uninfected young women during pregnancy



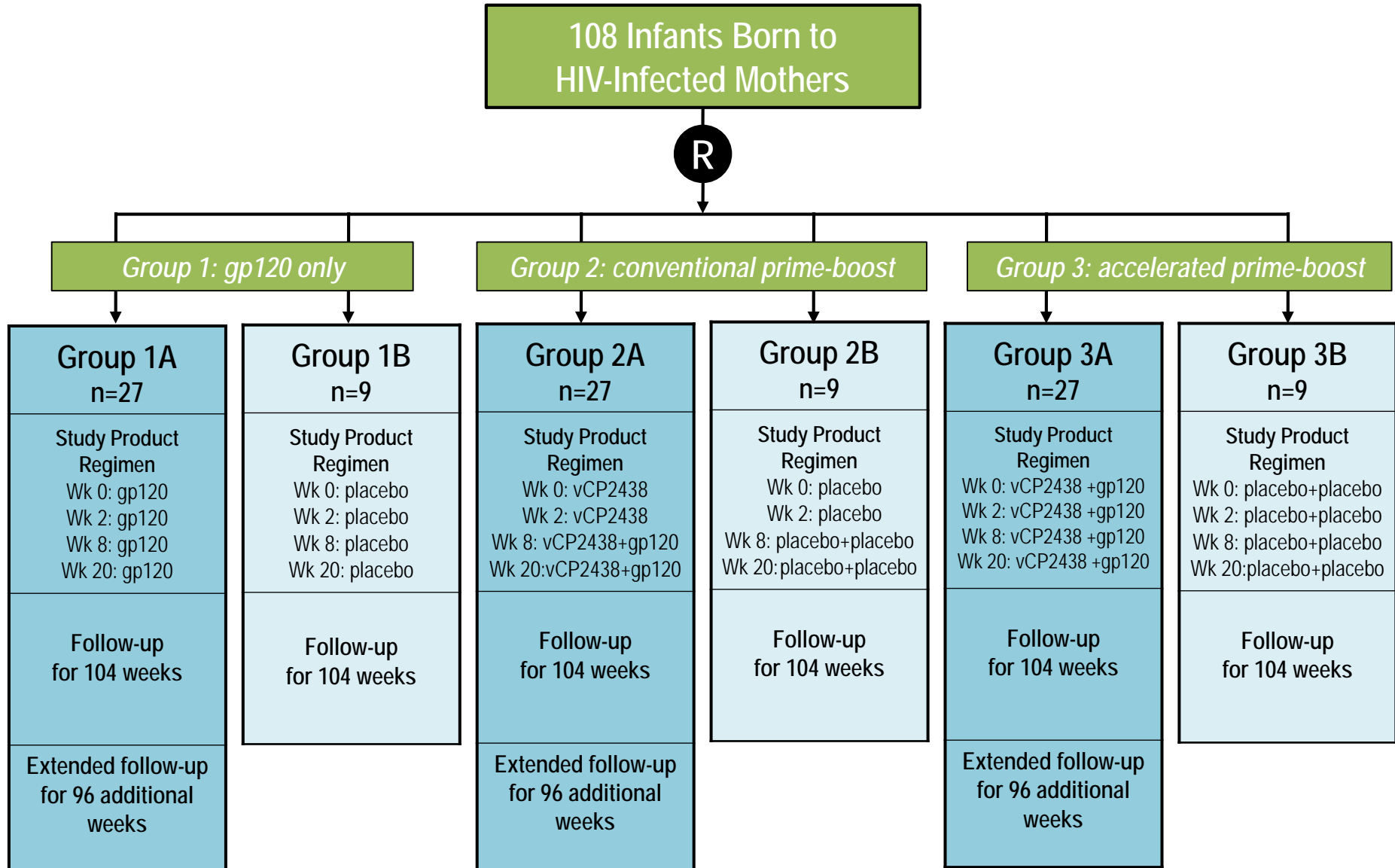
Study Highlight: IMPAACT 2004

HIV Vaccines for Infants

- Study in development within the **Prevention** Research Agenda
- Purpose: Safety and immunogenicity of Clade C ALVAC-HIV (vCP2438) and bivalent Subtype C gp120/MF59®
- Same vaccine product as in HVTN 100 and HVTN 702



IMPAACT 2014



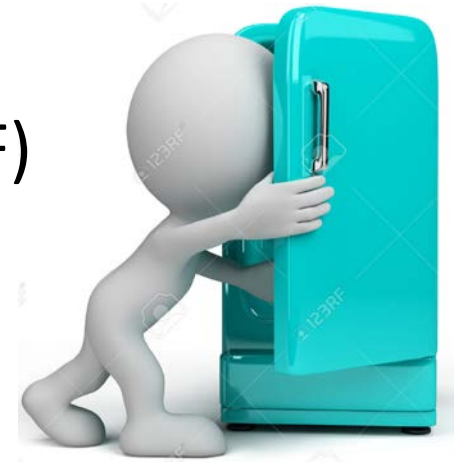
Plans for the Prevention Agenda

- Phase I/II, Placebo-Controlled study of safety & immunogenicity of Clade C ALVAC-HIV (vCP2438) & Bivalent Subtype C gp120/MF59[®] in South African Infants (IMPAACT 2004)
- Phase I study to evaluate safety & immunogenicity of HIV-1 envelope sequential vaccine (EnvSeq-1) immunization in HIV-exposed infants (Capsule 523)
- Long acting ARV formulations in pregnancy



Samples Shipped This Year

- Site laboratories to repositories:
 - ✓ 21 laboratories shipped to BRI
 - ✓ 23 laboratories shipped to Fischer
- Shipped almost 230,000 samples of about 1 million stored at sites
- From five studies
 - ✓ PROMISE (1077HS, 1077BF, 1077FF)
 - ✓ P1078
 - ✓ P1060



Early Career Investigator Program

- 2015 Cycle: Fourteen submissions, with three funded
 1. **Florence Momplaisir:** Effects of Perinatal Depressive Symptoms on Maternal ARV Adherence, HIV Viral Suppression and Infant Outcomes
 2. **David Bearden:** Biomarkers of Immune Activation and Cognitive Impairment in Children with HIV
 3. **Anne Neilan:** HIV-infected Adolescents and Viral Dynamics: Individual and Population Impact
- 2016 Cycle: Three submissions, with decisions pending and funding expected by September 2016



Upcoming Meetings

- IMPAACT leadership retreat in January 2017
 - Interface between the lab and the SC agenda
- Annual Meeting in May 2017

More details to come!



