

AVAC

Global Advocacy for HIV Prevention

The Next-Generation of Biomedical Prevention: *Fasten Your Seatbelts*

Mitchell Warren, Executive Director

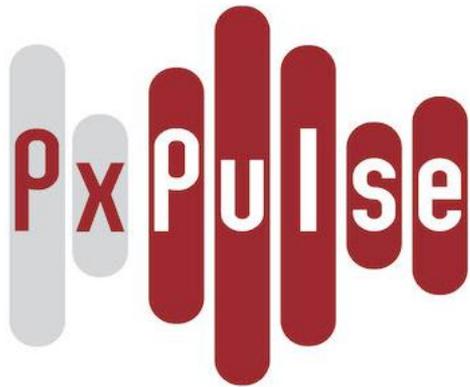
16 October 2019

PEPFAR Scientific Advisory Board

Outline

- The Science of Choice
- Timelines and Pipelines for Context
- The Oral PrEP Experience
- Possible Future Experiences
- Balancing the Portfolio; Product Considerations; People Considerations

The Science of Choice



The Science of Choice: The future of HIV prevention research

<https://www.avac.org/podcast/science-of-choice>

To Think About Now

- Where is the greatest unmet need for prevention?
- What products will people want AND use?
- What trial designs can best answer the questions fastest and ethically?
- How will we deliver “next generation” prevention?
- How to best “balance our portfolio”?
- How do we keep R&D part of the “ending AIDS” narrative?

New Biomedical Approaches

Upcoming efficacy trial results: The future of HIV prevention



Vaginal ring



Oral PrEP



Long-acting injectable



Antibody



Preventive HIV vaccine

JANUARY 2018 JANUARY 2019 JANUARY 2020 JANUARY 2021

Dapivirine (HOPE/MTN 025)

Dapivirine (DREAM/IPM 032)

F/TAF (DISCOVER – MSM/TG)

FDA
Approval –
for some

Possible
regulatory
opinion

F/TAF (Name TBD – women)

Cabotegravir (HPTN 083)

Cabotegravir (HPTN 084)

VRC01 (HVTN 704/HPTN 085)

VRC01 (HVTN 703/HPTN 081)

ALVAC (HVTN 702/Uhambo)

Ad26 (HVTN 705/HPX2008/Imbokodo)

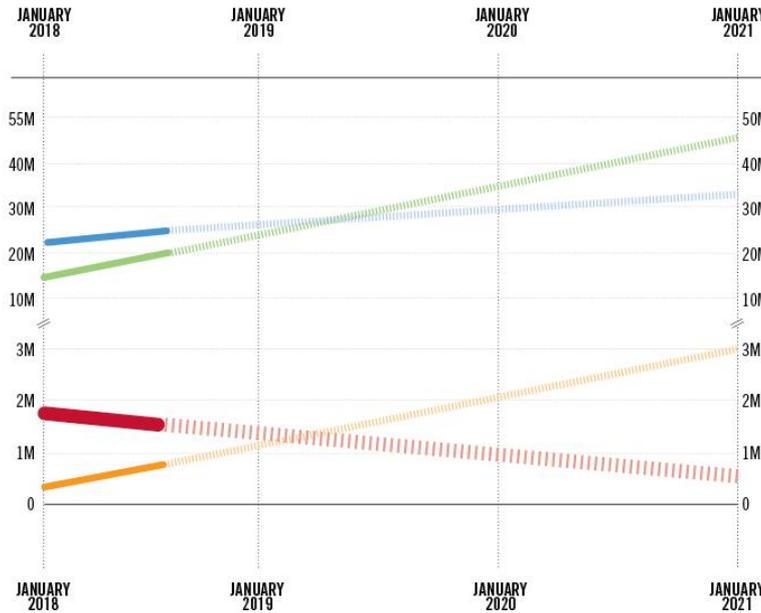
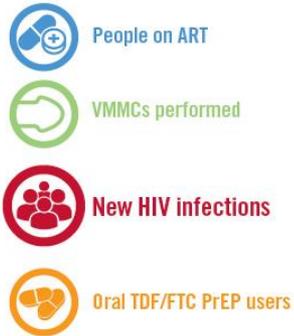
Ad26 (HVTN 706/HPX3002/Mosaico)

Visit www.avac.org/pxrd for trial status updates.

