

What's New & Next in HIV Prevention

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Outline

- Targets made – and missed
- Language check
- Prevention journeys – for programmes and for people
- The oral PrEP experience – and the potential of a “prevention platform”
- The product pipeline
- Decisions, decision-makers and the future







UNAIDS 2020 targets: Where we landed

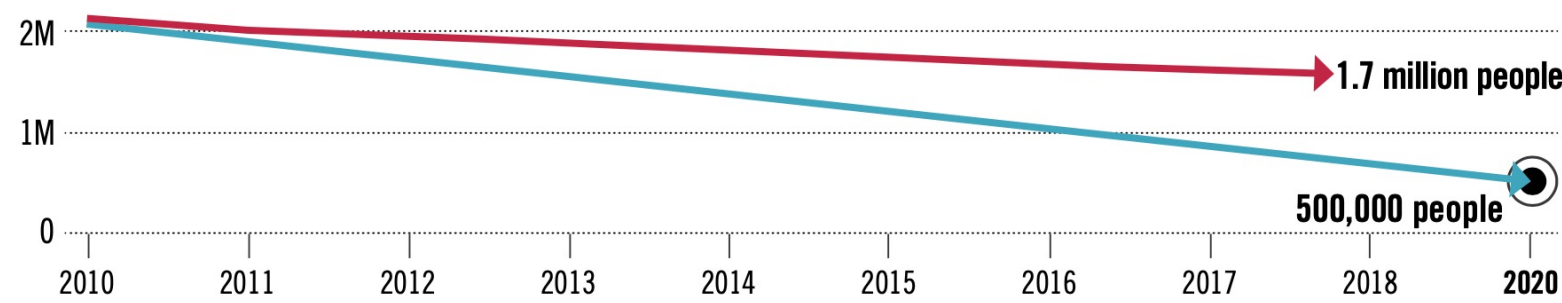


What Model Assumed

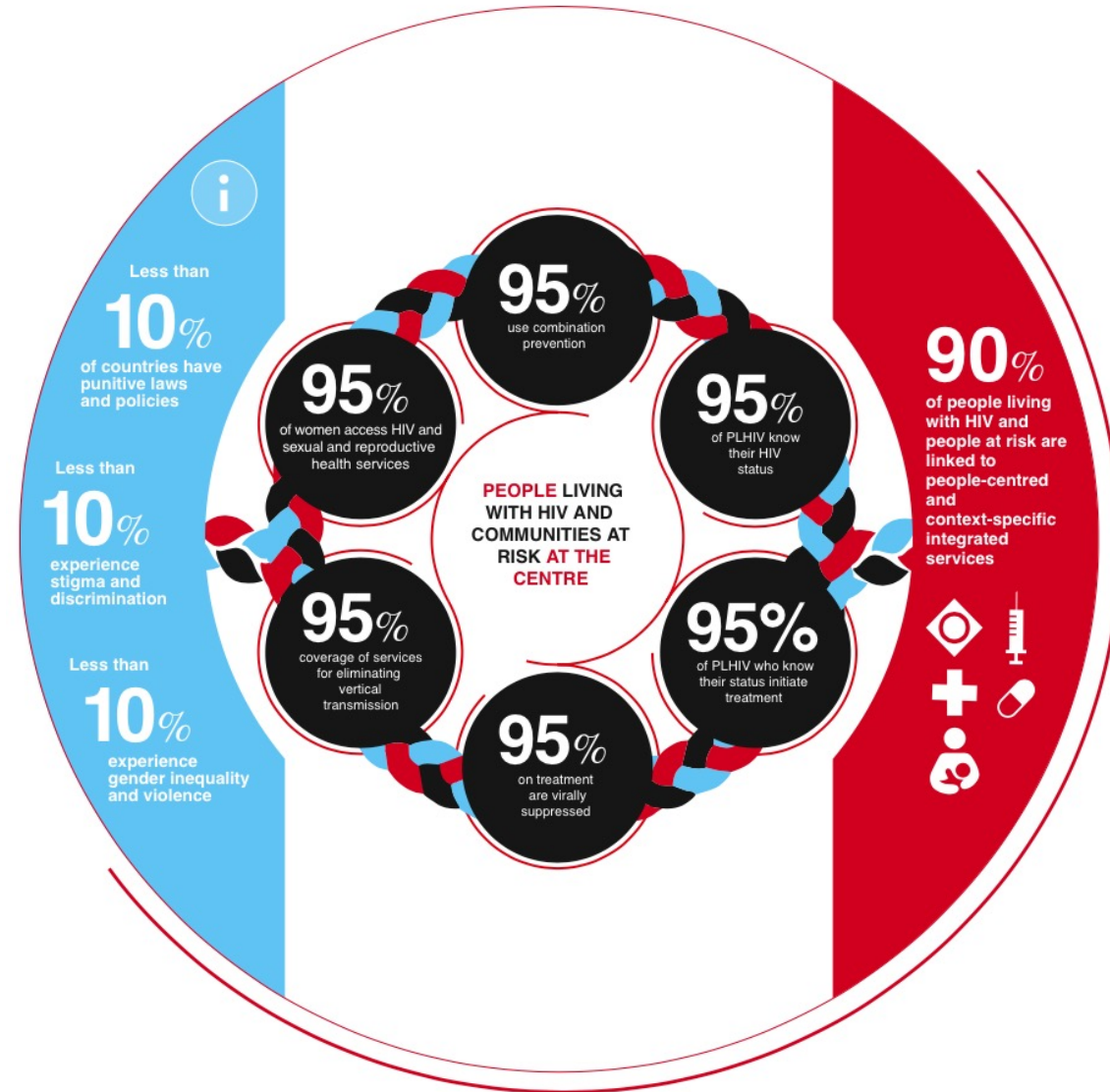
-  90% key population covered
-  90% of AGYW (key locations)
-  >6bn condoms (SSA) per year
-  3m PrEP
-  5m VMMC per year
- 
 - Funding (additional \$6.5bn per year)
 - Testing, treatment, virologic suppression in PLHIV worldwide: 90-90-90

What Was Implemented

- 
 - 47% for sex workers
 - 33% for gay men & other MSM
 - 32% for PWID*
-  34% of AGYW in key locations covered**
-  <3bn condoms (SSA)*** per year
-  Approx 385,000 PrEP****
-  4.1m VMMC per year in 2018
- 
 - Flat funding
 - Testing, treatment, virologic suppression in PLHIV worldwide: 79-78-86 with large disparities



