Designing for the Future

Community Perspectives for HIV Prevention Trials

Grace Kumwenda

Clinical Trial Design Summit, Johannesburg, South Africa

11-12 June 2025

AVAC
Advocacy. Access. Equity.

Frameworks and Mechanisms

Priorities are anchored in:

- The GPP framework developed in response to the PrEP trial controversies in Cambodia and Cameroon in 2004 and 2005
- The People's Research Agenda launched in 2024 which provides collaboratively developed set of priorities for how prevention research should be conducted and what products should be developed
- Workshops and Dialogues by the Clinical Trial Design Academy for advocates
- Community Consultation on the design of MK8527 Efficacy Trial

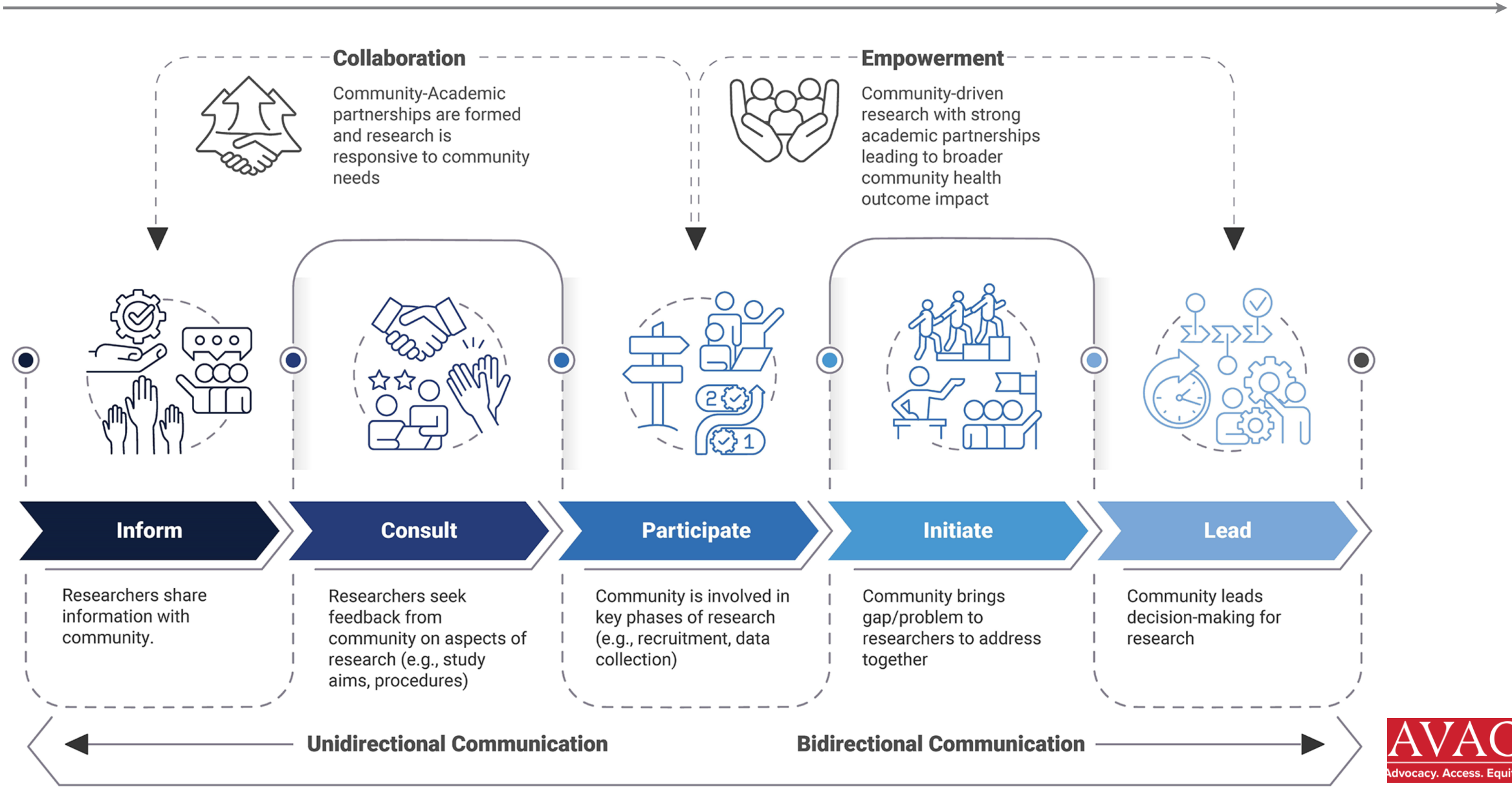
AVAC
Advocacy. Access. Equity.

Why Community Perspectives Matter

CDC, Ending the HIV Epidemic in the US 2023

AVAC
Advocacy. Access. Equity.

Early and Continuous Community Engagement



AVAC
Advocacy. Access. Equity.