— Open-label == Randomized controlled === In planning

UNCLASSIFIED

Trajectories to fast-track prevention targets: The present state of HIV prevention



Upcoming efficacy trial results: The future of HIV prevention



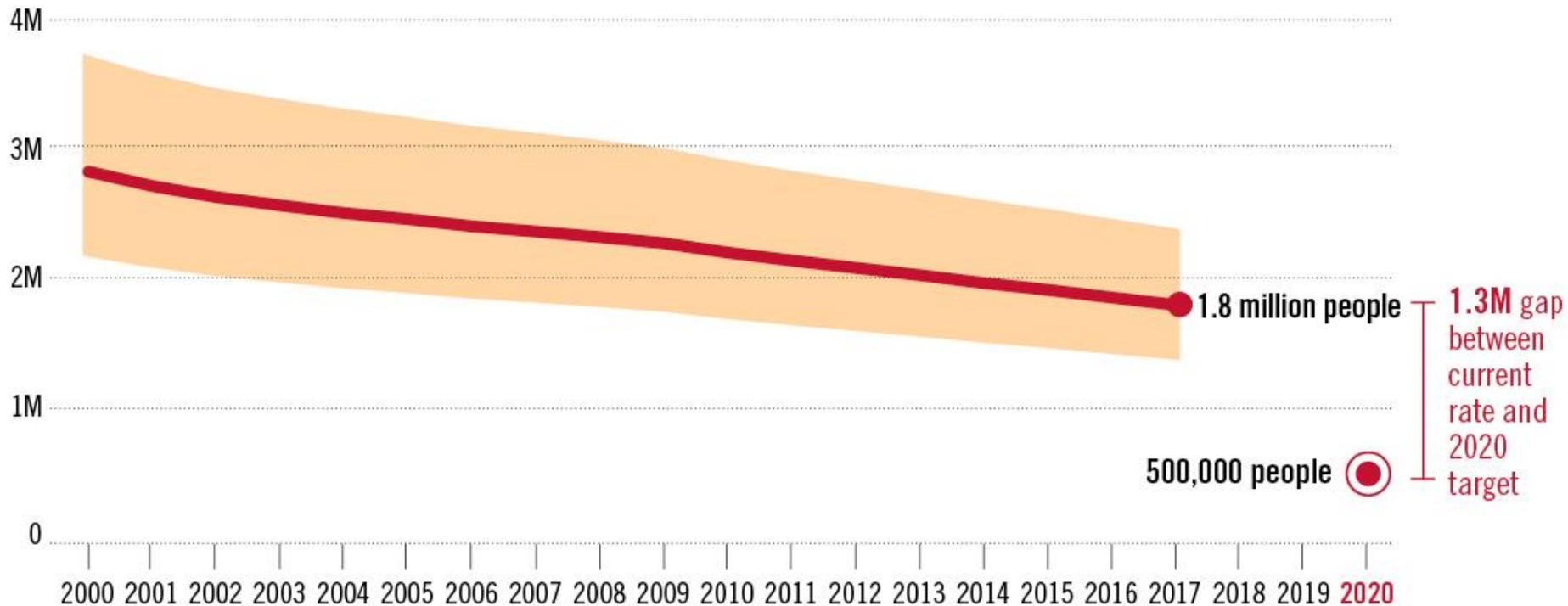
Visit www.avac.org/pxrd for trial status updates.

One Timeline, Two Stories, One Message

- With the current trajectory, we will miss targets for incidence reduction & scale up of primary prevention
- At the same time, we will see key trial results
- Need to tell these two stories, and support an evidence-based narrative
- Preparing for this is key!

