Preparing for a future with a range of MPT options

Jessica Rodrigues, AVAC

JULY 31, 2022

There is a market for an oral pill MPT

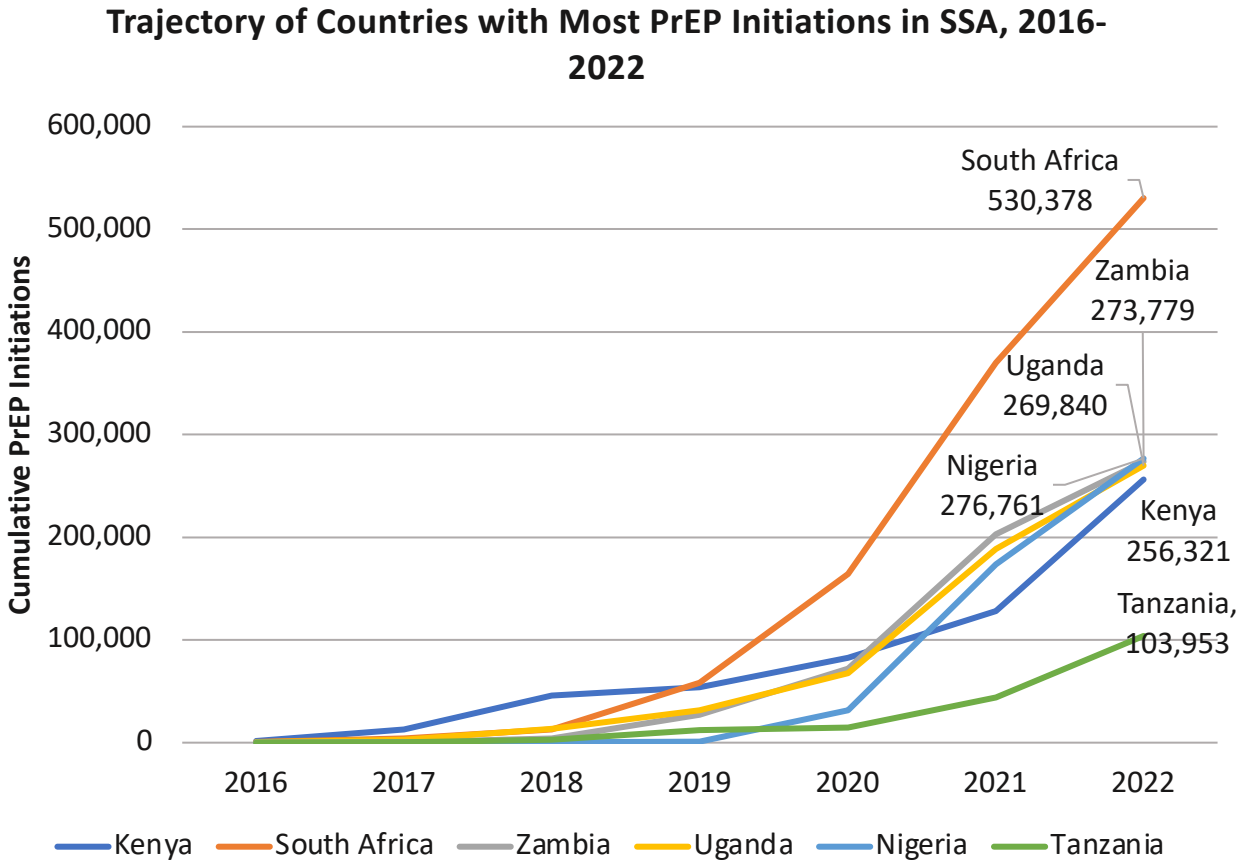
ECHO trial underscored the potential benefit of an MPT given high rates of HIV incidence among women using various forms of contraception

OC use has been stable over time in East and Southern Africa (ESA), even as LARC use increased; with high use in the US and globally

Oral PrEP uptake has grown rapidly in sub-Saharan Africa (SSA), especially from 2020-2022 **reaching almost 3 million new users**

Evidence that **women (and their partners)** prefer a user-controlled product that addressed **multiple health needs** with some preferring short-acting methods

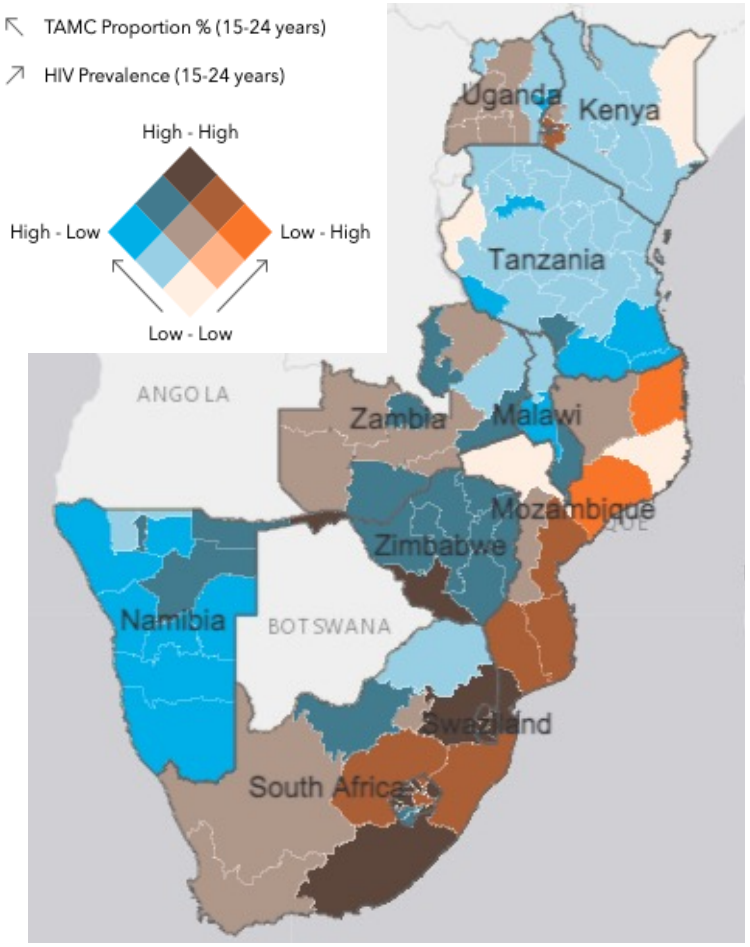
The Dual Prevention Pill (DPP) is an additional option and will be offered to women in the context of **informed choice** alongside other available contraceptive methods



FP2030 Data Dashboard; AVAC, Global PrEP Tracker, https://data.prepwatch.org/

MPTs could help address unmet prevention needs

HIV prevalence and total addressable market for contraception (TAMC) data show substantial overlap of unmet need for FP and HIV prevention, indicating high potential for MPTs



Kenya has relatively lower need, though regional pockets show promise for MPTs and DPP, given higher OC use, % non-FP users.