UNAIDS 2020 targets: Where we landed



Prevention Paradigm circa 2006

Different Strokes for Different Folks		
Method	Contraception	HIV Prevention
Behavior	✓	✓
Barrier Methods	✓	✓
Gels	✓	
Rings	✓	
Oral pill	✓	
Injectables	✓	
Implants	✓	
Surgical procedures	✓	
Treatment		

Prevention Paradigm 2021 and beyond

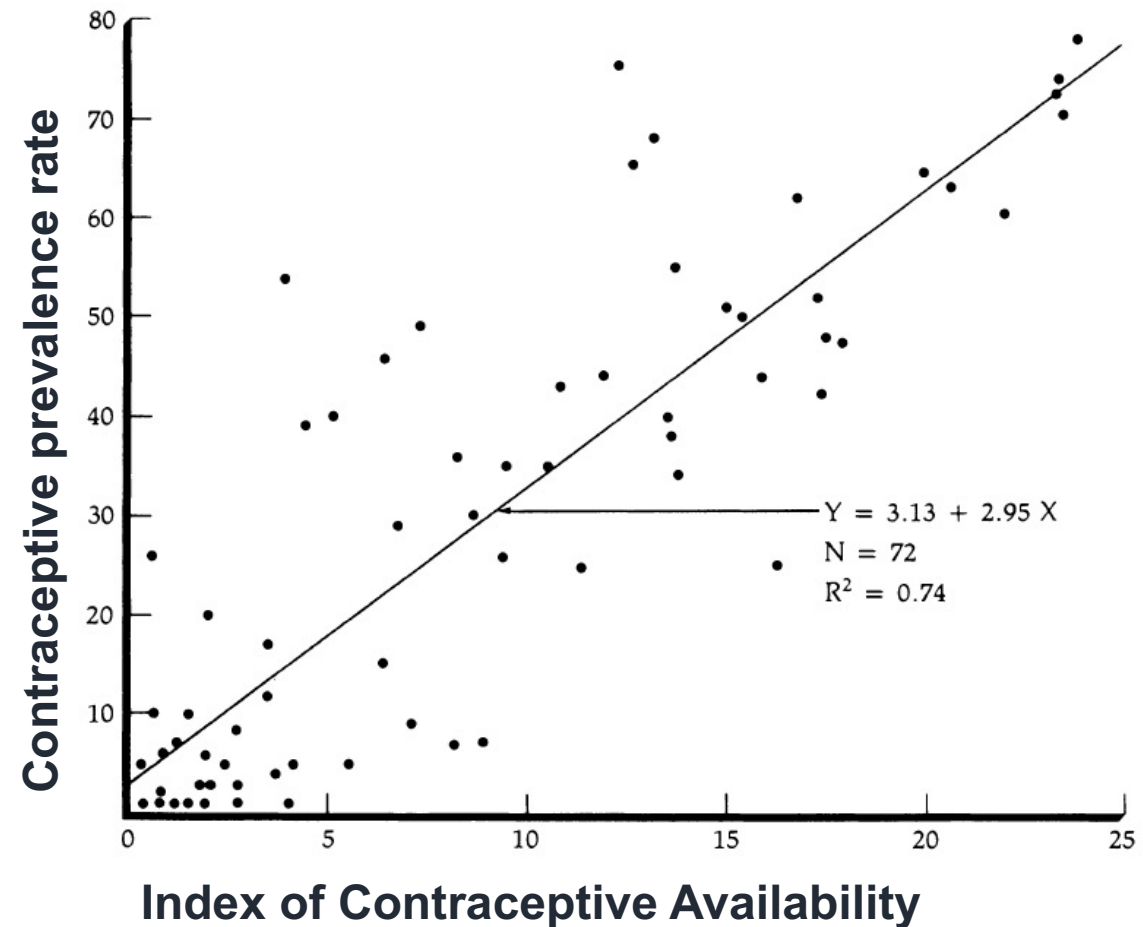
Different Strokes for Different Folks		
Method	Contraception	HIV Prevention
Behavior	✓	✓
Barrier Methods	✓	✓
Gels	✓	✓ – not registered
Rings	✓	✓ – EMA positive opinion; WHO PQ
Oral pill	✓	✓ ✓ (for some) ? – monthly, dual px in development
Injectables	✓	✓ – ARV ? – 1 bNAb, 1 vax in Phase 3, 1 new ARV entering Ph 3; others in development
Implants	✓	? – multiple in preclinical
Surgical procedures	✓	✓
Treatment		✓

Language Check

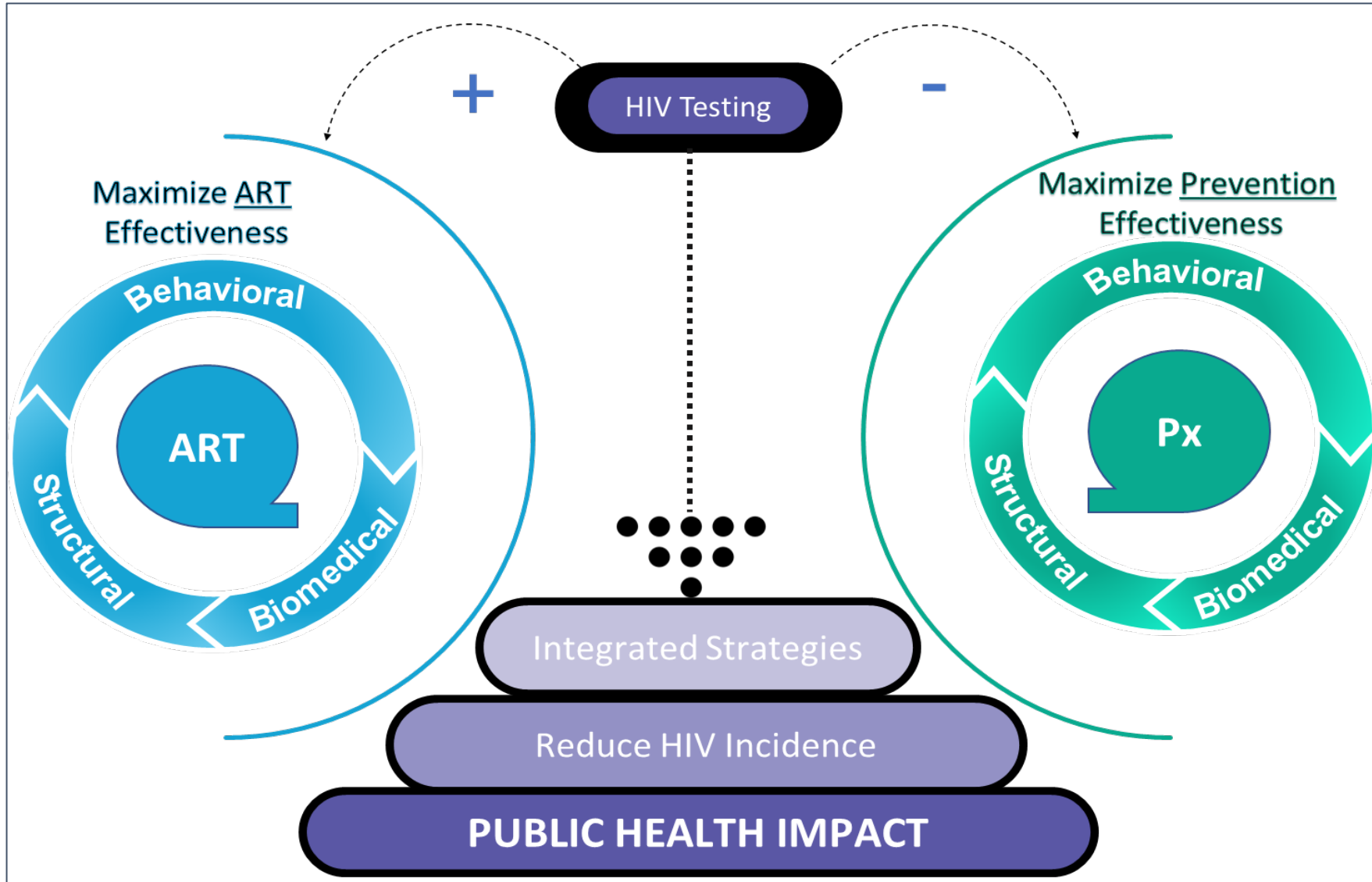
- Options
 - Biomedical methods that are safe and effective
 - Requires R&D of additional options to add to the “method mix”
- Choice
 - The ability for an individual to select from an array of options
 - Requires policy makers, donors, governments & implementers to make the “mix” available, accessible & affordable