And We're Missing the Target – Badly

Global Number of New HIV Infections, 2000-2017 and 2020 Target

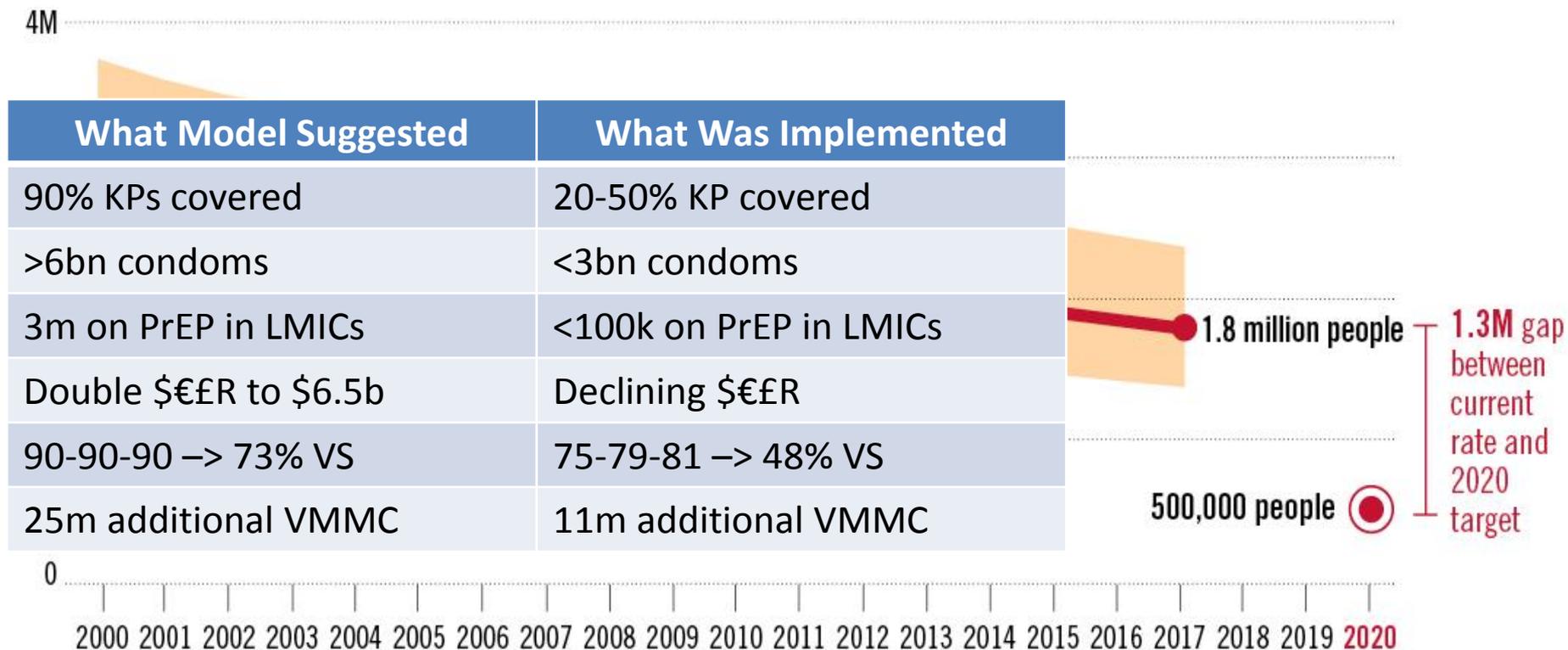


Source: UNAIDS. *Miles to Go—Closing gaps, breaking barriers, righting injustices*. July 2018. Accessible at: www.unaids.org/en/resources/documents/2018/global-aids-update.

AVAC Report 2018: *No Prevention, No End*
www.avac.org/report2018

Where Are We?

Global Number of New HIV Infections, 2000-2017 and 2020 Target



Source: UNAIDS. *Miles to Go—Closing gaps, breaking barriers, righting injustices*. July 2018. Accessible at: www.unaids.org/en/resources/documents/2018/global-aids-update.

HIV Px R&D Spectrum

Currently available

-  HIV treatment for people living with HIV
-  Oral PrEP with TDF/FTC
-  PrEP
-  Voluntary medical male circumcision
-  Male & Female Condoms
-  Syringe exchange programs

In regulatory review

-  Dapirine vaginal ring
-  Oral PrEP with F/TAF

In development: Efficacy trials Under way

-  Long-acting injectable
-  Preventive vaccines
-  Broadly neutralizing antibodies

In development: Various pre-clinical and clinical

-  Long-acting Oral PrEP
-  Preventive vaccines
-  Long-acting implants
-  Broadly neutralizing antibodies
-  Inserts
-  Patches
-  Multipurpose vaginal ring
-  Combo Oral PrEP/OC
-  Inserts
-  Enema

R&D Pipeline – Future

Upcoming efficacy trial results: The future of HIV prevention



Vaginal ring



Oral PrEP



Long-acting ARVs



Antibody



Preventive HIV vaccine

JANUARY
2020

JANUARY
2021

JANUARY
2022

JANUARY
2023

- Initial regulatory opinion in 2020; possible in market 2021
- Multipurpose ring in Ph 3 in 2022

- Efficacy trial of F/TAF in South Africa begins in 2020
- Possible dual pill to market by 2021
- Monthly pill in Ph 3 in 2021

- CAB/LA results 2022; possible to market 2023/4
- Implants into Ph2/3 in 2021 – which implant, and which active drug

- Implications of AMP results in 2020 – prompting “what next” discussions
- Combo bNAbs – but which combos? – in Ph2/3 in 2021

- ALVAC result in 2021-22; possible licensure in SA?
- Ad26 results in 2021-23; possible licensure of “global vax”?
- PrEPVacc begins enrollment in 2020
- Other strategies in development, but no clear path to Ph 3