South Africa has moderate-to-high need for FP and HIV prevention, with certain provinces exhibiting higher % OC use.

Zimbabwe has high OC use and HIV prevalence rates across the country, with higher overlap in the Matabeleland South province.

iMPT, MPT Target Population Identification Mapping Tool, https://theimpt.org/mpt-target-population-identification-mapping-tool/.

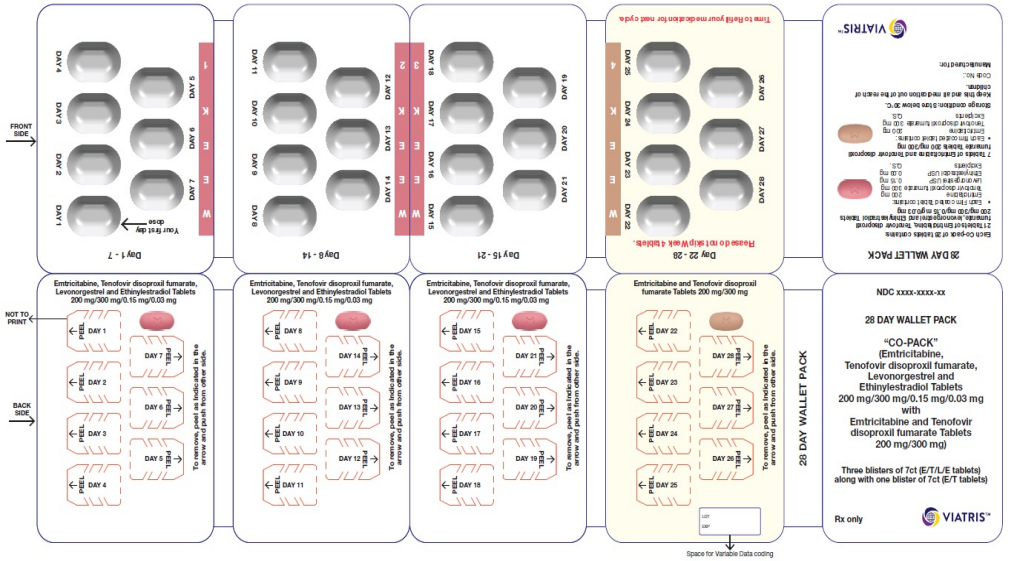
The DPP is the MPT furthest along in the pipeline

- Viatris developing **co-formulated tablet with 28-day regimen** (TDF/FTC, oral PrEP + LNG/EE, combined oral contraception (COC))
- **Different color pills** for 21 vs. 7 days (dark pink and light peach, respectively)
- **Packaging will be wallet pack** with tear-off weekly sheets with instructions on them
- Pill color, packaging, brand names **validated with women**
- **Branding/secondary packaging** will have women's lifestyle feel
- Longer term, Population Council/Medicines360 to **develop F/TAF-based DPP**

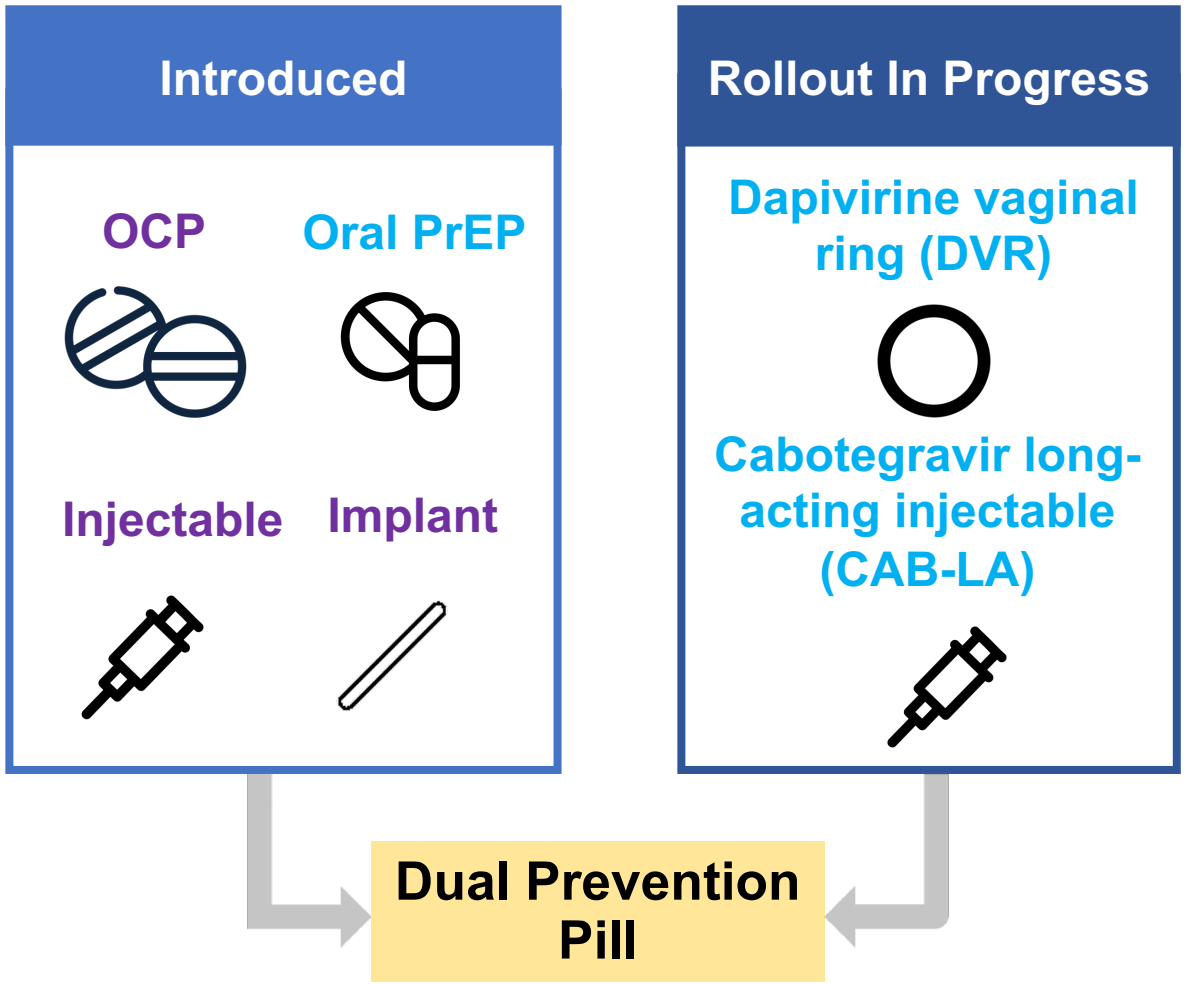
Viatris plans to file for regulatory approval with US Food & Drug Administration in early 2024

