

### Research & Reality

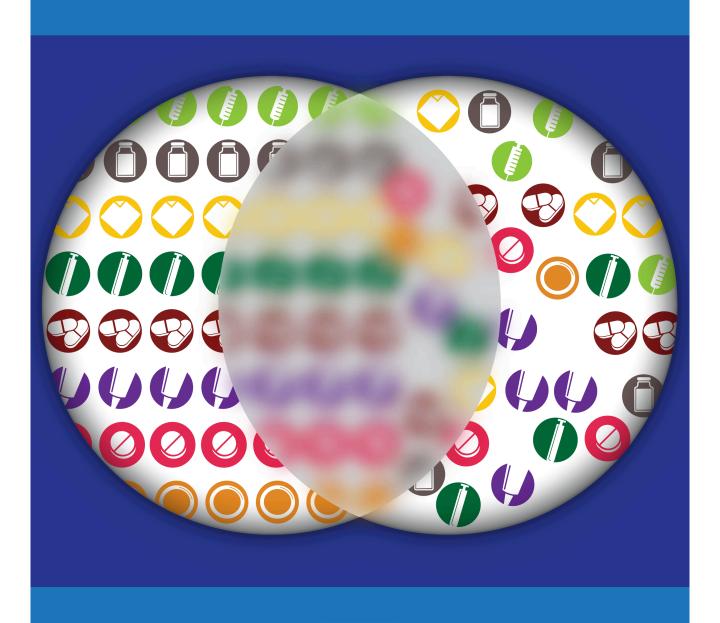
What to expect in 2014 – and where should prevention advocates put our energy?

Mitchell Warren Executive Director, AVAC 26 February 2014

## Today's Call

- Overview of the 2014 timeline and development of AVAC's analysis
- Snapshots of some key issues
- What's on your mind?

### **AVAC REPORT 2013: Research & Reality**







#### The HIV Prevention Research-to-Rollout Continuum, December 2013

### Develop Demonstrate Deliver

**Early Trials** 

**Efficacy Trials** 

**Post-Trial Access** 

Demonstration Projects

Product Introduction

Scale-Up

**TasP** Treatment as prevention using antiretrovirals is effective. Real-world impact depends on linking testing, treatment programs and adherence support.

**VMMC** Voluntary medical male circumcision reduces men's risk of HIV by roughly 60 percent. Scale-up is accelerating and must be sustained.

**ORAL PrEP** Demonstration projects of daily oral tenofovir-based pre-exposure prophylaxis (PrEP) are underway, but once they are completed, unanswered questions will remain. Strategic implementation plans are still needed.

**ARV-based gels and rings** Results from ongoing microbicide trials will be pivotal for the field. Now is the time to plan for rollout and/or follow-up research.

**Vaccines** Recent breakthroughs have energized the field, but a licensed product is still years away. Sustained support is key.

Multipurpose technologies Tachnologies that

Technologies that could prevent pregnancy, HIV and/or other STIs are in early clinical trials.

Long-acting ARV injectables Antiretrovirals are being designed to provide protection for HIV-negative individuals—and minimize adherence challenges. Look for efficacy trials in 2016. The "research-to-rollout" continuum encompasses the many steps between an initial scientific concept and a new tool offered in an effective public health program. Today, HIV prevention research advocacy is needed at every stage. It is critical to sustain support for research to *develop* game-changing tools such as microbicides or an AIDS vaccine; pilot projects that *demonstrate* the impact of emerging tools like pre-exposure prophylaxis (PrEP); and public health programs that *deliver* combination prevention including treatment as prevention and voluntary medical male circumcision (VMMC) for maximum impact. To learn more visit *www.avac.org*.