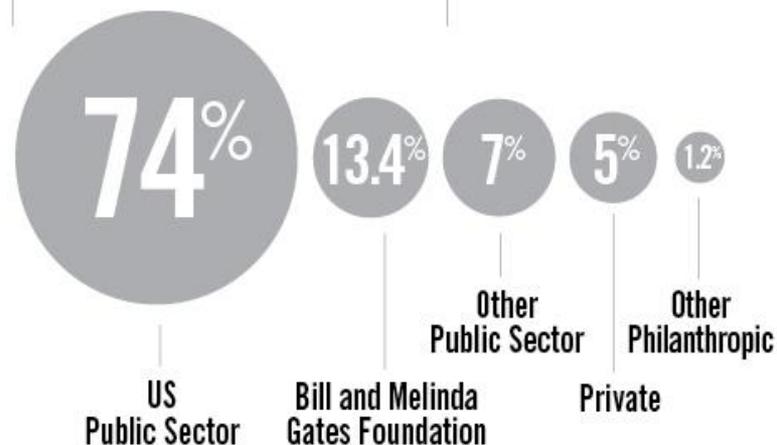
R&D Resource Tracking

Composition of the Global HIV Prevention R&D Investment Base, 2017-2018

2017

US\$1.13 billion

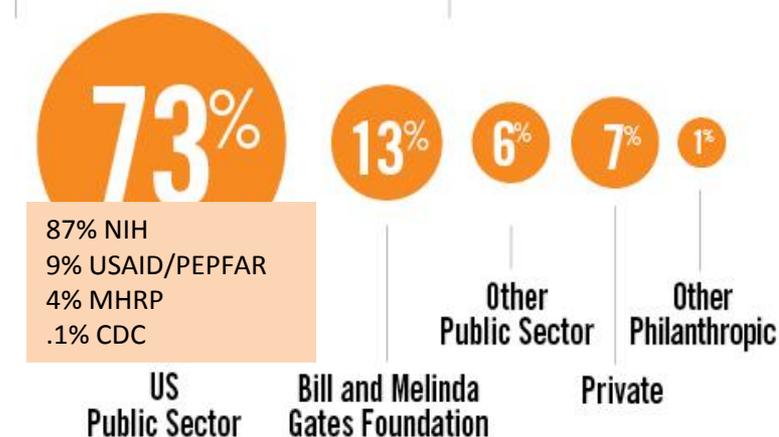
87% of total funding



2018

US\$1.14 billion

86% of total funding



* *Other Public Sector* includes funding outside the US public sector; *Other Philanthropic* includes funding outside the Bill and Melinda Gates Foundation

Product Considerations

For each product, understand and balance:

Clinical

- Biologic efficacy
- Dosing
- Reversibility
- Side effect profile
- Systemic/Topical