Figure 1: Proposed DPP tablet colors

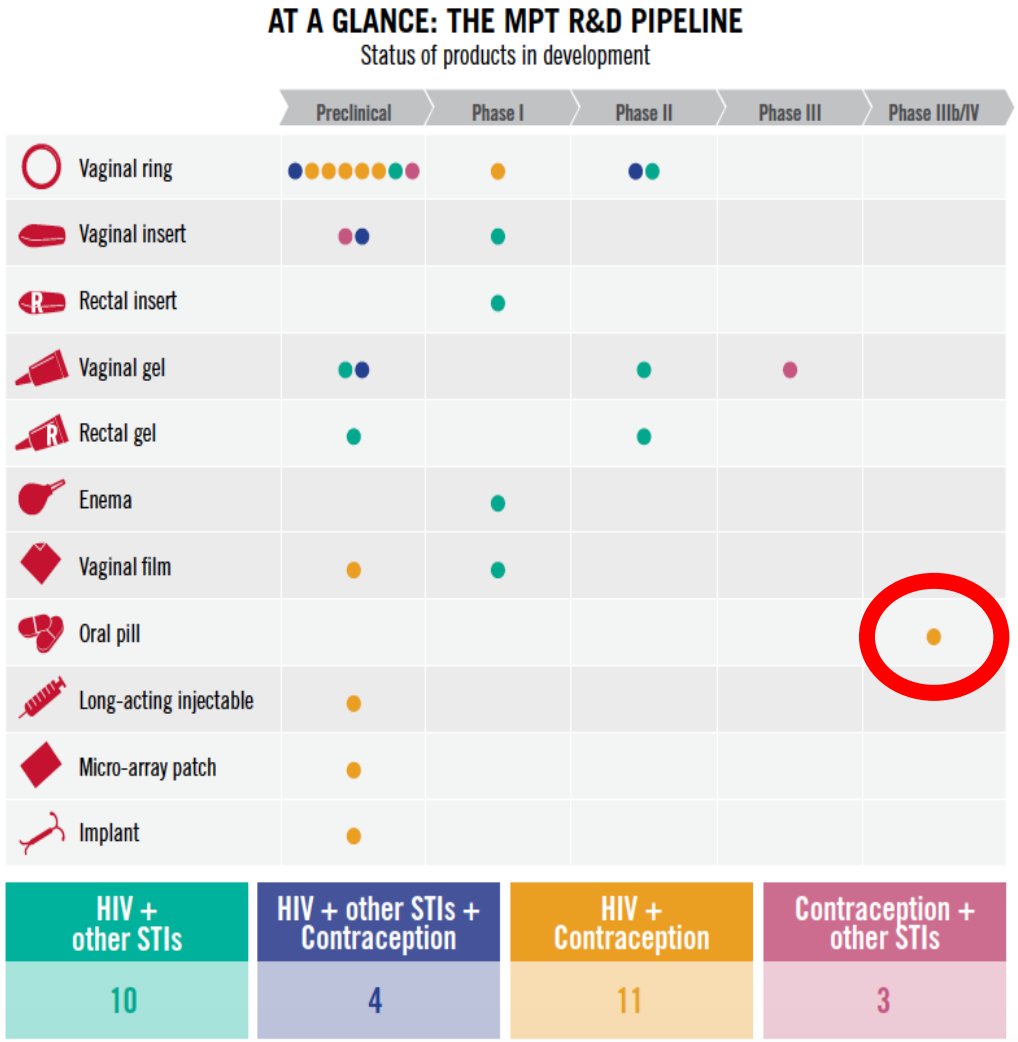
Figure 2: Illustrative mock-up of DPP packaging by Viatris



The DPP is poised to be the first MPT to reach the market since the condom



Key: Contraception HIV prevention



AVAC, Advocates' Guide to Multipurpose Prevention Technologies (Mar. 2021)

The DPP can generate lessons for future MPTs

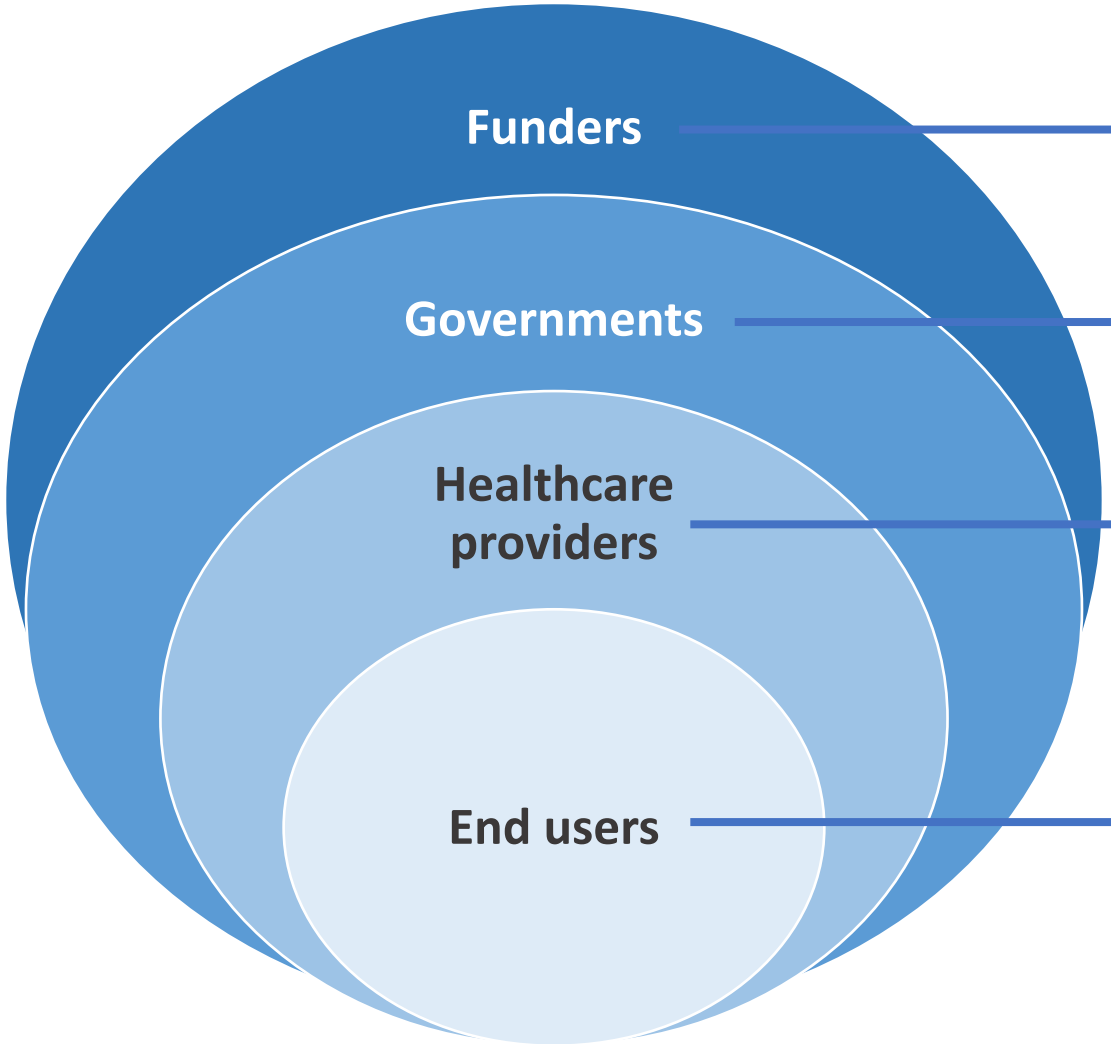
Future MPTs are likely to build on the **health system adaptations, regulatory, delivery and financing** lessons generated from DPP introduction and scale-up