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Oct- Dec	HIVR4P inaugural conference, Cape Town, South Africa October 28-31	> Increased collaboration across HIV prevention research areas				
Dec	WHO/UNAIDS announce new global VMMC total	A new deadline for reaching the target of 20 million procedures; more frequent global progress updates				
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### PEPFAR Country Operational Plans

- Made every year, but every second year requires more work by PEPFAR
  - Those years are known as "COP heavy" years: 2014 is "COP heavy"
- US government document with input from national governments
  - Includes PEPFAR priorities, budgets, targets and implementing partners in the country
- Drafted by USG country team

  Insert Civil Society
  - → Sent to DC
    - → Changes made
      - → Approved or "red lighted"
- Uganda team in 2012 helped get the COP red lit, staff changes, huge changes toward scale up!
- Also, possibility to influence Global Fund

### Influencing PEPFAR Country Operational Plans(COPS)

An Advocate's Guide

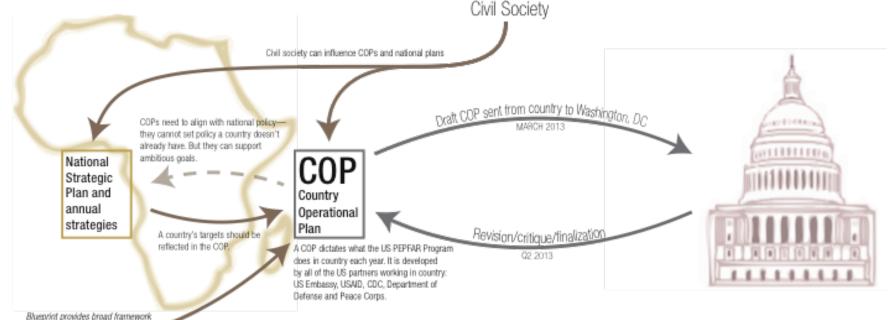
#### Country-Level Advocacy Points

- Ensure the COP is ambitious and consistent with the PEPFAR Blueprint
- Use PEPFAR commitments to influence national plans and policies—e.g. Blueprint statement that PEPFAR will support national programs implementing the WHO guidelines for treatment of serodiscordant couples.
- . It is PEPFAR's obligation and your right that you be meaningfully involved



#### **US-Level Advocacy Points**

- . Lobby to increase overall PEPFAR funding
- . Ensure COP targets match Blueprint goals
- Amplify specific country concerns





for Country Operational Plans

PEAR BALLEPRINT

full report at: http://1.usa.gov/U4BNII

Priority is combination prevention: VMMC, ART, PMTCT, testing, condoms, and programs targeting key populations (p15).

Support for plans incorporating Option B+, treatment at a CD4 count of 350 and above, and treatment for the positive partner in serodiscordant couples (p 19). Financial assistance may be available to countries that need them to implement these programs.

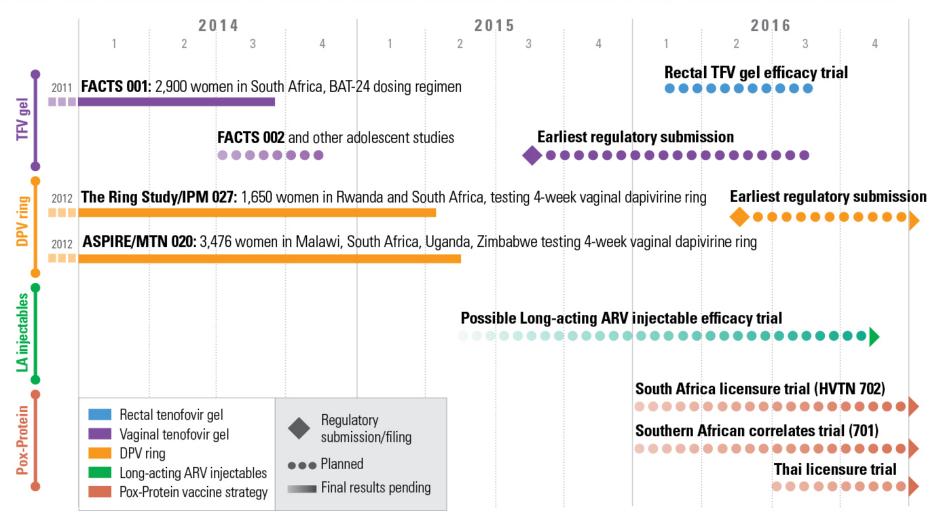
PEPFAR is reorienting its approach in order to increase country financial commitments and ownership (p 44).