Choice Matters

- WHO systematic review (231 articles) showed increased choice associated with:
 - **Increased persistence** on chosen method
 - **Better health outcomes**
 - **12% increase in contraceptive prevalence for each additional method**
- Similar to contraceptive needs: different people have different HIV prevention needs at different times



Universal Test & Connect



Parallel Universes/Journeys

Users

What do I want?

Who do I want to talk with about sex and relationships?

Do I want an HIV test?

Where do I want to get an HIV test?

Do I need and want HIV prevention?

What kind of HIV px do I want?

Oral, ring, injectable, condoms, DPP?

Where and from whom do I want it?

Providers & Health Systems

Who is at risk?

Where do I find them?

When I can test them?

What do I tell them?

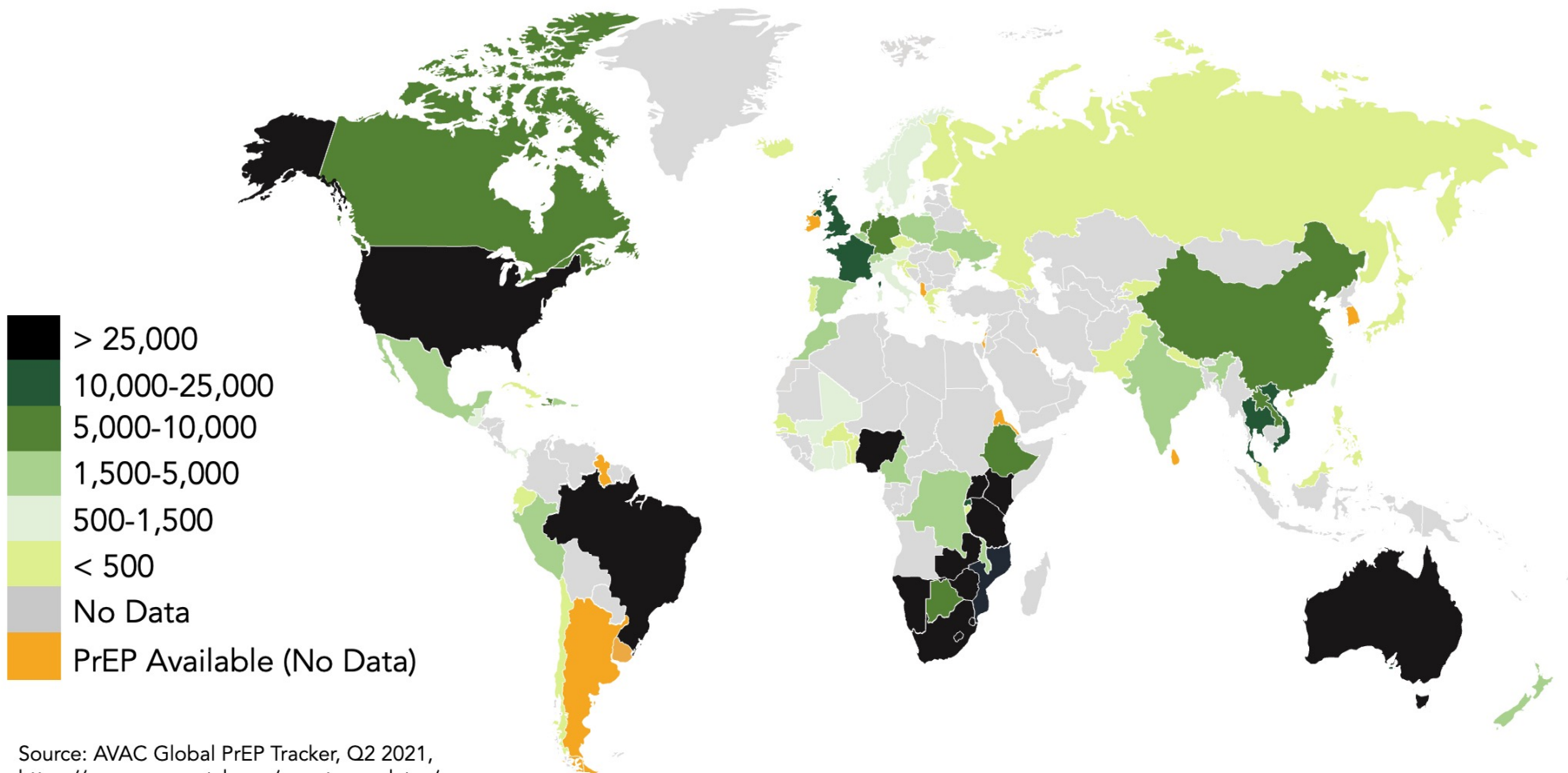
Where can I provide px info and products to them?