Funding **HIV and SRH innovations** would benefit other MPTs in the pipeline. Investment in the DPP could **signal to governments that MPTs are a priority**

Foster integration of HIV prevention and sexual and reproductive health (SRH) services to deliver a dual-indication product

A **user-controlled, co-formulated pill supports convenience** and may motivate increased knowledge, use and adherence. Women and couples prefer a dual-purpose product, even as an oral formulation

Key questions we will address to deliver the DPP and MPTs



*How will **MPTs be funded** amid a shrinking funding envelope for HIV prevention and SRHR?*

*How can **integration of HIV/FP programs** be strengthened?*

*How can **providers be supported** to deliver the DPP/MPTs?*

*How can **end users be reached** with information on and supported to use the DPP/MPTs?*

Demand, delivery and data for decision-making: How market preparation for the DPP is reimagining prevention programs for a future with MPTs

Title	Presenter	Time
Introduction: Preparing for a future with a range of MPT options	Jessica Rodrigues, AVAC (co-chair)	17:45 10 min
Who is most likely to use the DPP and how might we engage them effectively? Using HCD research to design demand generation and marketing plans for the DPP	Wawira Nyagah, AVAC	17:55 15 min
How can providers counsel on the DPP as a novel, combined product? Recommendations and process for reconciling oral PrEP and COC counseling guidance	Dr. Lisa B. Haddad, Population Council	18:10 15 min
Cost-effectiveness of the DPP for HIV and contraception across different populations in Western Kenya and South Africa	Dr. Anna Bershteyn, NYU Grossman School of Medicine	18:25 15 min
How can planning for the DPP help build platforms for future MPTs? Integrating HIV and FP programs to accelerate delivery of new MPTs with proven approaches	Dr. Nyaradzo Mavis Mgodi, University of Zimbabwe (panel moderator/co-chair)	18:40 30 min
Key takeaways: Ingredients for the successful rollout of MPTs	Jessica Rodrigues, AVAC (co-chair)	19:10 5 min

Who is most likely to use the DPP and how might we engage them effectively?

Using HCD research to design demand generation and marketing plans for the DPP

Wawira Nyagah, AVAC

JULY 31, 2022

The approach

- Ethnographic approach: **repeated immersion sessions to build trust** with participants provided opportunity to **unlock deep audience insights** – broader values and identities, as well as how influence works among partners, friends, family

- **Holistic view of our audience**, rather than a sexual and reproductive health (SRH) lens. Understanding existing times and places where conversations about sex/relationships take place provides an **opportunity to increase share of mind**

- Fieldwork in **3 key markets**: Kenya, South Africa and Zimbabwe. Opportunity to generate insights in Kenya (not part of initial HCD research or acceptability studies), fill evidence gaps in South Africa and Zimbabwe

Need vs. early adoption

- In East and Southern Africa, where the DPP is initially planned for introduction, **65% of new HIV infections** in adults are amongst women aged 15 and over[1]
- **16% of women of reproductive age** have unmet need for contraception[2]

HOWEVER

- DPP early adopters most likely to be current OCP and/or PrEP users[3, 4]
- OCP market much larger than the PrEP market – although PrEP usage continues to grow[5, 6]
- OCP users skew urban, older, married and wealthier. Those with an unmet need for family planning tend to be younger and less wealthy[5]

Mismatch between early adopters vs those with greatest need potential.
Consider launching to early adopters while making sure campaign is relevant to those with unmet FP need when distribution grows.

[1] UNAIDS, 2021; [2] UNFPA, 2021; [3] Shapley-Quinn et al., 2019; [4] Weinrib et al., 2018; [5] DHS 2014, 2015, 2016; [6] AVAC, Global PrEP Tracker, data.prepwatch.org

Motivators and barriers

- **Receptive to DPP, concerned about associations with HIV**; less stigma with OCP but many go to great lengths to conceal its use
- **Big life-stage and mindset shifts** (e.g., living situation, relationship, becoming a mother) likely trigger her adoption of DPP
- DPP brings greater **choice and empowerment**, which may conflict with some of the gender roles women adopt
- Might be at risk of receiving 'backlash' from male partner if he discovers she is taking DPP in secret; however, she could **find a champion in her partner if he is involved and educated on DPP and its benefits**

Emerging DPP personas

- Representation of similar data and insights about potential DPP users' **behaviors, attitudes, goals and pain points** – and ideally have a human face, with a name and biographical information
- Based on **qualitative research**
- **Ongoing analysis** to build on:
  - Differences between countries and urban vs rural
  - Integration of media data on influencers and channels
  - Final mapping/prioritisation of most likely users for the DPP, and high-potential category entry points

Enjoyment outside marriage

Early 30s, started using PrEP after beginning an affair with another man

Likelihood to accept DPP

Attributes

- Relationship goals
- Family values
- Caring for children
- Religious values
- Social status/respectability
- Career goals
- Enjoyment