GPP in Practice: MK8527

Community input into design of efficacy program

- Global pre-protocol community consultation
- Community Protocol Reviews
- Global Community Advisory Board

Expected continuous community engagement and monitoring of trial conduct

- Global Community Advisory Board
- Clinical Trial Design Academy for advocates
- Broader Stakeholder Engagement

A 2-day consultation with 24 global advocates – from North & South America, East & Southern Africa, Europe and Asia, representing a broad range of populations – along with researchers, ethicists, statisticians conducted in 2024

AVAC
Advocacy. Access. Equity.

Objectives and Core Questions

The consultation was organized to incorporate advocate and ethicist input into efficacy program planning and future protocol(s) for MK-8527 and to build a cadre of advocates who are well-informed about the trial and who can serve as liaisons to wider constituencies as it progresses.

Questions we sought to answer

1	2	3	4	5
What is the role for a monthly PrEP pill?	How best to swiftly determine efficacy?	Beyond efficacy, what else do we want to know, and how best to structure that research?	How do we build in choice throughout the process?	How do we plan now to ensure equitable access?

AVAC
Advocacy. Access. Equity.

Proposed Framework

Advocates suggested core principles to guide recommendations

The consultation yielded nuanced perspectives and recommendations on all aspects of the research-to-rollout process

These inputs can be considered as part of a stepwise framework linked to the clinical development process – and attached to core principles that guided more detailed discussions and ultimate recommendations

Efficacy

Keep it simple to demonstrate efficacy as swiftly as possible.

Sub-studies

Ensure representation and ask the right questions to understand population needs and user preferences.

Implementation Research

Start planning now for open-label studies that will help ensure widespread access and use.

Access

Advocates demand a commitment to access that recognizes the inadequacies of previous efforts and serves to address them.

> **"This is a group of people who believe this is going to be a successful endeavor. How do we contribute to its success, how do we accelerate progress, and how do we get it in the hands of the people who need it?"**

AVAC
Advocacy. Access. Equity.

Overview of Emerging Priorities

Efficacy

- Prioritize monthly oral compared to daily oral with counterfactual placebo
- Provide a choice at enrollment and link those who want access to CAB or DVR to programs that offer them, randomizing those who want oral to trial
- Include cisgender women in the US, and transgender men and non-binary individuals in efficacy trials
- Ensure robust adherence counseling
- Ensure post-trial access
- Ensure representation of geographies & populations based on clear criteria

Sub-studies and/or parallel studies

- Assess acceptability and choice
- Ensure inclusion of PWID and answer key question on adherence – ***and organize follow-up consultation***
- Explore drug-drug interactions, including gender-affirming care
- Ensure data related to use during pregnancy and lactation
- Ensure robust stakeholder engagement plans, looking toward access
- Determine time to onset of protection, forgiveness, and tail through PK studies

Implementation Research

- Provide evidence for WHO guidelines
- "Choice" OLE
- Understand issues around service delivery, innovation, de-medicalization
- Ensure community-based adherence support
- Potential use as PEP
- Conduct cost modelling – including delivery costs – to develop cost of infection averted
- Understand PrEP switch/start/stop
- Ensure evidence to influence policy change

Access

- Planning for generic manufacturing
- Ensure a licensing structure – whether direct or via MPP – that ensures access in Latin America/Asia/Eastern Europe
- Engage advocates/ stakeholders throughout planning process
- Map barriers and enablers now and ongoing process

AVAC
Advocacy. Access. Equity.

Core Recommendations: Efficacy trials

Cis-gender women

- US inclusion
- Strive for geographic diversity
- PLPs included
- Adolescents after sentinel cohort

MSM and TG

- More inclusive to include TGM and gender non-binary
- Enrollment goals for vulnerable pops.

Comparator: Broad consensus that a pill-to-pill comparator (with counterfactual*) would offer a simple, straightforward approach. Further discussion and review of alternatives (i.e., other monthly options) are warranted.

Adherence: Build in robust adherence support to empower participation.

** Note, the group did not have a robust discussion about a counterfactual method; flagged for advocate input in follow-up*

Attendees broadly agreed that we should **move with all due speed to establish efficacy.** Additional questions around preference, use-cases and real-world use could be included in sub, parallel and/or follow-on studies.

> ***"First let's answer 'does it work, is it safe.' And then we can ask how it compares in a choice landscape."***

AVAC
Advocacy. Access. Equity.

Answering questions beyond safety and efficacy

Core Discussion Topics

PWID	Consult further on how to include them and when to study them (e.g. in context of phase 3 study or a separate focused study).
Pregnant and Lactating	Consider PURPOSE design of allowing pregnant and lactating participants to continue in trial..
Drug-Drug	Understand drug-drug interactions including PWID, contraceptives, gender-affirming hormones etc.
PEP	Consult further on how a study could be done ethically and informatively on PEP – currently limited regulatory pathway forward.
Forgiveness and Tail	Plan PK studies to understand time to protection, forgiveness period (estimated 1 week) and drug tail

Attendees broadly agreed that there are numerous important questions to be answered alongside the primary question of efficacy.