What px options can I provide them?

Oral, ring, injectable, condoms, DPP?

Global PrEP landscape – 9 years in

PrEP Initiations by Country, June 2021



3 million people
with access
to PrEP

**Actual total
initiations
(approx.):
1.3 million**

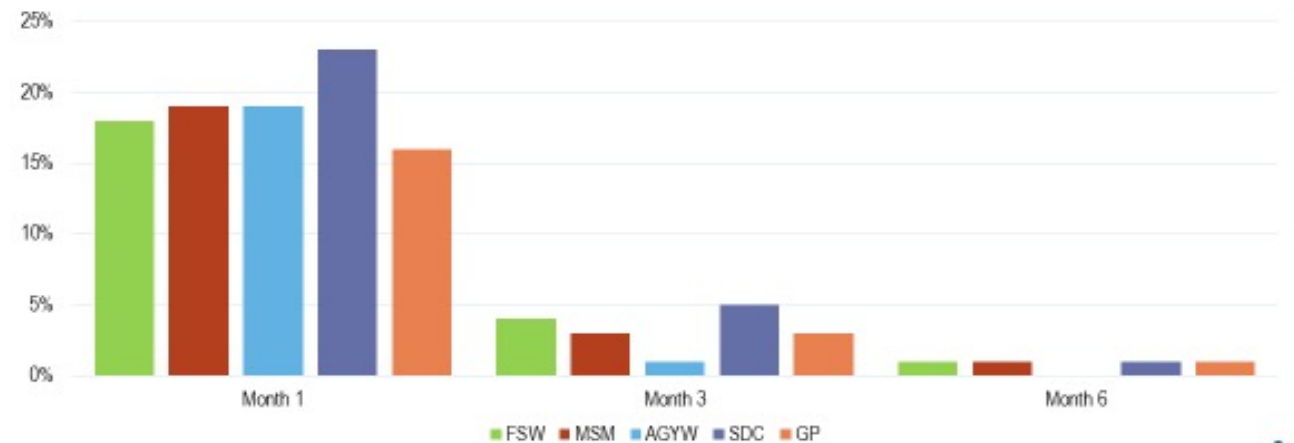
Source: AVAC Global PrEP Tracker, Q2 2021,
<https://www.prepwatch.org/country-updates/>

But these don't always translate to continued use

PrEP continuation rates tend to decline significantly by 3 months after initiation across all populations¹

Study	Country	Continuation Rates (M=month)
POWER ²	Kenya, South Africa	43% (M1); 20% (M3)
PrIYA ³	Kenya	MCH Clinic: 39% (M1); 12% (M6)
		FP Clinic: 41% (M1); 24% (M3); 15% (M6)
EMPOWER ⁴	South Africa, Tanzania	73% (M1); 61% (M3); 34% (M6)

Lesson 1: Continuation Rates are Low and Vary by Population Type⁵

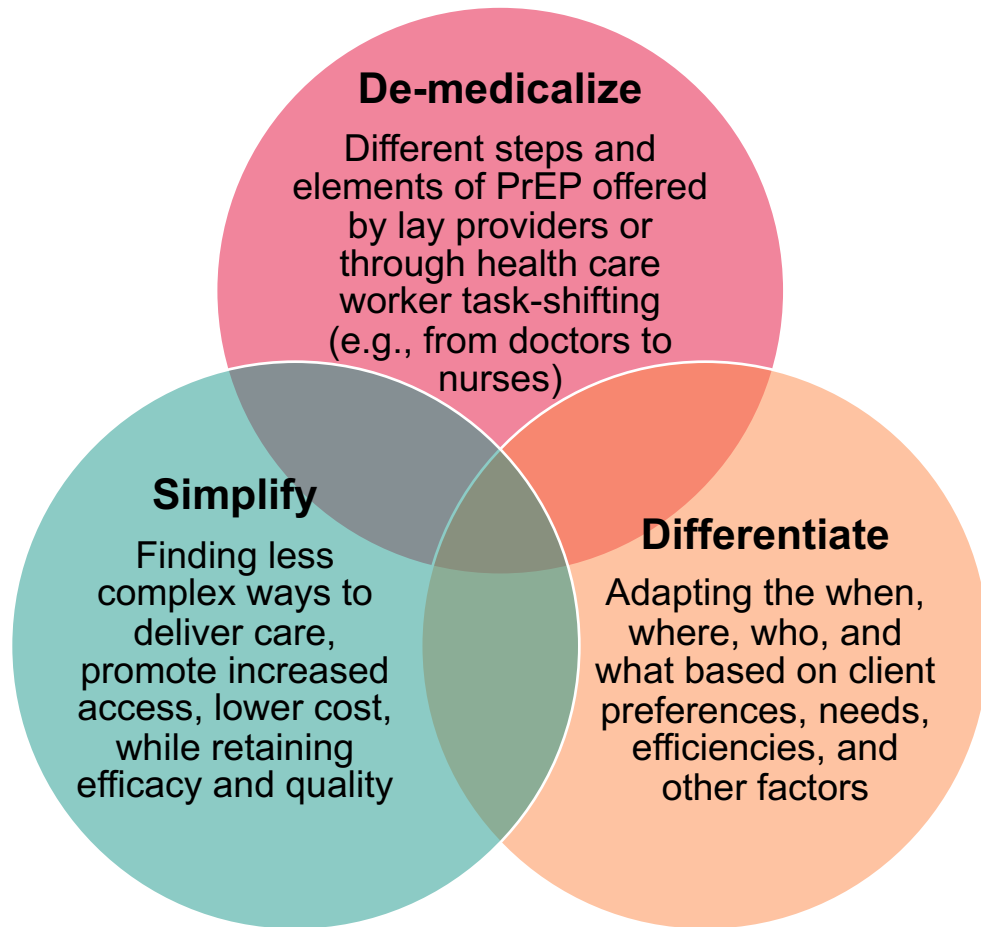


Source: ¹ Rodrigues et al., Starting and staying on PrEP: a scoping review of strategies for supporting and improving effective use of PrEP, HIV R4P (2021); ² Rousseau-Jemwa et al., Early Persistence of HIV Pre-exposure Prophylaxis (PrEP) in African Adolescent Girls and Young Women (AGYW) from Kenya and South Africa, HIV R4P (2018); ³ Kinuthia et al., Pre-exposure prophylaxis uptake and early continuation among pregnant and post-partum women within maternal and child health clinics in Kenya: results from an implementation programme (2019); Mugwanya et al., Integrating preexposure prophylaxis delivery in routine family planning clinics: A feasibility programmatic evaluation in Kenya (2019); ⁴ Delany-Moretlwe et al., Empowerment clubs did not increase PrEP continuation among adolescent girls and young women in South Africa and Tanzania - Results from the EMPOWER randomised trial, AIDS 2018 (2018); ⁵ Jilinde (2019).

