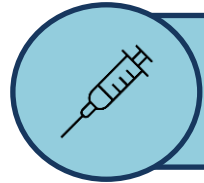


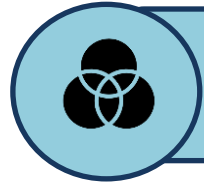
HPTN Future Research Agenda

Wafaa El-Sadr and Mike Cohen
October 6, 2020

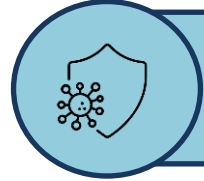
Priority Areas as per RFA



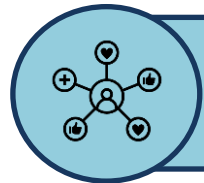
Identify **novel ARV-based methods and delivery systems** for HIV prevention



Develop **multi-purpose technologies (MPTs)** for HIV prevention as well as for contraception, prevention of other STIs



Evaluate **broadly neutralizing antibodies (bnAbs)** alone or in combination that prevent HIV acquisition, in collaboration with the HVTN



Design and conduct population-specific **integrated strategy studies** that combine biomedical, socio-behavioral and structural interventions for HIV prevention to maximize their effectiveness

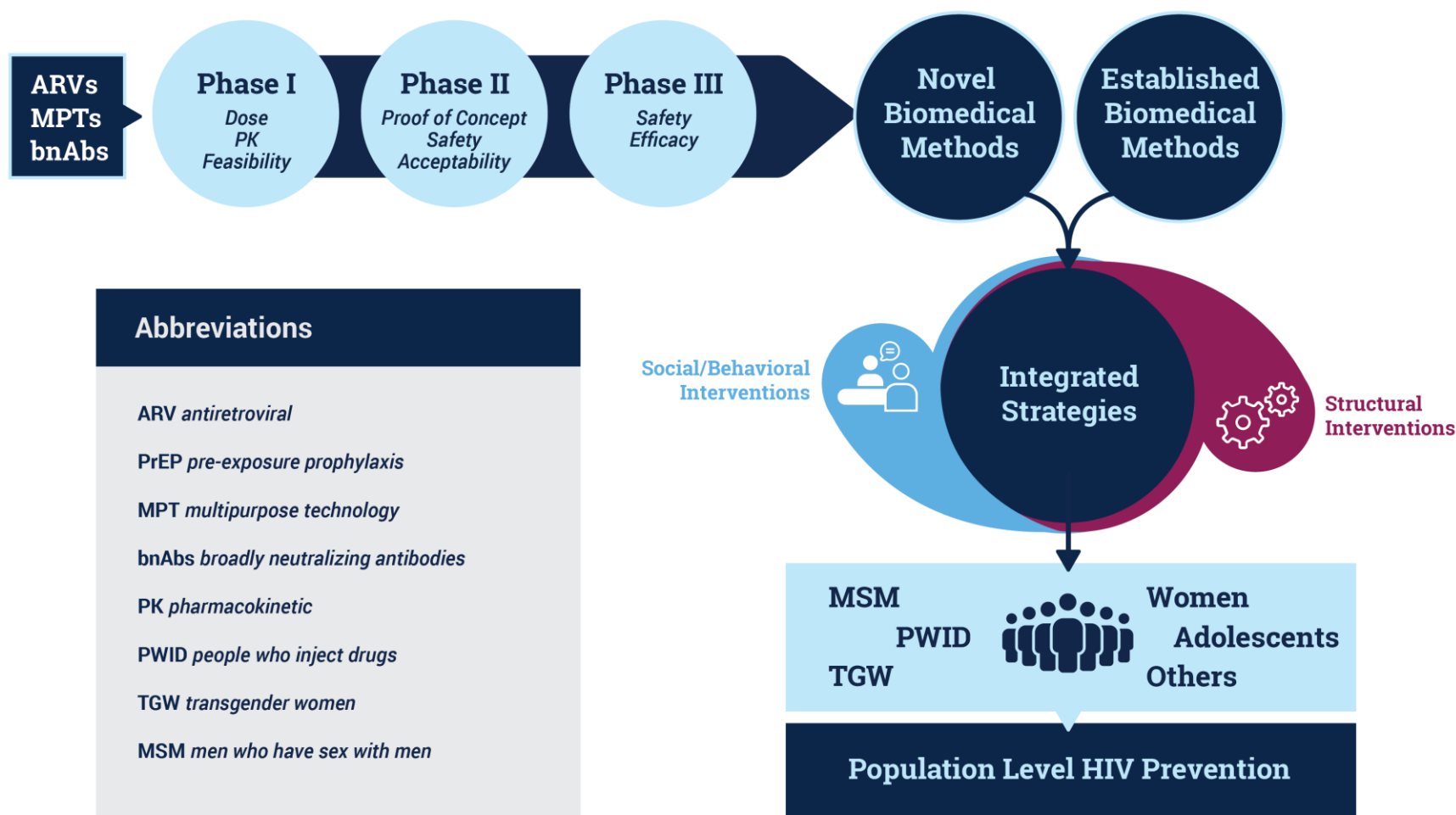
HPTN Mission

- **Develop new biomedical interventions:**
 - *Novel ARV methods and delivery systems*
 - *Multi-Purpose Technologies (MPTs)*
 - *Broadly neutralizing antibodies (bnAbs)*
- **Optimize integration of proven interventions to achieve high effectiveness and impact:**