Engaging civil society in the COP process is a priority. Small grants are available for ongoing advocacy work. (p 46).





#### Biomedical HIV Prevention Efficacy Trials, 2014–2016\*\*



- \* Trial end dates are estimates; due to the nature of clinical trials, the actual dates may change. For full trial details, see www.avac.org/pxrd.
- <sup>+</sup> This table only includes efficacy evaluations of biomedical strategies in HIV-negative people. There are ongoing pilot and demonstration projects of oral PrEP, an open-label evaluation of 1% tenovfovir gel in the community where CAPRISA 008 took place, and numerous Phase I and II trials of other options.

# A field on the verge of change

What it will take to find new prevention options for women:

- Don't abandon vaginal gels and other user-dependent methods for women – and prepare for additional efficacy trials
- Invest in studies of why women participate in research
- Differentiate between trial participants and end users
- Measure methods to improve adherence
- Plan for success, applying lessons from oral PreP
- Prioritize informed civil society involvement

#### ARV-Based Prevention Pipeline (December 2013)

	PRECL	INICAL	РНА	SE I	РНА	SE II	PHAS	E III	PHASE IV
	MAb	GRF	MVA	TFV/ FTC	MVA	TFV Rectal Use	DAP	TFV	TDF/ FTC
	DAP	MIV 150	TDF	TFV					ACTIVE DRUG
	GRF	TFV	TMC 278	DAP/ MVA				TPE/ FFY	Maraviroc Tenofovir disoproxil fumarate/emtricitabine Tenofovir/emtricitabine
			TFV	744		Vaginal film  Vaginal gel	1	TMC 278 MIV 150 GRF	Ripilvirine MIV-150 Griffithsin
			MAb	MIV			ı injectable	TFV TDF DAP	Tenofovir Tenofovir disoproxil fumarate Dapivirine
	oral pills, v films, long-	aginal rings, va acting injectal	d prevention p aginal and rect ble ARVs. Not p	150 roducts includes al gels, vaginal pictured are a		Vaginal tab  Vaginal ring		744 MAb	GSK744 Monoclonal antibody
			<b>,</b> For up-to		n on the ARV-bas abase at <i>www.av</i>		n pipeline, visit the HIV		

# Research Reality Check 1



#### **Vaccines**

- Maintain funding to build on recent breakthroughs.
- Connect the vaccine agenda to combination prevention.
- Ensure RV144 follow-on trials begin by 2016.

#### **Hormonal Contraceptives and HIV**

- Expand the range of existing contraceptive methods.
- Provide clarity on how to operationalize WHO guidance.
- Move ahead with a clinical trial.