Lessons Learned for PrEP Implementation

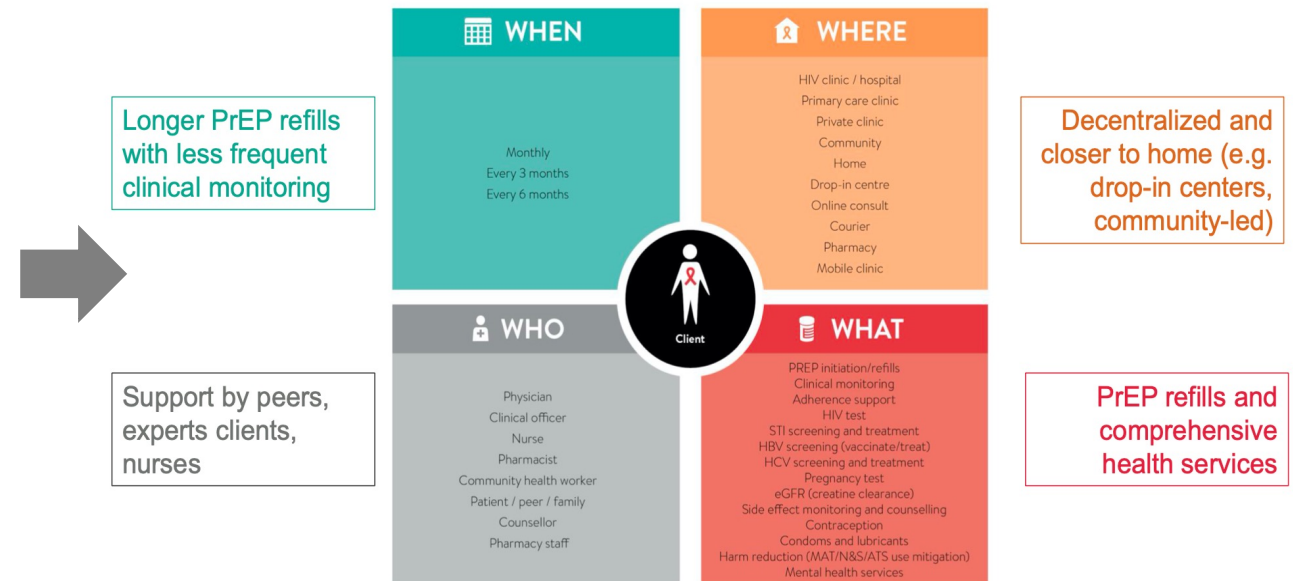
- **Invest in and expand demand generation** – socialize PrEP for general population while implementing outreach tailored to specific user segments
- **Replicate successful approaches**, prioritizing service delivery models that help users access and stay on PrEP if they want
 - Build on adaptations that have expanded due to COVID-19: differentiated delivery models, mHealth, multi-month dispensing, HIV self-testing
 - Integrate PrEP with other SRH services
 - Promote peer, partner, and continued use support interventions
 - Community-led, accessible, non-discriminatory services
- **Increase resource allocation to HIV prevention** to facilitate national scale-up
- **Introduce future HIV prevention options** via channels and approaches preferred by potential users

Differentiate, Simplify and De-Medicalize



Building blocks for differentiated PrEP

Adapting the when, where, who and what




Kim Green, HIVR4P Satellite: Bringing PrEP to the people: Democratizing access to PrEP through differentiated delivery before, during, and after COVID-19, 4 Feb 2021

Lessons Learned for SEARCH

PLOS MEDICINE

HIV incidence after pre-exposure prophylaxis initiation among women and men at elevated HIV risk: A population-based study in rural Kenya and Uganda

Catherine A. Koss , Diane V. Havlir, James Ayieko, Dalsone Kwarisiima, Jane Kabami, Gabriel Chamie, Mucunguzi Atukunda, Yusuf Mwinike, Florence Mwangwa, Asiphos Owaraganise, James Peng, Winter Olilo, Katherine Snyman, [...], Laura B. Balzer
[view all]

Published: February 9, 2021 • <https://doi.org/10.1371/journal.pmed.1003492>

- Population-level offer of PrEP with rapid start and flexible service delivery was associated with 74% lower HIV incidence among PrEP initiators compared to matched recent controls prior to PrEP availability
- HIV infections significantly lower among women who started PrEP
- Universal HIV testing with linkage to treatment and prevention, including PrEP, is promising approach to accelerate reductions in new infections in generalized epidemic settings

Dapivirine Vaginal Ring

- Flexible silicone vaginal ring developed by IPM
- Woman-initiated
 - Self-inserted monthly
 - Discreet
 - Does not interfere with sex
 - Excellent safety profile; non-systemic
- ARV dapivirine (developed by Janssen/J&J) slowly released over one month
- Reduced HIV risk in Phase III trials: 35% in The Ring Study, 27% in ASPIRE
- Open-label extension studies saw increased adherence, suggested greater risk reduction (increasing to 63% and 39% from Phase III)
- First long-acting HIV prevention product



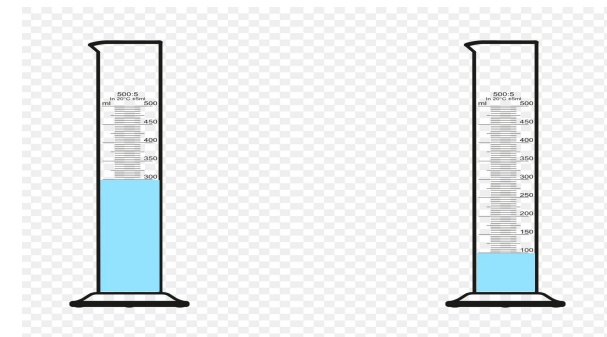
Dapivirine Vaginal Ring

- On July 24, European Medicines Agency (EMA) announced a positive scientific opinion on DVR as an additional HIV prevention option for cisgender women age 18 and older in developing countries to reduce their HIV risk
- Considered under EMA's Article 58, in cooperation with WHO, to “facilitate access to essential medicines in developing countries using the same rigorous standards as for products intended for use in the European Union”
- In November 2020, WHO prequalified DVR; and in January 2021 recommended DVR as an additional option
- EMA/WHO combination expediting submissions to African National Medicines Regulatory Authorities (NMRAs) in 2021
- Incorporated in PEPFAR 2021 Country and Regional Operational Plan (COP/ROP) Guidance