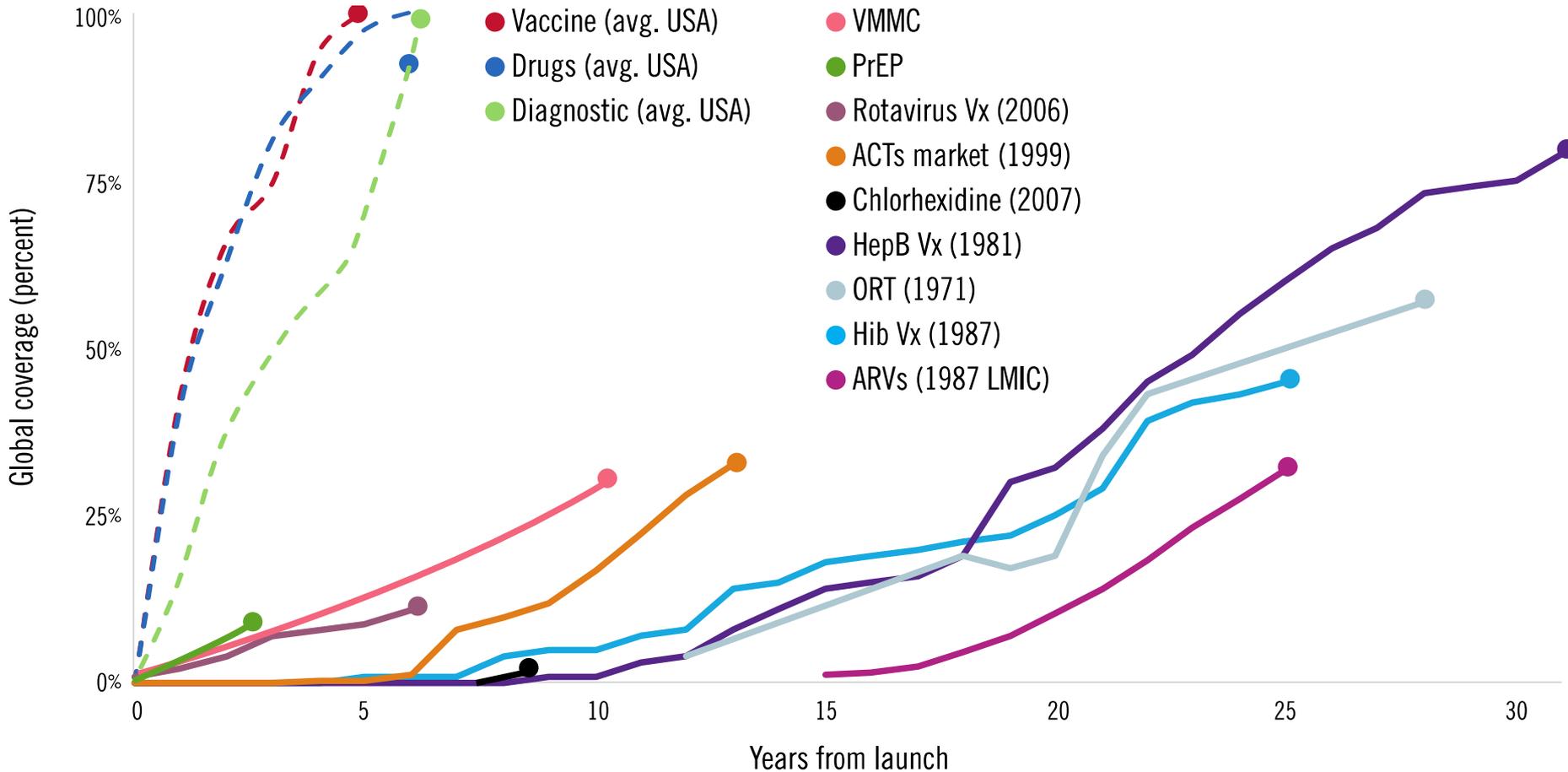
Policy & Programs

- Delivery channel(s)
- Health system burden
- Product cost
- Program cost
- Provider training

Personal

- User effectiveness
- User preference
- User burden
- Discretion of use
- Contribution to stigma

But What If It Works?



Product launch year is shown in parentheses.
 LMIC = Lower- and middle-income countries

Figure courtesy of Dana Hovig, Bill & Melinda Gates Foundation.

The Oral PrEP Experience

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



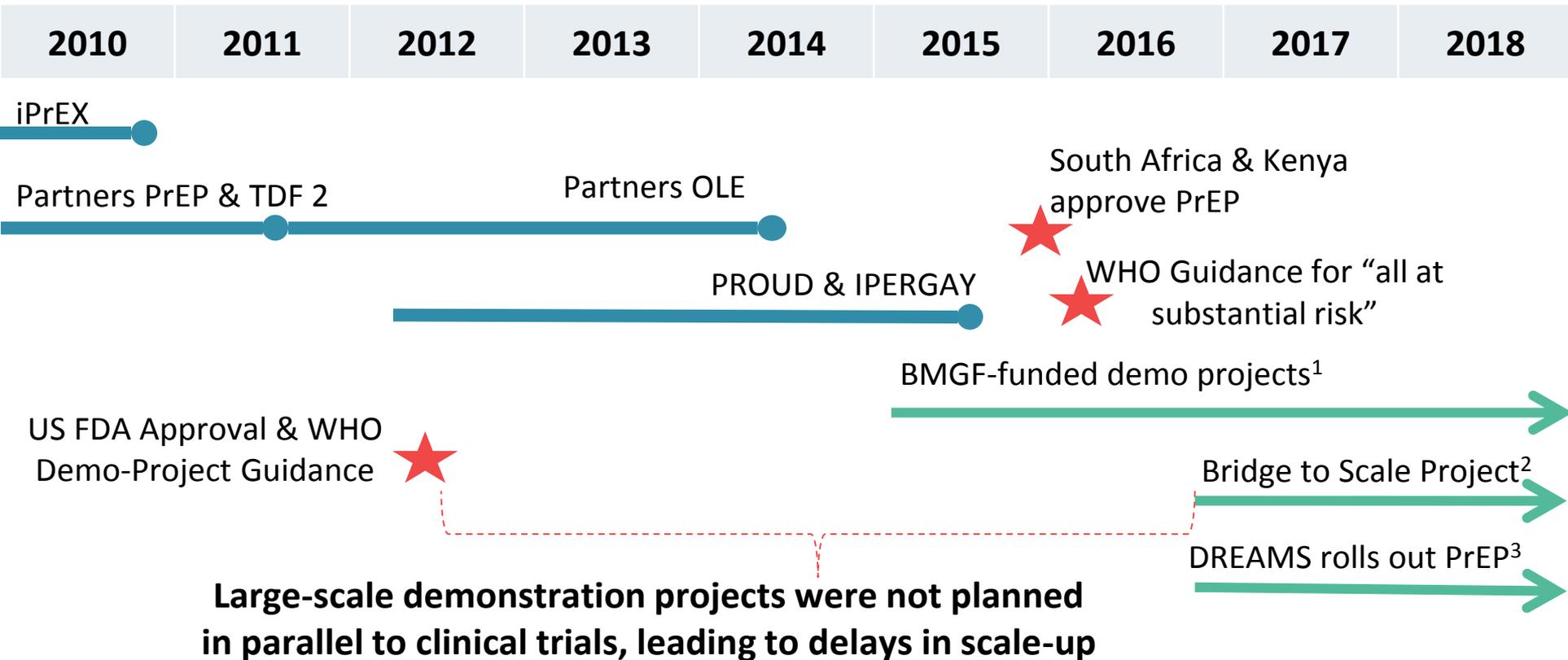
Data from research was not well timed to inform decision making at global or country level