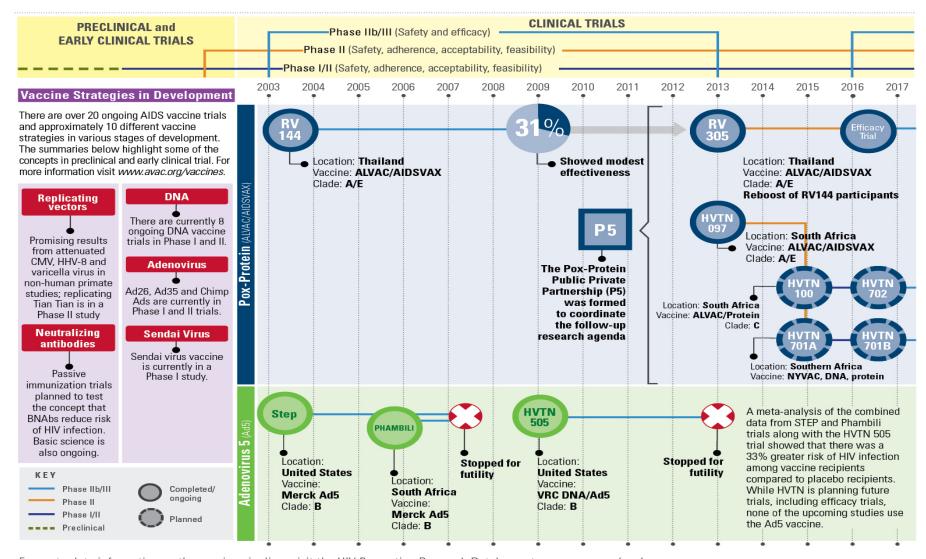
Design
and conduct
complex
trials

The AIDS vaccine field and the arena of hormonal contraception and HIV risk are both grappling with questions about how to proceed when there is uncertainty about whether a product may have caused harm. Even with—or because of— these questions, it is important to move forward with carefully designed research. This requires funding, clear messaging and smart trial designs.



#### AIDS Vaccine Research: An overview (December 2013)

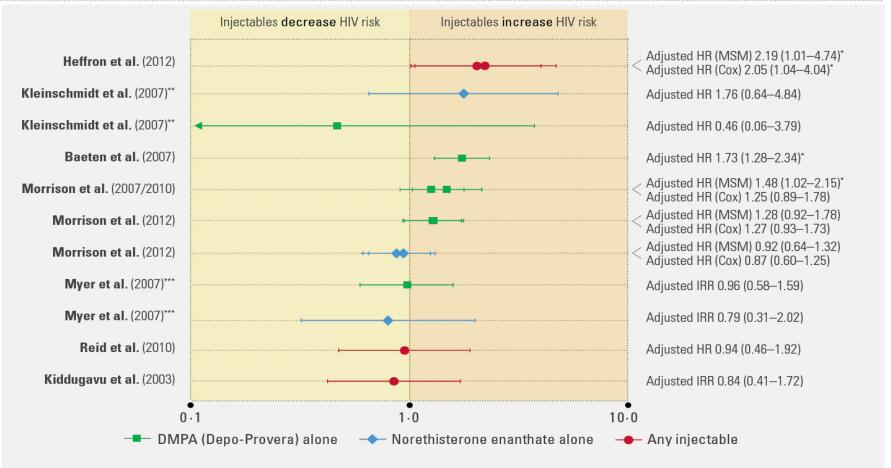
This graphic shows the big picture of AIDS vaccine concepts and clinical trials in process and on the horizon. It is an intentionally simplified representation of a complex field. Some approaches are not listed, or described in full detail—and related arenas like therapeutic vaccines and cure research are omitted.



For up-to-date information on the vaccine pipeline, visit the HIV Prevention Research Database at www.avac.org/pxrd.

#### Use of Injectable Contraceptives and HIV acquisition: The data to date

This graphic summarizes the results of studies that gathered information on the relationship between injectable hormonal contraceptives and HIV risk. Different studies have drawn different conclusions. This is the reason for current uncertainty. None of these studies was designed to specifically evaluate this interaction. Discussions about a trial that would directly address the question are underway.



Source: CB Polis and KM Curtis. "Use of hormonal contraceptives and HIV acquisition in women: a systematic review of the epidemiological evidence." The Lancet (2013) http://dx.doi.org/10.1016/S1473-3099(13)70155-5

 Should there be a randomized controlled trial (known as ECHO) or not – that is a key question for hormonal contraceptives and HIV

## Research Reality Check 2



#### PrEP

Swift implementation of pilots projects and phased implementation in countries and communities where oral TDF/FTC-based PrEP is relevant; clear action on evaluating PrEP and developing policies in countries where it might be introduced over the long-term.