Long-acting Injectable Cabotegravir

- HIV integrase strand transfer inhibitor developed by ViiV/GSK – and an analogue of dolutegravir
- Nano-formulated, low-solubility crystalline drug suspended in an aqueous solution
- Two HIV prevention efficacy trials underway, under the HPTN, comparing CAB injections every two months to oral TDF/FTC
- CAB-LA in combination with injectable rilpivirine from J&J developed as a treatment (called Cabenuva)

	CAB-LA	DMPA-IM
<i>Location</i>	Gluteal muscle (buttocks)	Upper arm or gluteal muscle (buttocks)
<i>Frequency</i>	Every 2 months	Every 3 months
<i>Volume</i>	3 mL	1ml



Long-acting Injectable Cabotegravir

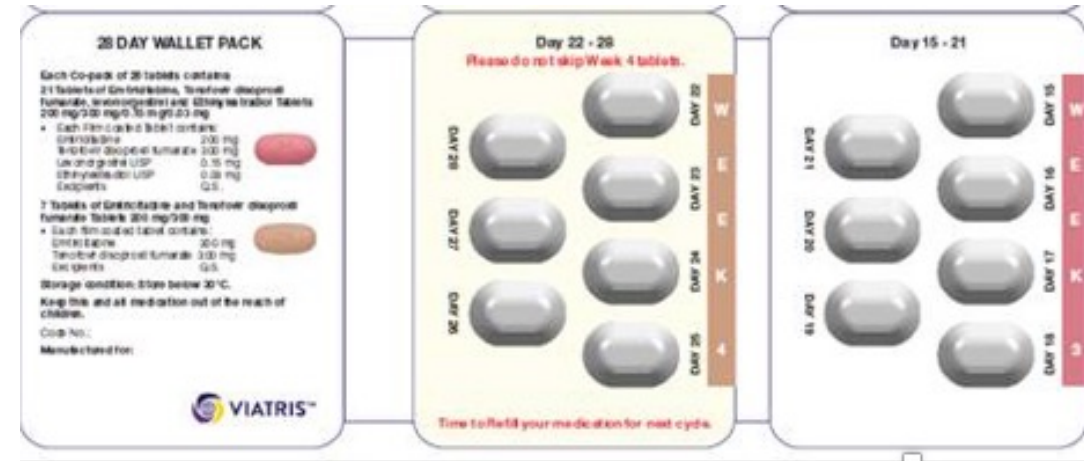
	Total Infections	Infections in CAB-LA Arm	Infections in oral TDF/FTC Arm	Hazard ratio in CAB LA vs. FTC/TDF arm
HPTN 083 Started December 2016	52 Incidence 0.81%	13 Incidence 0.41%	39 Incidence 1.22%	0.34 (95% CI 0.18-0.62) 66% risk reduction
HPTN 084 Started November 2017	38 Incidence 1%	4 Incidence 0.21%	34 Incidence 1.79%	0.11 (95% CI 0.04-0.32) 89% risk reduction

Long-acting Injectable Cabotegravir

- Understand breakthrough infections, adherence and potential resistance profiles – and the potential pharmacologic “tail”
- Currently moving to offering all participants choice between the two safe and effective options
- Formal Open Label Extension phase of trials in development
- Additional sub-studies and sub-analyses underway for various sub-populations
- ViiV publicly stated its commitment to file for a broad label for all populations at risk and are in process of compiling data and discussing pathways with various regulatory agencies (FDA, EMA, and SAHPRA)
- Earliest regulatory submission in 2021; approval 2022

Dual Prevention Pill

- A single co-formulated tablet containing TDF/FTC and combined oral contraceptive with levonorgestrol and ethylene estradiol (COC)
- Bioequivalence study to compare bioavailability of co-formulated tablet to TDF/FTC and COC separately ongoing
- File for regulatory approval possible in 2022
- Could be packaged in a blister pack – like COCs, and unlike the classic “rattling PrEP pill bottle”
- End-user research and market preparation underway



Developing and Introducing a Dual Prevention Pill

Oral PrEP & oral contraceptive for HIV and pregnancy prevention



Background

A coalition of partners is developing a novel Dual Prevention Pill (DPP) for prevention of pregnancy and HIV acquisition in high-need countries. Women in sub-Saharan Africa are disproportionately affected by HIV compared to men, and 214 million women of reproductive age in the developing world have an unmet need for contraception.¹ In particular, young women ages 15-24 in sub-Saharan Africa account for 71 percent of new infections in their age group and 29 percent of new infections among adults in the region.² As the “youth bulge” results in millions of young people entering their reproductive years,³ it will impact efforts to end the HIV epidemic and reduce unintended pregnancies. It is critical to ensure all women have access to both contraception and HIV prevention.

Project Goal

Rapidly and successfully introduce a daily oral pill for HIV and pregnancy prevention.

A coalition of organizations, including AVAC, the Clinton Health Access Initiative (CHAI), Mann Global Health, Mylan and the Population Council are implementing the DPP project. These efforts are supported by the Children's Investment Fund Foundation (CIFF), the Bill & Melinda Gates Foundation (BMGF), the U.S. Agency for International Development (USAID) and WCG Cares.

Now What?

- Build px platforms with condoms (M&F) and oral TDF/FTC programs that can integrate DVR, CAB-LA & DPP – while assessing specific service delivery needs that might be needed for an injectable
- [Common Agenda to Plan for Ring Introduction](#), developed by PEPFAR/USAID-funded OPTIONS Consortium with IPM; updated with PROMISE & CHOICE
- Gates-funded [Biomedical Prevention Implementation Collaborative \(BioPIC\)](#) working with ViiV and numerous stakeholders (including Global Fund and PEPFAR) to develop a comprehensive, coordinated product introduction and access strategy – currently being updated given early results of HPTN 083 and 084
- Similar work funded by CIFF for the DPP

Learning from and Building on Oral PrEP

Oral PrEP Implementation Studies

Post-approval studies and projects

131

Distinct post-approval oral PrEP implementation projects and studies; most were small-scale

Countries

68

Different countries conducted projects including multiple in the same country (e.g. 25 in one country)

Stakeholders

54

Different organizations involved in oral PrEP implementation research

Key Takeaways from early Oral PrEP rollout



Post-approval studies were not all designed to address decision-maker questions



Data from research was not well timed to inform decision making at global or country level