 - *Biomedical*
 - *Socio-behavioral*
 - *Structural*

Discovery

Impact

HPTN Scientific Agenda: Conceptual Framework



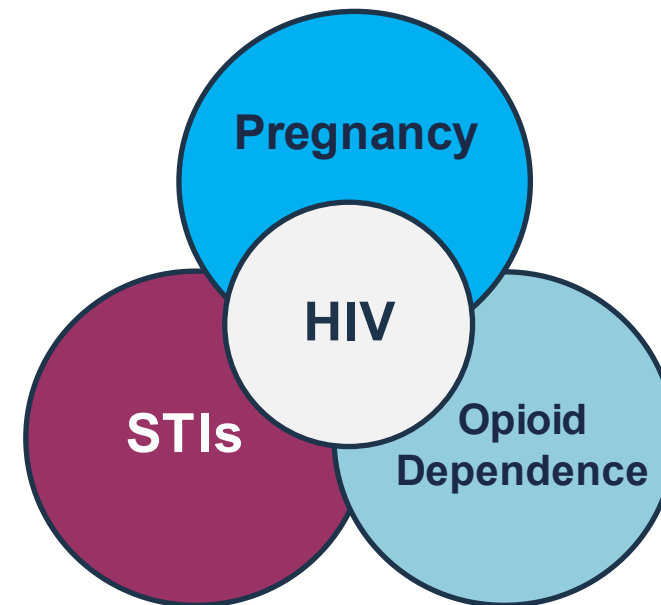
Aim 1: Design and conduct studies of long-acting antiretroviral (ARV) agents and delivery systems for pre-exposure prophylaxis (PrEP)

- Identify promising ARV for PrEP
- Test products through phase 1-3 drug development studies
- Evaluation various delivery systems e.g. injections/infusions, implants, patches and topical products with promising systemic effects
- Collaborate with partners to access new agents and delivery systems



Aim 2: To design and conduct studies that evaluate multipurpose prevention technologies (MPTs) that concurrently prevent HIV and pregnancy, other sexually transmitted infections or opioid dependence

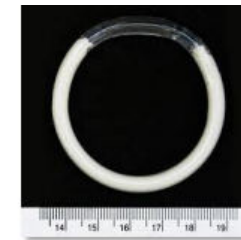
- **MPTs of interest (examples):**
 - **HIV prevention + contraception**
 - Vaginal rings and inserts
 - Implants and devices
 - **HIV prevention + STI prevention**
 - **HIV prevention + opioid dependence management**
 - Long-acting substance use medications (oral, injection, and implant)