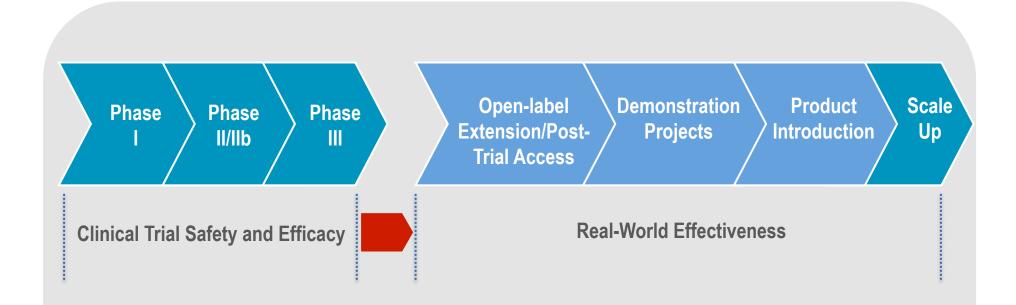
#### **Male Circumcision**

Roll out VMMC including surgical procedures, non-surgical devices and early infant male circumcision in countries that meet WHO-recommended criteria. Link rollout to strategic national plans, sustained funding, and targets set for maximum impact on the epidemic.

Map the pathway beyond pilot projects

Pilot projects work if they are part of a strategic plan—if some thought has been given to what will happen once results emerge. This has been done, to a large extent, with projects involving nonsurgical devices for VMMC; there is less clarity and planning for demonstration projects of daily oral PrEP.

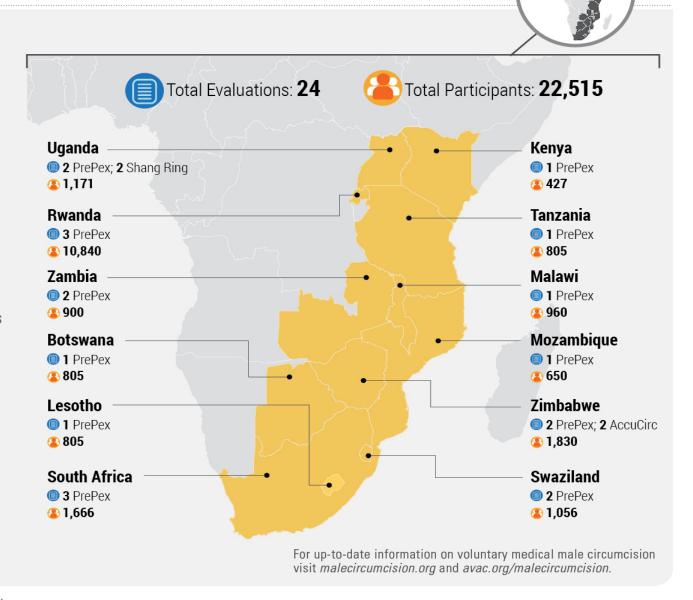
### Research to Rollout: A schematic road map



Highlighted in darker blue are the areas where biomedical HIV prevention research has the most experience to date. The "gap" between positive effectiveness data and access for trial participants and their communities is less familiar territory – as are the steps in lighter blue.

#### **Voluntary Medical Male Circumcision (VMMC) Device Evaluations**

There is a range of evaluation studies underway to learn more about how non-surgical devices can be used for adult male circumcision. These evaluations, also called implementation pilots, address questions about safety, efficacy, etc. The World Health Organization has already determined that one device, known as PrePex, meets required standards of quality, safety and efficacy for international use. Evaluations of PrePex and other devices will provide information on how to use these strategies in the real world. Most evaluations are enrolling, ongoing or recently completed. Results can be expected within a year.



#### Planned PrEP Demonstration Projects in Resource-Poor Settings as of December 2013

There are a range of planned or ongoing demonstration projects or open-label extension studies happening in the United States and Europe. This table includes those few projects in resource-poor settings that are not linked to one of the efficacy trials. A complete list is available at <a href="https://www.avac.org/prep.">www.avac.org/prep.</a>