Complex, fragmented stakeholder landscape

The Way Forward

Requirements of Collaboratively Planning for Successful Introduction:

Mapping decision-maker questions against studies

Planning in parallel with clinical trials

Shared strategy developed by diverse stakeholders

Ideal Scenario for Future Px Products:



Post-approval studies are **well designed** to address decision-maker questions



Data from research is **well timed** to inform decision-making at global and country level



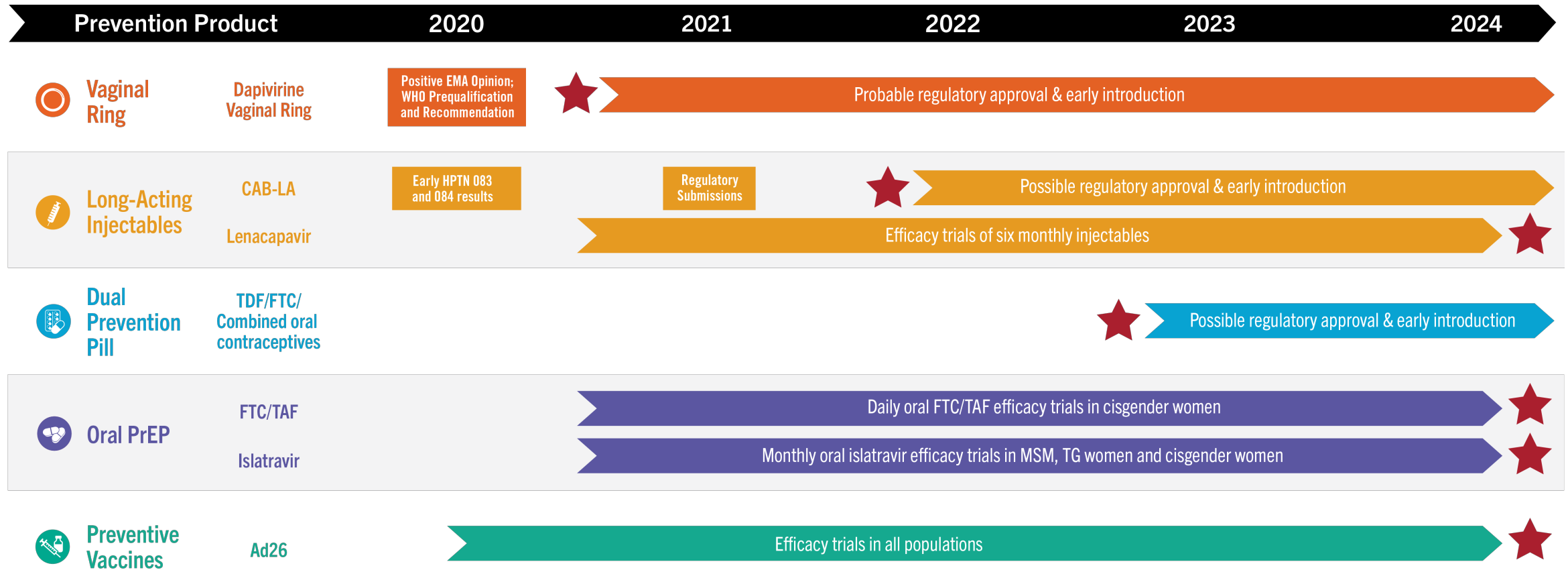
Coordinated stakeholder landscape with roles agreed upon in advance

New Px in PEPFAR COP 2021

- Teams should consider developing multi-year plans that show how PrEP can contribute toward epidemic control and that incorporate new prevention modalities including CAB-LA and DVR and that allow incorporation of new agents as they are approved.
- COP21 expansion of access to oral PrEP combined with communication within the OU as to the inclusion of CAB-LA and/or DVR will provide an important platform for the introduction of these and other new biomedical prevention intervention options.
- As CAB-LA and DVR become available, like oral PrEP, they should be presented with thorough information on all available HIV prevention options, including each method's relative efficacy and safety, as well as counseling and adherence support, allowing for an informed client choice regarding a biomedical HIV prevention option.
- Those who prefer an alternative to oral PrEP or are unable to adhere to daily dosing, may soon have new options to consider as part of a comprehensive biomedical prevention program. Building on family planning research, it is anticipated that by expanding access to and use of a range of HIV prevention products, saturation can be more effectively achieved.
- For COP21, especially in countries where CAB-LA and DVR trials occurred, OU teams are encouraged to identify implementation needs for the addition of these agents as part of the menu of HIV prevention options for women. Possible areas to consider OU engagement are regulatory approval, enabling policies, service provider education, service delivery channels, and demand generation.

Years Ahead in HIV Prevention Research

Time to Market



March 2021

★ Earliest time to market

Good Px News in the Midst of Madness

Px Option	Populations	Next Steps	Time to Market
Male & female condoms	All at risk	Market at scale	Approved for decades
VMMC	Heterosexual men	Re-energize post-COVID restrictions	2007 Recommended in 14 priority counties in E/SA since
Daily Oral TDF/FTC	All at risk	Scale-up demand creation and support for continuation	2012 US approval ; 2015 first African approvals
Event-driven Oral TDF/FTC	MSM	Integrate as per guidelines	2019 WHO recommendation
Daily Oral TAF/FTC	All except “those at risk via receptive vaginal sex”	Efficacy trial in cisgender women in Africa start 2021	2019 FDA partial approval; ±2024 for cisgender women
Dapivirine Vaginal Ring	Women	WHO guidelines; National regulatory approvals & product intro in 2021	2020 positive EMA opinion and WHO pre-qualification; late 2021 intro
Dual Px Pill (TDF/FTC/COC)	Women	Bioequivalence studies ongoing	Likely earliest approvals ±2022
Injectable Cabotegravir	Studied in multiple populations	Regulatory submissions mid-2021	Likely earliest approvals ±2022
Monthly Oral Islatravir	To be studied in multiple populations	Two efficacy trials to start 2021	Likely earliest approvals ±2024
Six-monthly injectable Lenacapavir	To be studied in multiple populations	Two efficacy trials to start 2021	Likely earliest approvals ±2024
Ad 26 Vaccine	Studied in multiple populations	Two efficacy trials continuing – one fully enrolled; one enrolling	Likely earliest approvals ±2024
VRC 01 bNAb infusion	Studied in multiple populations	No overall efficacy, but proof of concept Multiple combo bNABs in development	NA – not intended for licensure