Delivery Options for MPTs

Co-formulated:

Multiple API formulated into a single dose



Vaginal ring
containing ARV plus
LNG

Co-administered:

Two independent products
used together



Two implantable rods, one containing ARV, the
second containing contraceptive

Co-packaged:

Two different doses packaged
together in a single product
for simultaneous co-use

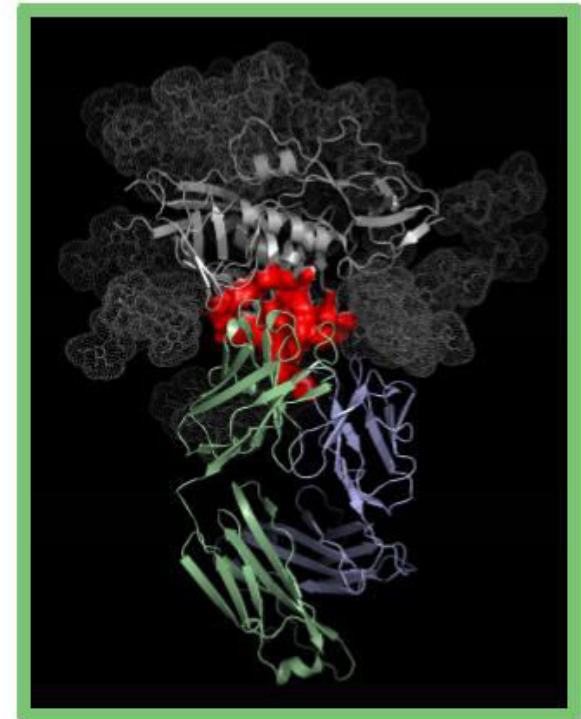


Two tablets, one containing ARV, the
second containing contraceptive

Aim 3: To design and conduct studies, in collaboration with HVTN, to evaluate broadly neutralizing antibodies (bnAbs) alone or in combination for PrEP.