Trial/project	Sponsor/funder	Location	Population	Status
Partners Demonstration Project			Serodiscordant couples	All four sites open and enrolling as of August 2013; results expected in 2016.
LVCT and SWOP	Implemented by national partners in collaboration with WHO, UNAIDS, O'Neill Institute of Georgetown University, London School of Hygiene and Tropical Medicine, Imperial College London; funded by Bill & Melinda Gates Foundation	Kenya	Young women, female sex workers and MSM	Formative research in planning phase.
Nigerian National Agency for the Control of AIDS		Nigeria	Serodiscordant couples	Formative discussions underway.
Wits Reproductive Health and HIV Institute  Durbar (DMSC) and Ashodaya Samithi		South Africa	Female sex workers	Expected start date of February 2014, with expected completion September 2016.
		India	Female and transgender sex workers	Feasibility study underway.
Implementation of PrEP	Oswaldo Cruz Foundation	Brazil	MSM and transgender women	Starting January 2014.

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## Research Reality Check 3



#### Testing/Diagnostics

Scaled-up and efficient testing programs with high levels of linkage to evidence-based prevention, treatment and care.

Swift execution of a research agenda on testing modalities and affordable diagnostics that meets emerging needs.

#### **Treatment as Prevention**

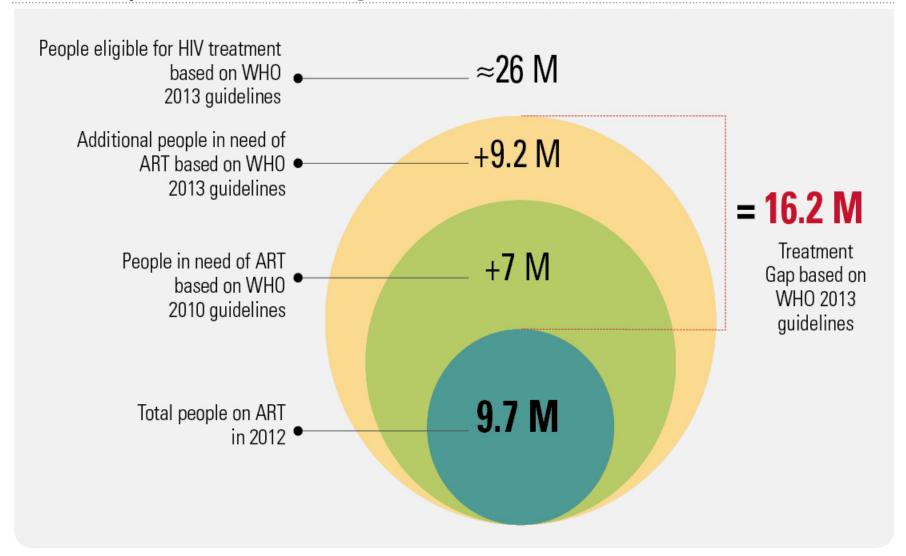
Accelerated adoption of new comprehensive WHO guidelines on ARVs for treatment and prevention, with majority of countries implementing by end of 2014.

Investment and innovation in viral suppression

ART doesn't preserve health and reduce transmission risk—virologic suppression does. It's an essential distinction that prevention advocates need to help amplify. We need to pay at least as much attention to what is happening after people start ART, as we do to how many people start at all. Virologic suppression—having a viral load that is at or close to undetectable—is key.



# The Global HIV Treatment Gap : Existing people on ART versus people eligible under past and current WHO guidelines



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#### Viral Load Testing Delivers Systemic Benefits from the Individual to the Institution

People living with HIV



I know if my treatment is working. I have the tools to get to "undetectable"! If necessary, I can switch to more effective drugs earlier, before I get sick.

Treatment provider



It's easier for me to identify and define treatment failure. I find out sooner when treatment isn't working. I know when to offer adherence counseling and when to switch treatment.

Program manager



I have better information about treatment adherence and health outcomes across my program.

Policy makers, National government



We can monitor community-wide progress toward the goal of "undetectable". We can identify areas that need more attention.

Donors, Global health actors



We can reduce global HIV incidence by reducing viral transmission within communities.

Médecins Sans Frontières/Doctors without Borders (2012). Undetectable: How Viral Load Monitoring Can Improve HIV Treatment in Developing Countries. http://www.msfaccess.org/content/undetectable-how-viral-load-monitoring-can-improve-hiv-treatment-developing-countries (Accessed November 7, 2013).