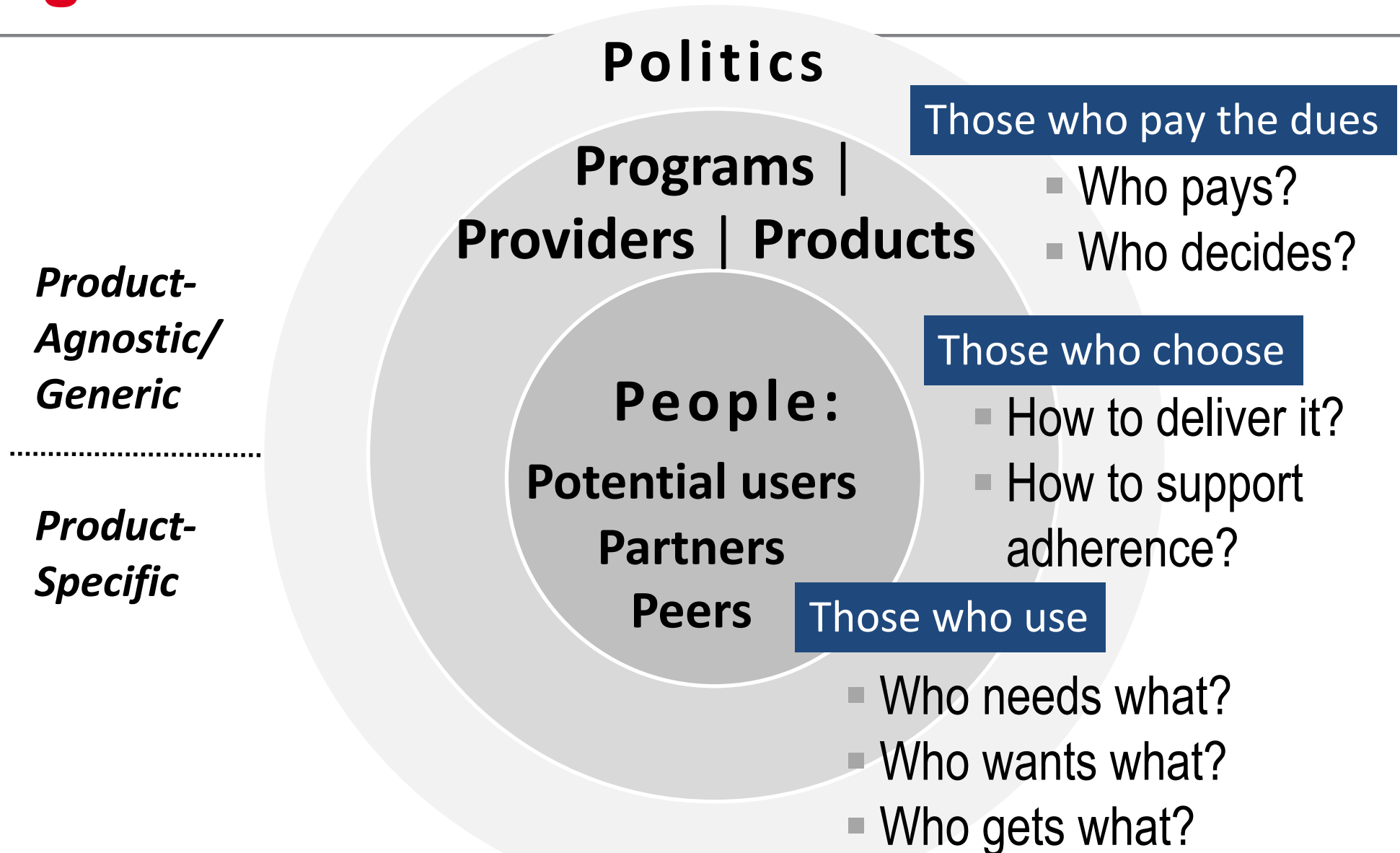
Product Considerations

For each product, understand and balance:

Clinical	Policy & Programs	Personal
<ul style="list-style-type: none">■ Biologic efficacy■ Dosing/duration■ Reversibility■ Side effect profile■ Systemic/Topical	<ul style="list-style-type: none">■ Delivery channel(s)■ Health system burden■ Product cost■ Program cost■ Provider training■ Demand creation	<ul style="list-style-type: none">■ User effectiveness■ User preference■ User burden■ Discretion of use■ Contribution to stigma

AND, it's never just "the product" – it's the program

Programmatic Considerations



Conclusion

- More safe and effective px options – entering market & in development
 - But oral TDF/FTC only PrEP option widely approved and with clear programmatic guidance, targets, product availability, etc.
 - Now timely to integrate DVR and CAB-LA into px programming
- No one option will be THE choice for all people, all the time – or for one person, all the time
- Biomedical product use & coverage need not be perfect to have impact – see SEARCH results

Conclusion

Much accomplished; much to do:

- Fill the **product introduction gaps**:
 - Accelerate time from regulatory approval to intro to impact
 - Demand-creation and program platforms for prevention generally
 - Differentiated (and integrated) service delivery for px
- Fill the **product development gaps**:
 - Longer-acting & event-driven
 - User-friendly & developed WITH users
 - Dual-purpose & multi-purpose methods

Resources

- [AVAC World AIDS Day 2020 letter to the world](#)
- [Understanding the EMA Opinion and Next Steps for the Dapivirine Vaginal Ring](#)
- [An Advocates' Primer on Long-Acting Injectable Cabotegravir for PrEP](#)
- [Dapivirine Ring Early Introduction Considerations: 7 Country Analysis](#)
- [Biomedical Prevention Implementation Collaborative \(BioPIC\)](#)
- [Developing and Introducing a Dual Prevention Pill](#)
- [AMP-ticipation: Context and concepts for understanding the AMP Trials](#)
- [Platforms, Process, Partnerships, Payers and Participatory Practices that Drive Vaccine Development](#)

- www.avac.org
- www.PrEPWatch.org

Acknowledgements



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- Kristine Torjesen

BILL & MELINDA
GATES foundation

CIFF CHILDREN'S
INVESTMENT FUND
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COMPASS

HIV Prevention Market Manager | Accelerating Product Introduction
Informing Product Development
Reducing Time to Impact

Supported by the Bill & Melinda Gates Foundation

OPTIONS
OPTIMAL PREVENTION TECHNOLOGY INTEGRATION IN SETTINGS



Coalition to Accelerate and Support Prevention Research (CASPR)



Cooperative Agreement No. AID-OAA-A-16-00031
HIV Vaccine and Biomedical Prevention Research Project—Objective 3

PROMISE-CHOICE Partners



AVAC
25 Years and Counting