Complex, fragmented stakeholder landscape

Poor planning can limit immediate impact of biomedical prevention options

Timing is Everything

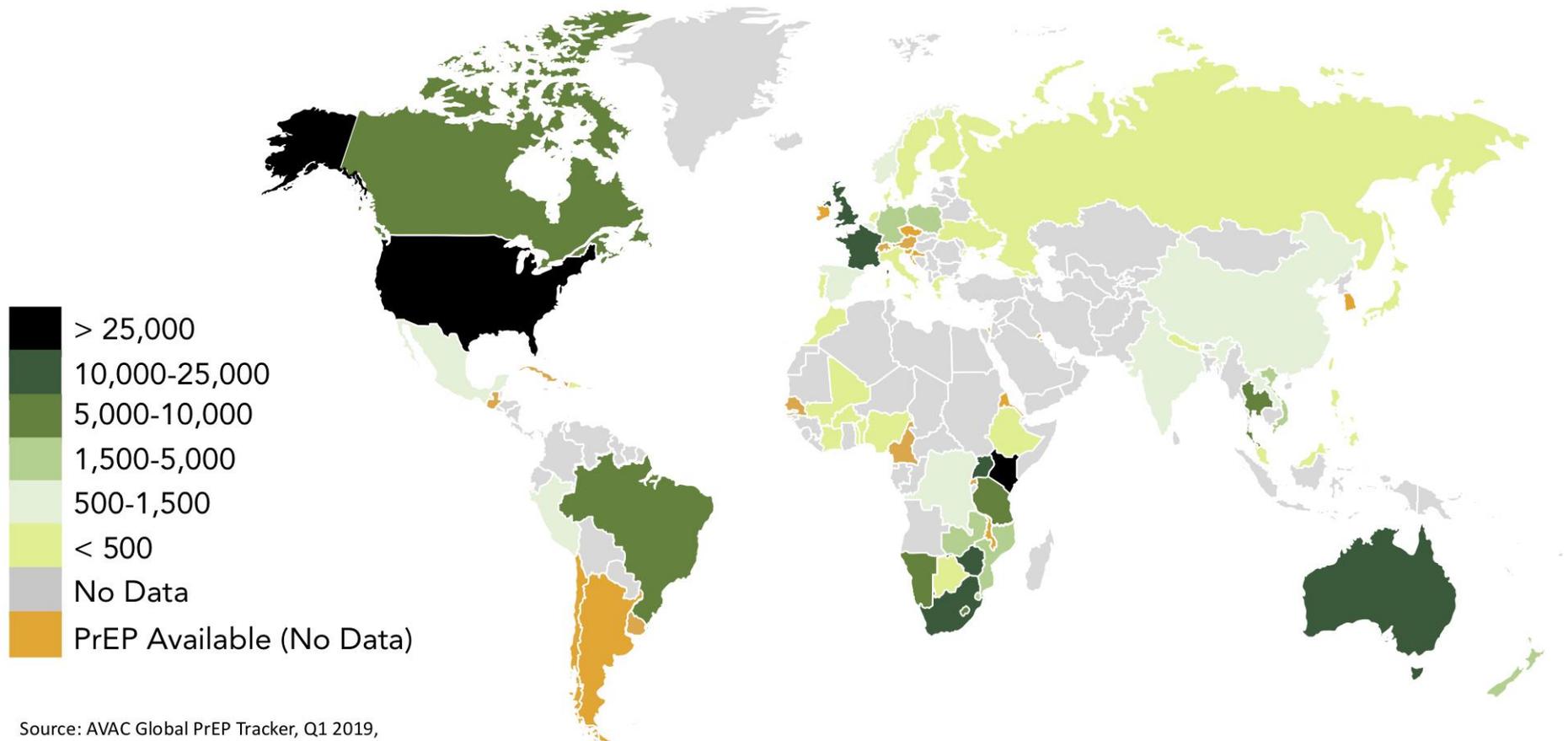


Note: NON-EXHAUSTIVE; (1) projects in Kenya, Uganda, South Africa, Senegal, Benin, India, Nigeria – enrolling an average of 1,000; (2) Bridge to Scale Implementation Project (Jilinde Project in Kenya, aiming to enroll 20,000; (3) DREAMS introduces PrEP in 5 countries