Whether these take the form of sub-studies or parallel or subsequent research, would need to be determined on a case-by-case basis. Again, with the understanding that adding complexity to efficacy trials may slow timelines.

Designing for the Future

Community Priorities and Considerations

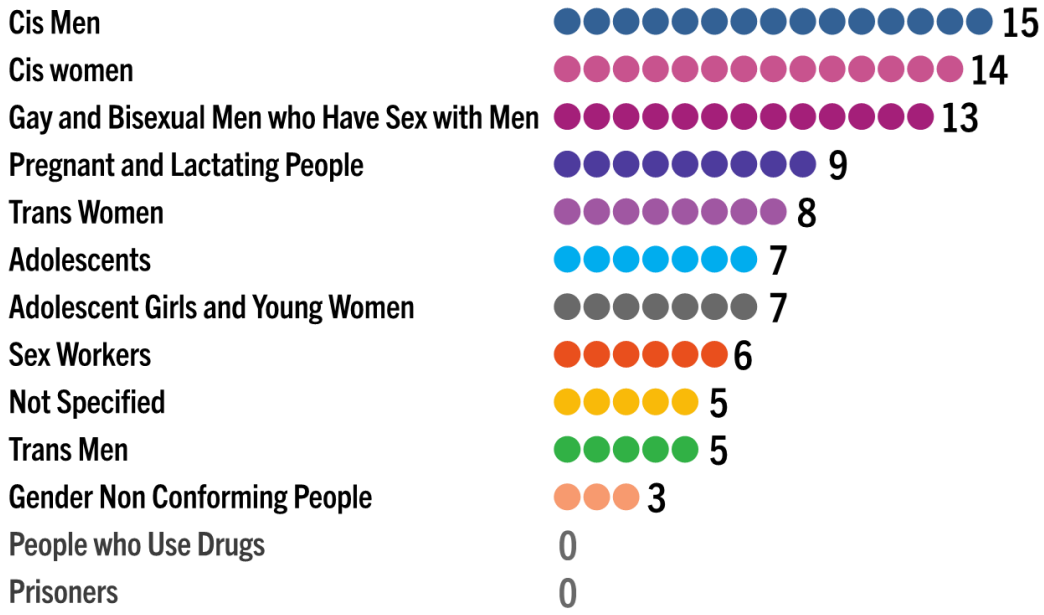
- **Ensure scientific rigor & safety**: Include pregnancy/lactation data, drug-drug interactions, PK studies on onset, tail, and forgiveness.
- **Center choice throughout trials**: Offer product options before, during, and after trials to reflect real-world preferences.
- **Ethical and transparent consent processes**: Participants must be supported to understand how designs impact them; consent must be ongoing, revisited at key decision points
- **Plan for ethical trial exits: E**fficacy trials should only move forward with clear plans for post-trial access, pricing, and potential scale up strategies.
- **Design for adaptability & learning**: Use flexible, adaptive designs grounded in past trial lessons and community insights.
- **Prepare regulators and ethics committees for the future:** Regulatory systems must evolve alongside science—with community voices included

Clinical trial innovation must go hand-in-hand with ethical evolution. It's time to build a future of research that is not just scientifically advanced, but also community-owned, inclusive, and justice-driven.

AVAC
Advocacy. Access. Equity.

Ensure Inclusive and Equitable Participation

- The R&D process must intentionally include:
  - AGYW (Adolescent Girls and Young Women)
  - PLP
  - PWID (People Who Inject Drugs)
  - Key populations including LGBTQ+ communities, sex workers, and migrants
- No population/Geography should be left behind in prevention innovation.



BioPIC Implementation Study Tracker

AVAC
Advocacy. Access. Equity.

Key Message

- Trial designs must be responsive to the lived experiences of highly impacted communities; Informed by community-generated research priorities and adapted to local realities (e.g., mobility, healthcare access, legal/policy risks)
- Community-centric approaches are as as important as scientific innovation.

AVAC
Advocacy. Access. Equity.

Resources

- GPP Guideline: http://www.avac.org/good-participatory-practice
- GPP Training & Implementation Tools: http://www.avac.org/gpp-tools
- Online Training Course: http://www.avac.org/gpp-online-training-course
- GPP for TB: http://www.cptrinitiative.org/resources/gpp-tb-resource-document/
- Stakeholder Engagement Toolkit: http://www.avac.org/resource/stakeholder-engagement-toolkit-hiv-prevention-trials
- Monitoring & Evaluation Toolkit: www.engagementforimpact.org
- HPTN Community Engagement Toolbox: https://www.hptn.org/community/educator-toolbox
- The Peoples' Research Agenda- https://avac.org/blog/introducing-peoples-research-agenda/

AVAC
Advocacy. Access. Equity.