Maintain relationship

Early 20s, started using OCP after boyfriend refused to wear a condom

Likelihood to accept DPP

Attributes

- Relationship goals
- Family values
- Caring for children
- Religious values
- Social status/respectability
- Career goals
- Enjoyment

Single but exploring

Early 20s, urban, started using OCP after leaving home and starting to date

Likelihood to accept DPP

Attributes

- Relationship goals
- Family values
- Caring for children
- Religious values
- Social status/respectability
- Career goals
- Enjoyment

Unfaithful partner

Started using PrEP when she suspected her husband had been unfaithful

Likelihood to accept DPP

Attributes

- Relationship goals
- Family values
- Caring for children
- Religious values
- Social status/respectability
- Career goals
- Enjoyment

New mother

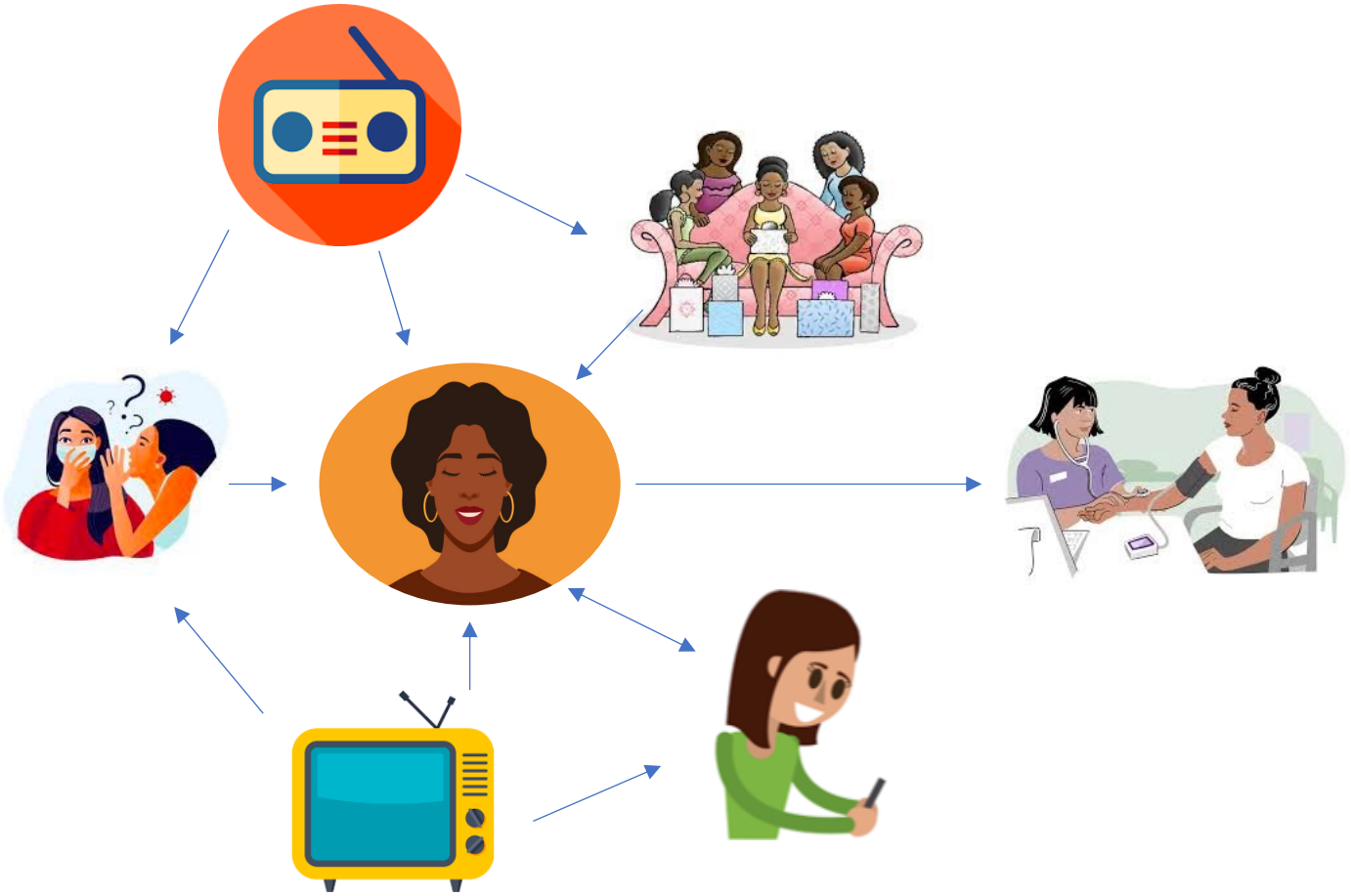
Married, new mother, started using OCP after birth, wants to delay next pregnancy

Likelihood to accept DPP

Attributes

- Relationship goals
- Family values
- Caring for children
- Religious values
- Social status/respectability
- Career goals
- Enjoyment

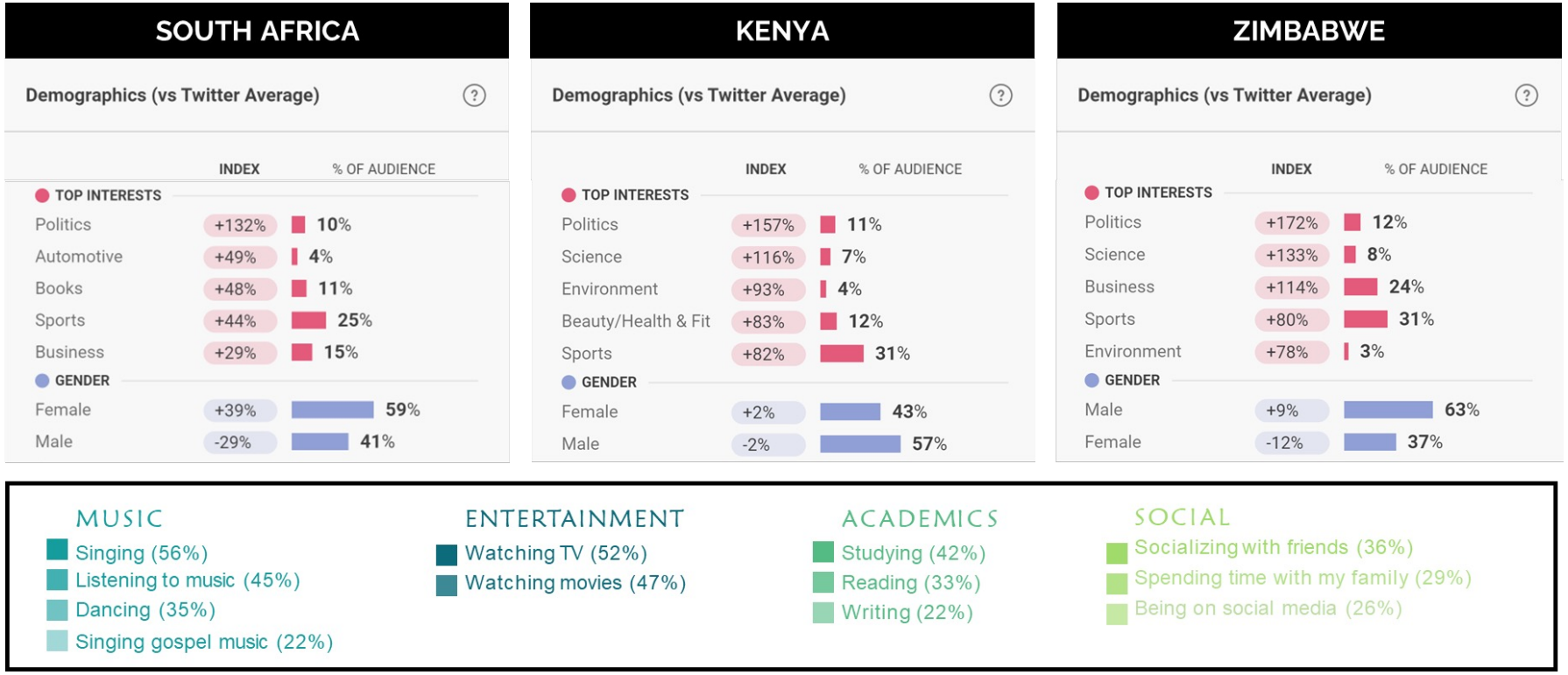
Information comes from multiple and complex sources