## Research Reality Check 4



#### **Combination Prevention**

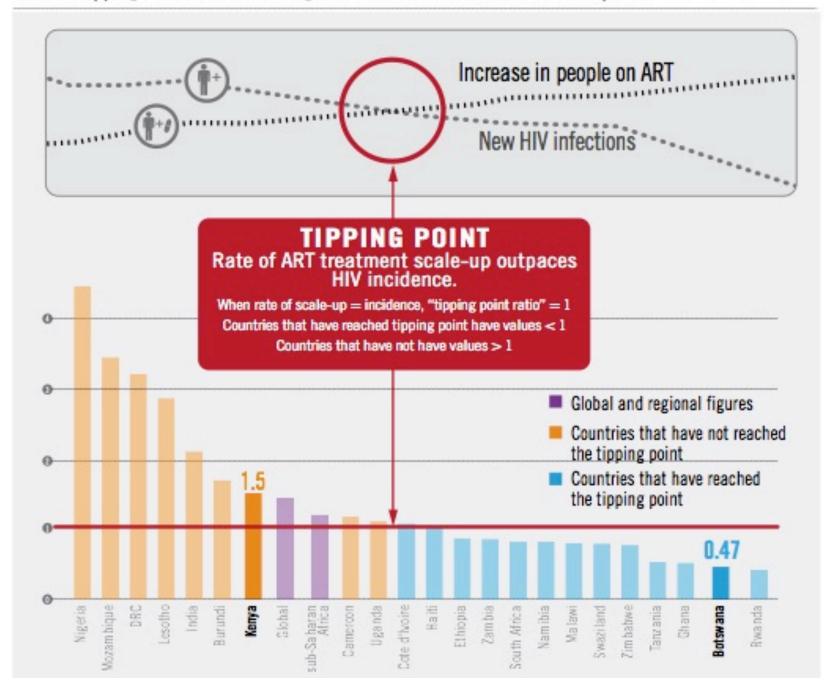
- Deliver evidence-based strategies in combinations that will have maximum impact on the epidemic.
- Support research that generates answers about synergistic use of multiple new prevention strategies.

### Partnerships movement from all sectors of

Build a movement from all sectors, calling for control of and then an end to AIDS.

Align models, programs and funding to stay on track to end AIDS To achieve ambitious targets for high-impact prevention and treatment, models and programs need to be connected in a feedback loop. This must be supported by full funding and visionary leadership at national and international levels.

#### The Tipping Point: Understanding a crucial milestone in the AIDS response



### The most recent bottom line(s)

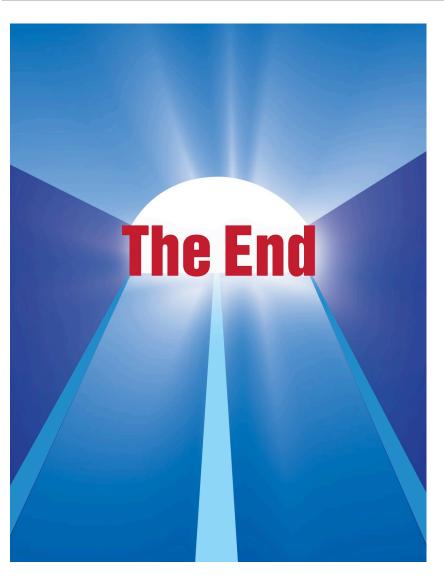
- Deliver what we have for immediate impact
- Demonstrate added benefit of new options as they become available
- Develop long-term solutions to end the epidemic
- Most of all, think and act in terms of combination prevention, rather than silver bullets or simple solutions

# What's on your mind?

- What are the issues uppermost on your mind?
- What needs action at a global level?
- What is on the "front burner" in different country contexts?

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### Thank You!



- For more information www.avac.org
- AVAC Report 2013: Research
   & Reality and all graphics to download at

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