- **Products of interest (examples):**

- bnAbs alone
- combination of bnAbs
- Tri-specific bnAbs



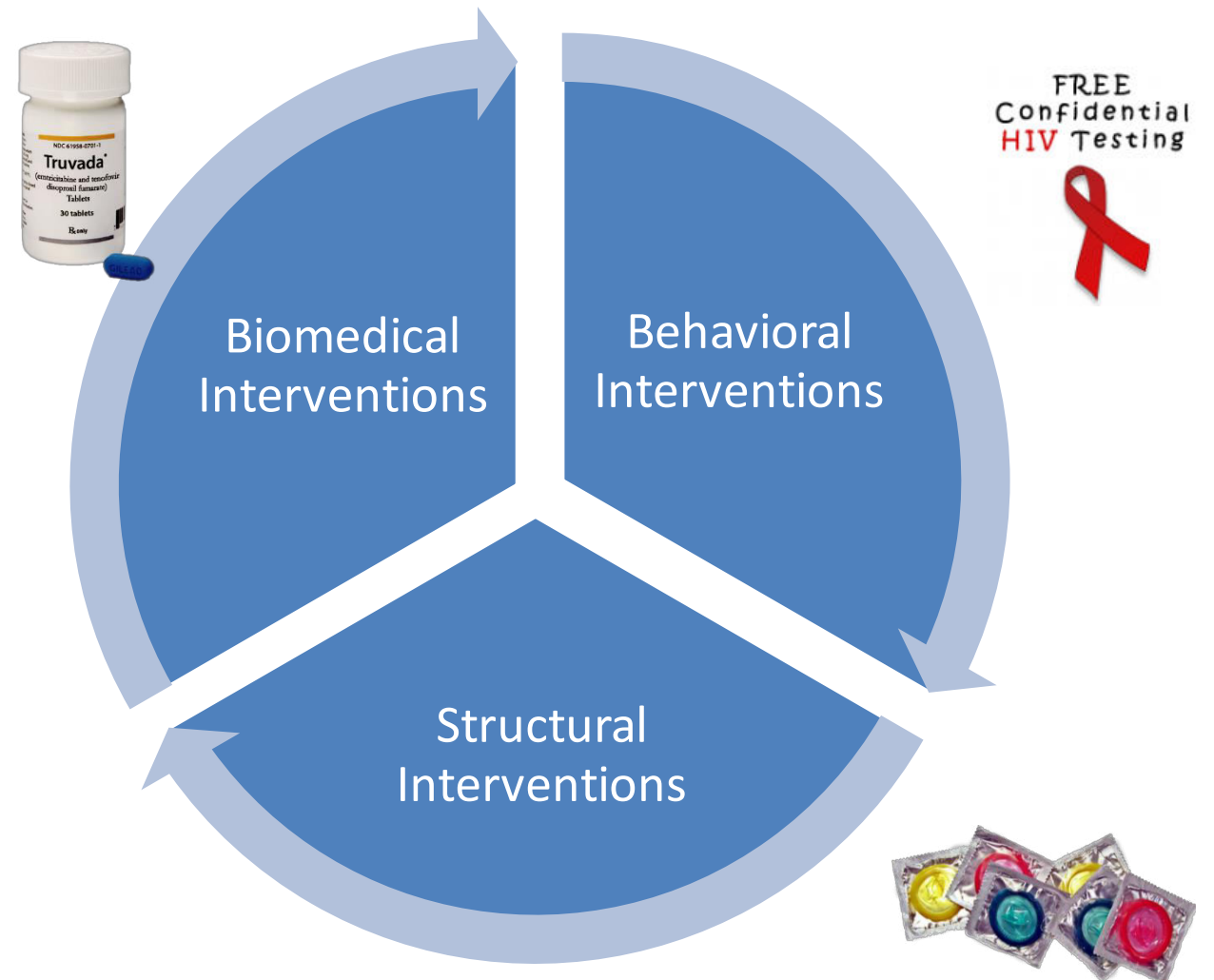
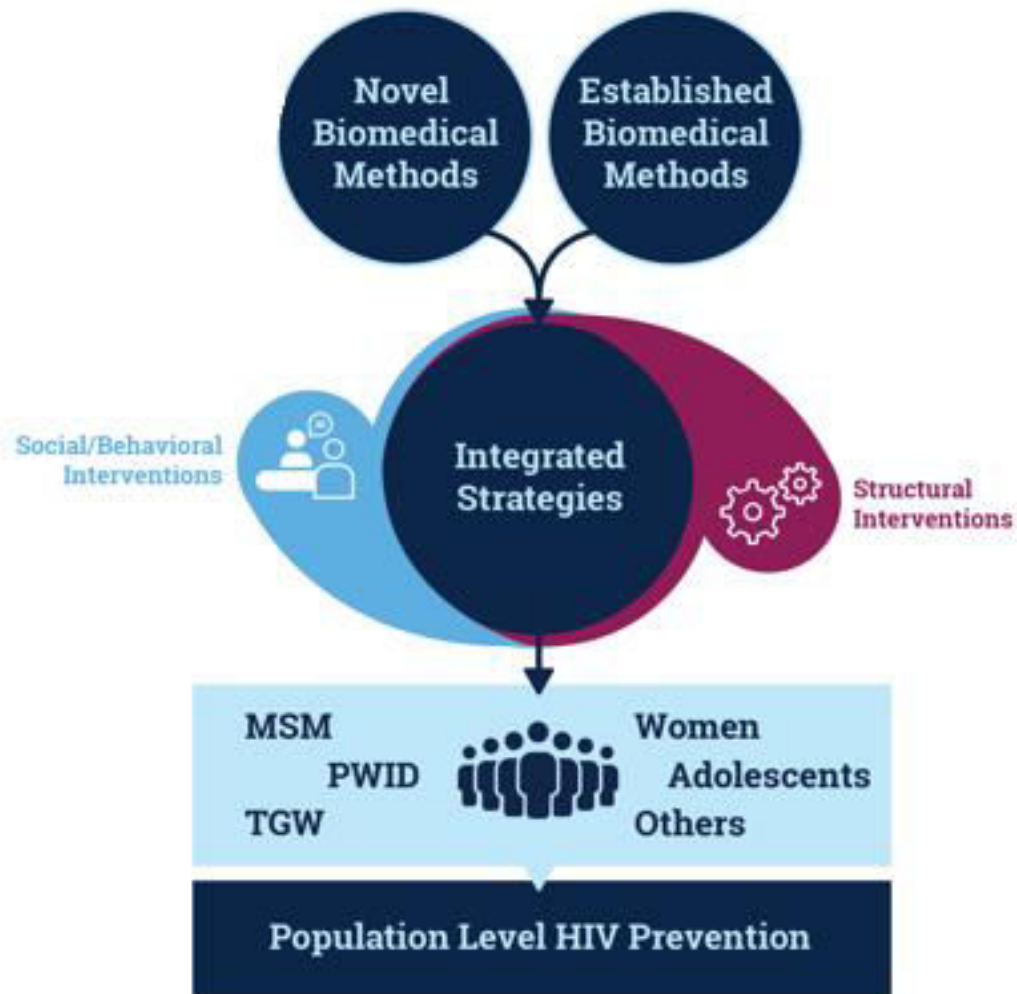
Gray: gp120