- **Sisters/aunties** and **close friends** inspire the greatest trust
- **Healthcare workers** (HCWs) verify/dispel myths and misinformation

‘Birth control’ communications compete for share of mind

Healthcare represents a tiny part of what our audience is thinking about. To increase share of mind, there is **opportunity to connect the DPP to broader interests** such as entertainment, spending time with friends.



Source: Brandwatch: Interests of those searching 'birth control' online; Example of key interests cited by FSW in Kenya

Communications have shifted from risk to empowerment framing

There has been a **significant shift in communications** for OCP/PrEP from risk-based motivations, towards more positive motivations such as empowerment, relationship building and choice.

How might these insights shape the demand generation strategy for the DPP?

Duality

Connect dual pill with dual benefits to women's dual identity. Position as brand which helps women navigate two sides of their lives: the empowered and the traditional. Dial up different parts of this identity for different audiences/channels.

Discretion

Position brand as supportive auntie/friend who helps women find empowerment in secret, while keeping up the appearance of respectability. Messengers will speak like a trusted friend and provide channels for anonymous discussion.

Preparedness

Tap into the feeling of confidence, savviness/ hustle and being on top of things, which women associate with OCP/ PrEP users. Explore being ready in relation to protecting the life women want to live vs protecting against the behaviours of others.

Enjoyment

Position as brand that's fun to engage with, speaks to motivations of enjoyment, pleasure, companionship. Make brand present in the moments – and with the people – that women feel this, e.g. women's meet-ups, bridal showers, entertainment, music.

How can providers counsel on the DPP as a novel, combined product?

Recommendations and process for reconciling oral PrEP and COC counseling guidance

Dr. Lisa B. Haddad, Population Council

JULY 31, 2022

Why address provider counseling for the DPP now?

The Problem

Providers will need training and support to help women decide if the DPP is right for them and properly counsel on instructions for use, which will be critical to foster confidence to start and stay on it

Integrated counseling for FP and HIV prevention not uniformly performed, but will be needed for the DPP and future MPTs

The Solution

Lessons learned from COC/oral PrEP can be consolidated now to inform counseling for the DPP and tested in acceptability studies

Sub-group formed to develop counseling recommendations, comprised of 8 HIV and FP experts with clinical and implementation backgrounds

Naming our assumptions

What the recommendations are and are not

- Recommendations for DPP counseling guidance **based on COC/PrEP guidance**, as product is not yet available for use
- Intended for counseling **after a woman has selected the DPP** as a prevention method
- Presumes **informed choice/voluntarism and range of methods available** were already discussed with client
- Presumes client is **eligible for the DPP** (e.g., received negative HIV test)
- Focused on counseling messages that are **DPP-specific**

Methodology to develop DPP counseling recommendations

1. **Map and categorize counseling messages** from OC/oral PrEP guidance, as well as relevant training materials and tools
2. **Identify for each topic where guidance overlaps and differs** between OC/oral PrEP and core elements to emphasize in DPP counseling
3. **Prioritize topics based on information available;** uptake, missed pills, side effects, discontinuation/switching, drug interactions, monitoring selected
4. **Consult additional evidence and experts to answer outstanding questions**, and develop recommendations for DPP counseling guidance
5. **Share recommendations** with Population Council and study teams to inform DPP acceptability studies in South Africa, Zimbabwe and HPTN 104 study protocol