Demo projects not well timed to inform decision making after regulatory approval

Oral PrEP Initiations – 7 Years On

PrEP Initiations by Country, April 2019



Source: AVAC Global PrEP Tracker, Q1 2019,
<https://www.prepwatch.org/country-updates/>

Key Oral PrEP Takeaways

- Go big or go home – small “demo projects” with hundreds of users won’t answer key questions of normative agencies & policy makers
- Design demo projects to answer actual programmatic scale-up questions
- Work with WHO early in the process to ensure any recommendations are helpful and not creating unnecessary barriers to scale

Avoiding Historic Delays with Intro

Full impact of recent advances—including VMMC & oral PrEP—delayed by years because of limited advance planning for roll-out:

- Limited research to identify & understand potential users until after efficacy
- Lack of coordinated plans for demonstration projects – e.g., many small studies; not big or consistent enough to draw conclusions
- Few tools for country-level decision makers e.g., estimated costs or impact of investments
- Slow recognition of importance of and investments in strategic demand creation
- Can't do everything, everywhere at initial launch

Planning for Success

Three Options – One Goal – Different Approaches and Timelines

Oral PrEP

In Market

Document lessons;
build platforms for next
gen PrEP

- Multiple stakeholders; funders; programs; guidance documents; tools

Dapivirine Ring

Demonstrated safe &
effective; under
regulatory review

Rapid planning for
potential intro in
2020/1

- IPM, Janssen & OPTIONS Consortium collaborating to prepare for possible intro

Long-acting injectable
cabotegravir

Two efficacy trials
currently enrolling

Develop strategic
framework to act on
results in \pm 2021

- HIV Prevention Market Manager and our Biomedical Prevention Implementation Collaborative (BioPIC) planning in parallel with the clinical trials to coordinate stakeholders and align on shared strategy, which ensures activities are well-designed, well-timed, and well-funded to meet the needs of global and country decision-makers

The Future Experience

Collaboratively Planning For Success

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

HIV prevention product pipeline offers exciting potential to curb incidence, but achieving impact will be challenging, and we will need to plan ahead