Red: CD4 binding site (CD4bs)

Purple & Green: VRC01 attached to the CD4bs

Photo: NIAID/NIH Vaccine Research Center (VRC)

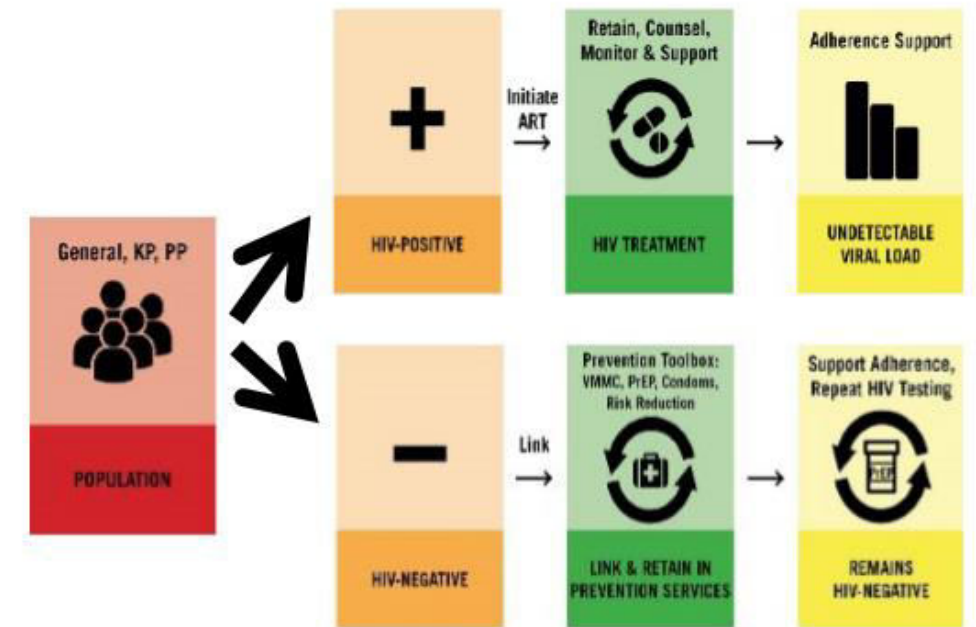
Aim 4: To design and conduct integrated strategies for HIV prevention



Aim 4: To design and conduct integrated strategies for HIV prevention

- **Approach**

- Focus on priority populations most impacted by HIV
- Tailor to individual and social contexts
- Embrace a status-neutral approach to avoid stigma of HIV
- Design different types of studies: e.g. vanguard and definitive studies
- Incorporate rapidly new tools and delivery methods



Integrated Strategies for Populations at Risk (U.S.)