Identified points of overlap/divergence to zero in on remaining questions

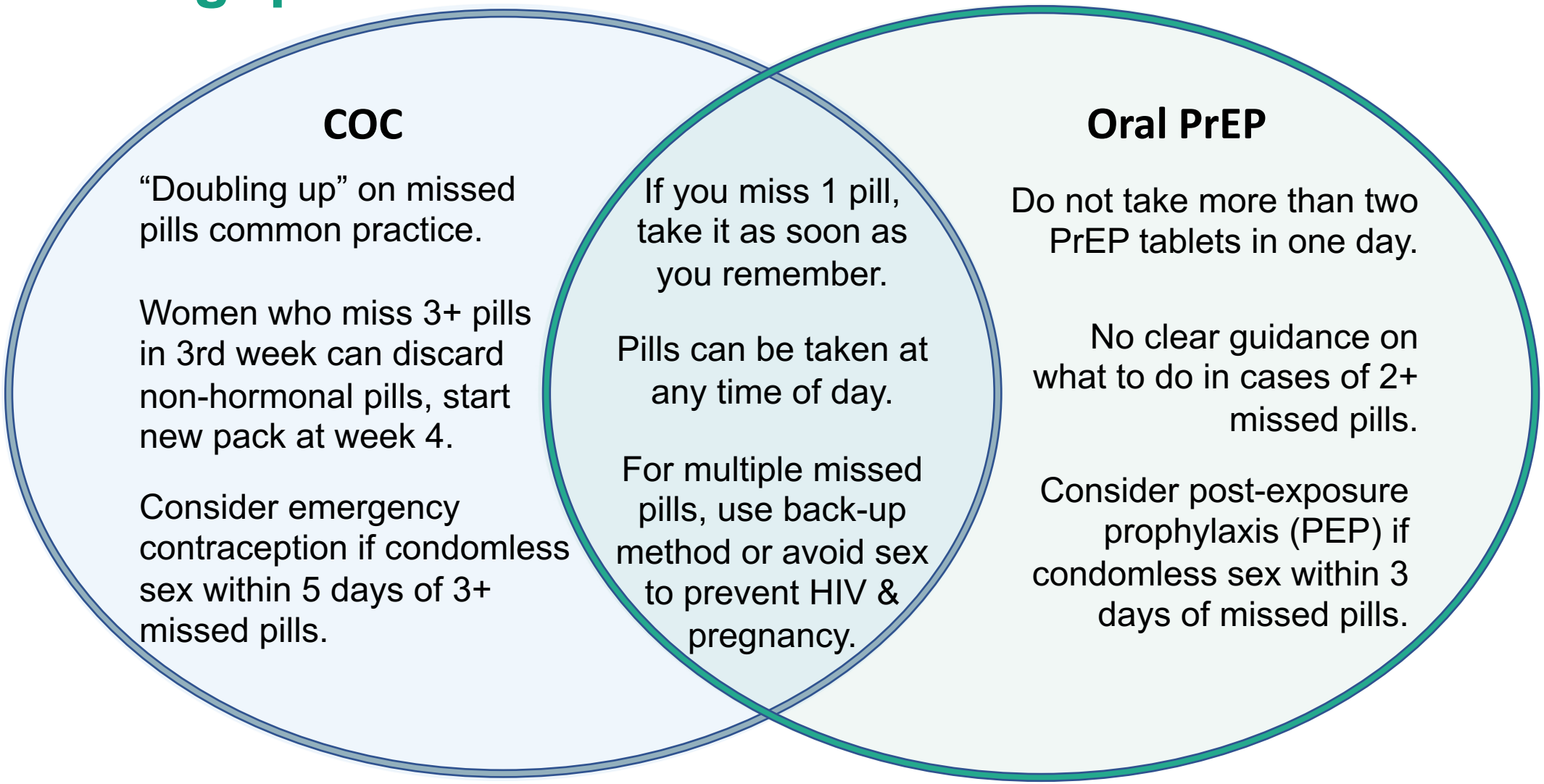
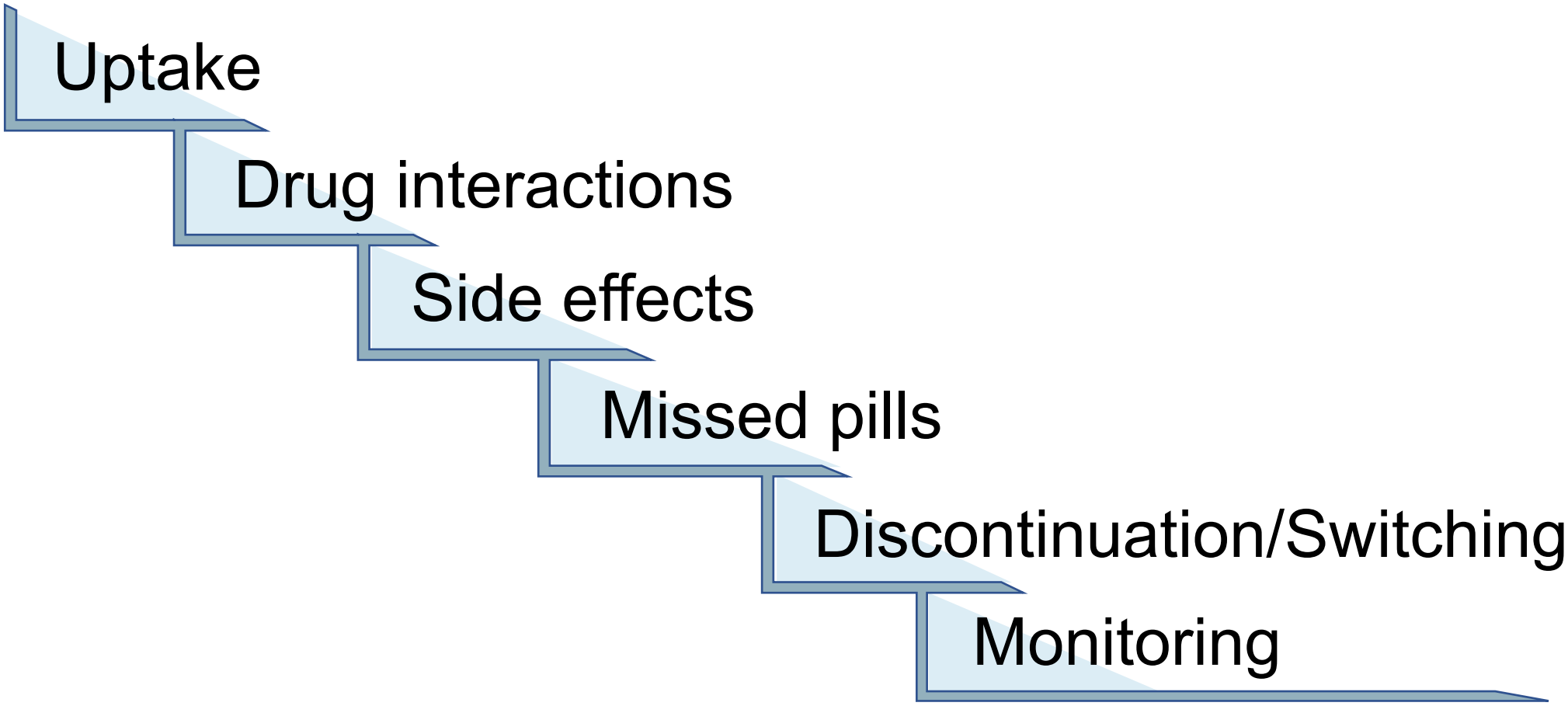