Different Questions; Different Trials

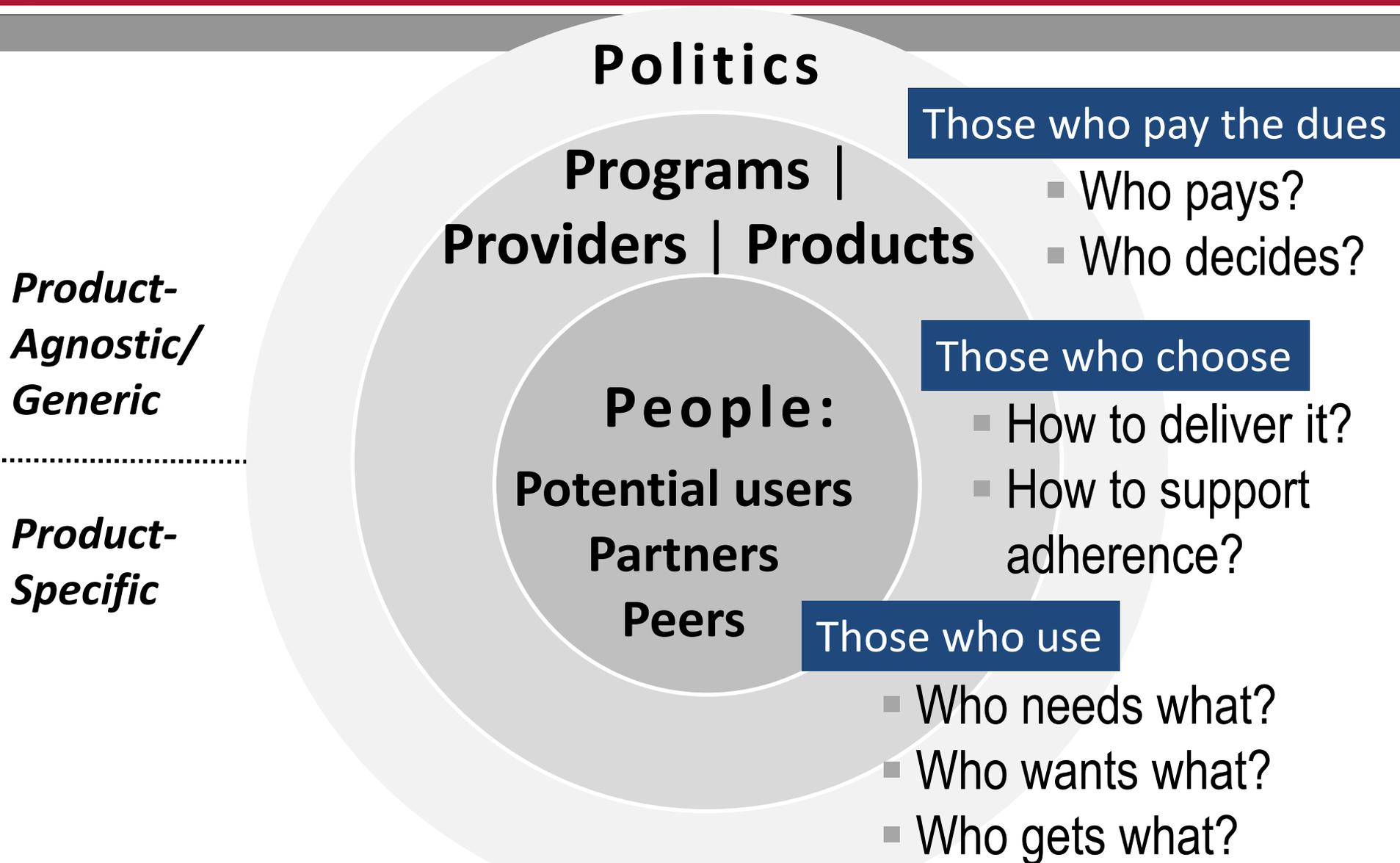
- What can the product do?
- What can providers and the health system do (or need to do)?
- What do users want – and where do they want it, how do they want, from whom do they want it?

Develop appropriate research agendas now to ask and answer key questions in all three streams simultaneously

What Next

- What have we learned from oral PrEP and end-user research?
- ...and which issues can be addressed in current efforts to improve oral PrEP programs, especially continuation rates?
- ...and which issues can be addressed with a dual pill?
- ...and which issues can be addressed with a vaginal ring?
- ...and which issues can be addressed with CAB-LA?
- ...and which issues can be addressed with next-gen px?
- ...and which issues cannot be addressed with specific px options, or are product agnostic?

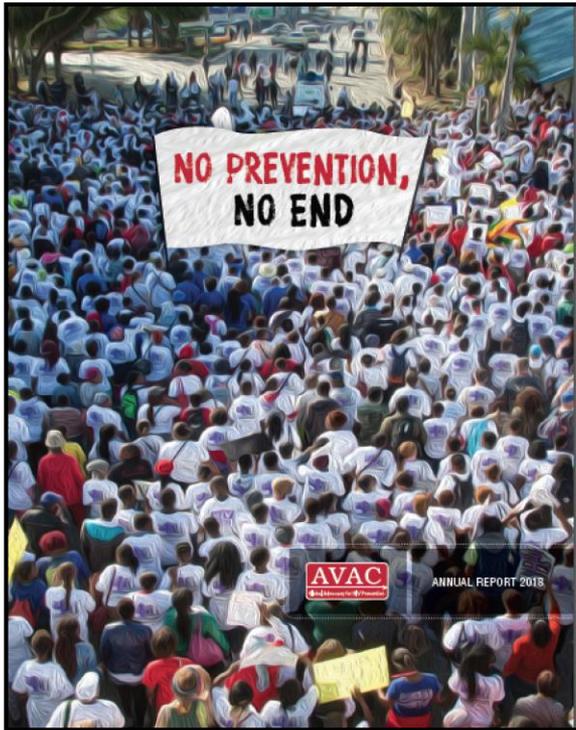
R&D, Introduction & Access



Bottomline

- Where is the greatest unmet need for prevention?
- What products will people want AND use?
- What trial designs can best answer the questions fastest and ethically?
- How will we deliver next generation prevention?
- How to best “balance our portfolio”?
- How do we keep R&D part of the “ending AIDS” narrative?

Acknowledgements



Thank you!

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

Coalition to Accelerate & Support Prevention Research (CASPR)



BILL & MELINDA
GATES foundation

HIV Prevention
Market Manager

Accelerating Product Introduction
Informing Product Development
Reducing Time to Impact



Supported by the Bill & Melinda Gates Foundation

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