U.S. Populations	Proposed Integrated Strategy (and Design)
MSM in U.S. (HPTN 096)	<ul style="list-style-type: none"> • County randomization in U.S. South • Study arms: Integrated community plus individual interventions vs. SOC • Interventions: <ul style="list-style-type: none"> • Community interventions: provider sensitization, community workshops • Individual interventions: status-neutral, client-centered coordination and intensive case management for adherence support
Young MSM (YMSM)	<ul style="list-style-type: none"> • Vanguard study with individual randomization • Study arms: <ul style="list-style-type: none"> • MHealth using apps and internet platforms for risk assessment, referral for HIV testing, care and prevention interventions, peer support • SOC: Facility-based SOC interventions
Women at risk	<ul style="list-style-type: none"> • Vanguard study with individual randomization • Study arms: <ul style="list-style-type: none"> • Community delivery of PrEP HIV prevention interventions, SMART design for intensified adherence support • SOC: Facility based SOC interventions
PWID (HPTN 094)	<ul style="list-style-type: none"> • Individual randomization • Study arms: <ul style="list-style-type: none"> • Mobile units at venues frequented by PWID (consisting of HIV, HCV, & STI testing, prevention/management, MAT, harm reduction, overdose education, naloxone) • SOC: Referral to facilities and programs in community

Integrated Strategies for Populations at Risk (Globally)

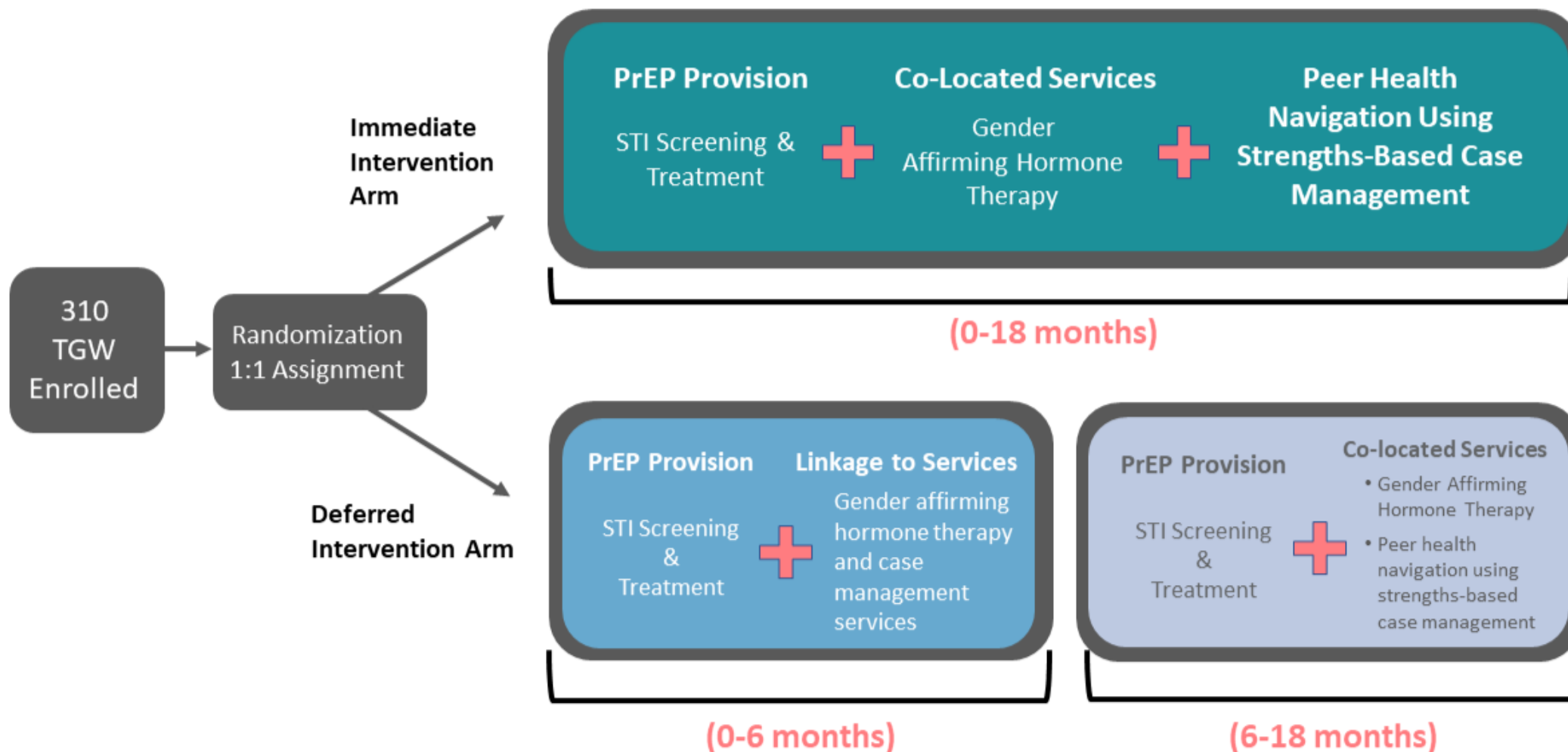
Population	Proposed Integrated Strategy (and Design)
Women in SSA	<ul style="list-style-type: none"> Cluster (family planning clinics) randomized step-wedge design Interventions <ul style="list-style-type: none"> Integrated strategies with HIV, STI and FP interventions, SMS texting, POC urine ARV with immediate feedback SOC
Heterosexual men in SSA	<ul style="list-style-type: none"> Individual randomization Interventions: <ul style="list-style-type: none"> Integrated strategies through mobile units at work and leisure venues frequented by men: HIV self-testing, status-neutral, HIV PrEP and ART with other health interventions, WhatsApp support by champions and peers SOC
MSM and TGW in SSA, South America and Asia	<ul style="list-style-type: none"> Two-level factorial design Interventions: <ul style="list-style-type: none"> Community plus individual interventions <ul style="list-style-type: none"> Community interventions: provider sensitization, community workshops, risk mitigation Individual interventions: Status-neutral approach, PrEP or ART, per HIV status, peer support SOC
TGW in Americas HPTN 091	<ul style="list-style-type: none"> Individual randomization Interventions: <ul style="list-style-type: none"> Co-located provision of PrEP plus gender-affirming hormones plus strength-based case management SOC
Non-injection substance users among MSM in Americas	<ul style="list-style-type: none"> Individual randomization Interventions: <ul style="list-style-type: none"> Mitrazapine, two-way text messaging reminders SOC

HPTN 091

Objectives

1. To assess acceptability and feasibility of delivering integrated **HIV prevention services co-located with gender-affirming hormone therapy** (GAHT) and peer-delivered health navigation supported by strengths-based case management (SBCM) for TGW.
2. To assess PrEP uptake and adherence (including PrEP persistence) in both the Immediate Intervention Arm and the Deferred Intervention Arm.

Integrated Strategies: HPTN 091

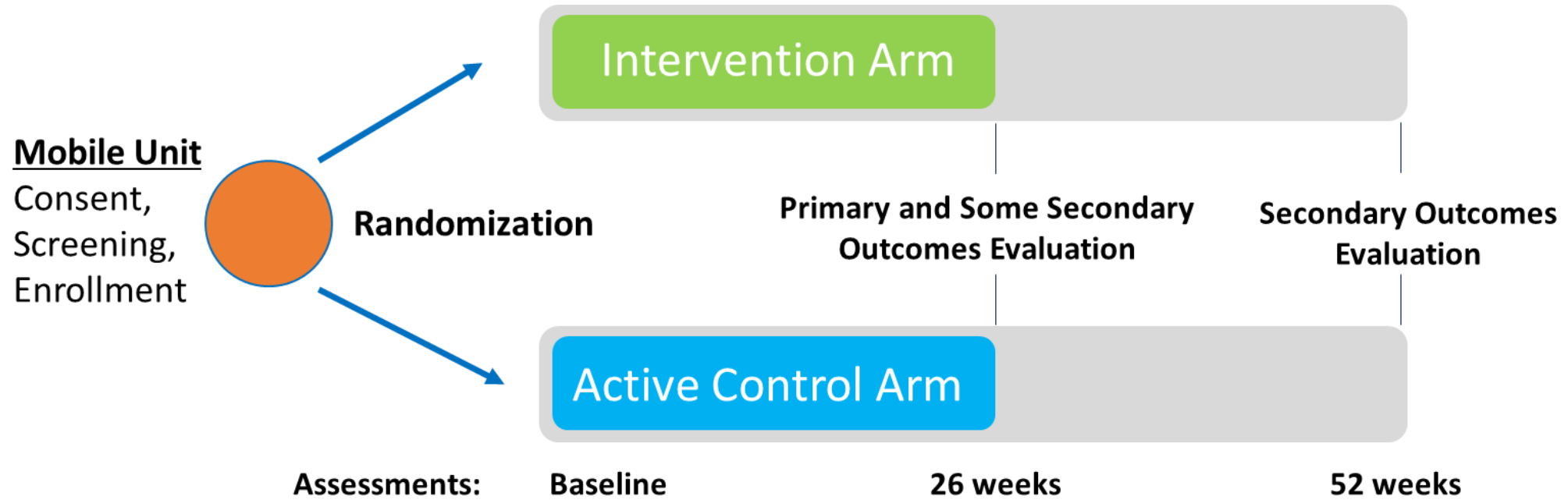


HPTN 094

- Evaluate “one stop” integrated services delivered in a mobile health delivery unit on uptake and adhere
 - medication for opioid use disorder (MOUD)
 - HIV treatment and prevention medications – to PWID improve uptake and adherence compared to a control arm that provides referrals to existing services at static facilities
- Two-arm, individually randomized, controlled, open label study



HPTN 094



INTERVENTION

“One stop shop” services in van, with peer navigation: MOUD, ART or PrEP, HCV, STI, primary care, and harm reduction

ACTIVE CONTROL

Navigation to health services available at community-based agencies

HPTN 096

To assess an integrated, HIV status-neutral, population-based approach designed to reduce HIV incidence among Black men who have sex with men (Black MSM) in the Southern US by increasing HIV testing, pre-exposure prophylaxis (PrEP) uptake and adherence, and viral suppression rates

HPTN 096: Mechanisms of Action

Integrated Strategy

Health Equity

Community Level

Social Media Influencers

Community Level

Intersectional Stigma Reduction

Organizational Level

Peer Support

Interpersonal Level

HIV/STI Testing

Individual Level

Mechanisms of Action

Multi-level Social
Support

Multi-level
Intersectional Stigma

Structural Barriers to
Healthcare Services

Individual-
level Agency

Outcomes

Viral
Suppression ↑

Positive Test

HIV Testing ↑

Negative Test

PrEP Use ↑

HIV
Incidence ↓

Moving the Science Forward

- **Science Committees:**

- Population-specific
- Responsible for informing HPTN science, generation and review of concepts
- Liaisons focused on specific agenda elements, e.g. Susan Buchbinder & Connie Celum for integrated strategies, Sharon Hillier for MPTs

- **Working Groups:**

- Cross-cutting expertise
- Inform HPTN protocol and concept teams
- Advance cross protocol harmonization and synergy

- **Chairs:**

Science Committees	Chair	Co-Chair
Adolescents at Risk	Audrey Pettifor	Linda-Gail Bekker
Sexual and Gender Minority	Kenneth Mayer	Beatriz Grinsztejn
Substance Users	Steffanie Strathdee	Nabila El-Bassel
Women at Risk	Ada Adimora	Philippa Musoke
Working Groups	Chair	Co-Chair
Biomedical Sciences	Jeanne Marazzo	Joseph Eron
Community	Melissa Turner	Ntando Yola
Ethics	Jeremy Sugarman	Jerome Singh
Socio-Behavioral and Structural Sciences	Ariane van der Straten	Julie Pulerwitz

Thank you