Figure 1: Illustrative example of missed pills guidance

Narrowed down priority counseling topics based on group consensus

Focused on what was important to understand for studies



Some topics were more complex than others

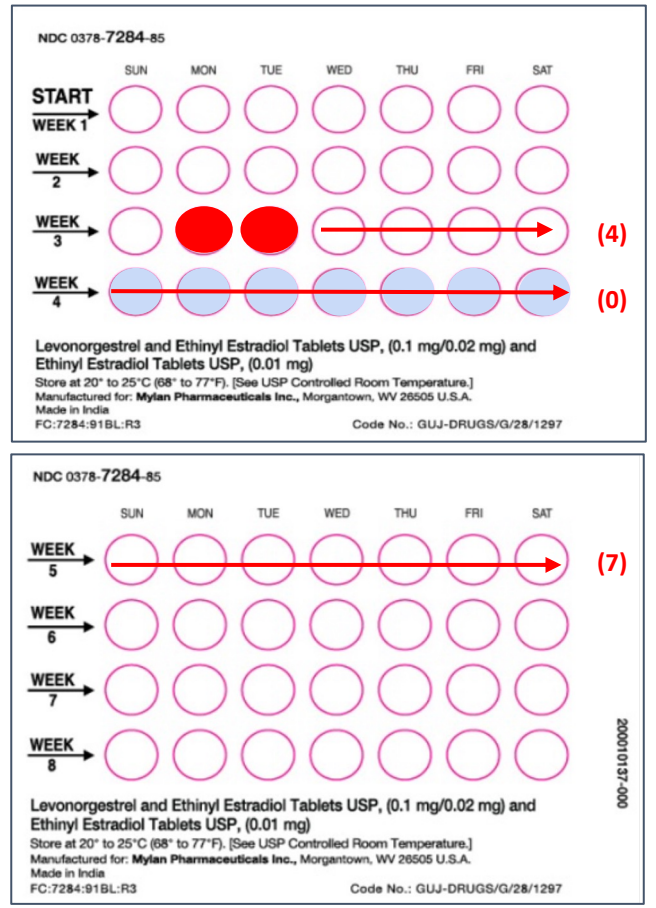
Missed pills posed unique challenges

- Depending on quantity and timing of missed COC pills, recouping pregnancy protection **can require use of a back-up method for up to 3 weeks** (Figure 2).

- To reduce user burden, DPP users may consider skipping week 4 (i.e., monthly bleeding) to recover pregnancy protection more quickly. However, week 4 of the DPP contains oral PrEP and thus **there are supply and cost implications of tossing DPP packs early**.

- While doubling up on missed COC pills is common practice, WHO permits “occasional” doubling-up on oral PrEP. There is **limited published evidence on toxicity of multiple PrEP doses in cisgender women**.

Figure 2: Considerations for DPP counseling recommendations on missed pills

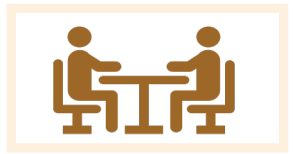


To resolve outstanding questions, we consulted experts and literature

Sub-group on provider counseling for the DPP met monthly to discuss available information and formulate recommendations

Conducted additional desk research beyond guidance and training tools on specific topics/questions

Solicited early input and guidance from DPP Consortium partners and Advisory Board, who are knowledgeable about DPP



Consulted external experts on specific topics/questions

Presented preliminary results to Wits RHI, implementing partner for DPP acceptability study in South Africa

Each topic involved important considerations relevant for counseling

Uptake

- Aligning time to reach protective levels of both DPP components (oral PrEP + COC)
- Ensuring daily dosing

Discontinuation/Switching

- Managing risk of HIV and unintended pregnancy when discontinuing/switching to another HIV prevention and/or contraceptive method

Drug interactions

- Differing contraindications for COC/PrEP

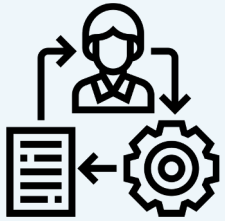
Side effects

- Determining which side effects are common vs. serious
- Typical time to resolution of side effects
- Potential changes to monthly bleeding

Monitoring

- Balancing monitoring recommendations with need and user burden, particularly for PrEP-naive users, who will be new to HIV testing requirements

Reflections for replicating process of reconciling oral PrEP/COC counseling guidance for MPTs



PROCESS

- **Important to have HIV and FP perspectives**, both clinical and implementation experts, involved
- **Share working versions** of counseling messages with trusted group of reviewers on a regular basis for iterative feedback and to access to outside expertise

COUNSELING MESSAGES

- **Balance** clinical and implementation implications (e.g., cost) of both products
- **Consider user burden**, desire and ability to use the method correctly and consistently
- **Consider provider burden**, including workload and comfort with counseling on a new method
- **Evaluate** what is safe and clinically-responsible to recommend vs. standard “real-world” practice

Acknowledgments

DPP Provider Counseling Sub-group members

- Dr. Lisa Haddad, Population Council
- Dr. Eva Lathrop, PSI
- Dr. Karin Hatzold, PSI
- Dr. Sanjay Hadigal, Viatris
- Andy Carmone, CNM, MSN, MPH, CHAI
- Meridith Mikulich, CNM, RN, USAID
- Jennifer Mason, USAID
- Chris Jones, Mann Global Health
- Danielle Harris, Catalyst Global (coordinator)
- Kate Segal, AVAC (coordinator)

Experts consulted

- DPP Consortium
- DPP Advisory Board
- Dr. Nyaradzo Mgodi, University of Zimbabwe-Clinical Trials Research Centre
- Dr. Mackenzie Cottrell, University of North Carolina
- Dr. Julie Dumond, University of North Carolina
- Wits RHI acceptability study team

Cost-Effectiveness of the Dual Prevention Pill (DPP) for HIV and Contraception Across Different Populations in Western Kenya and South Africa

Anna Bershteyn, PhD
Assistant Professor of Population Health
New York University Grossman School of Medicine
Anna.Bershteyn@nyulangone.org

IAS 2022 Satellite Session: Demand, delivery, and data for decision-making

July 31, 2022

NYU Grossman School of Medicine
Department of Population Health

CLINTON HEALTH ACCESS INITIATIVE

Motivation for cost-effectiveness modeling of the dual prevention pill (DPP)

- Health systems in sub-Saharan Africa face severe resource constraints
  - Introducing new interventions often requires re-allocating funding from alternative options
  - Interventions are beneficial only if they provide more health per $ spent than alternative options
- Cost-effectiveness analysis is used to estimate health benefits per $ spent
- Cost-effectiveness depends on:
  - Costs (commodities, delivery, overhead, impact on other costs)
  - Health impact (effectiveness, taking into account adherence)
  - The risk profile of the population, including how it changes over time (disease dynamics)
- Disease modeling is an important tool for cost-effectiveness analysis
  - Forecasts disease dynamics
  - Enables comparison of costs and population health with and without the technology
  - Results can be compared to benchmarks for cost-effectiveness of alternative options

Goal: Compare multiple DPP launch populations

Demographics

- Primary analysis: Women ages 25-49
- Additional analyses:
  - Adolescent girls and young women ages 15-24
  - Female sex workers
  - Women with HIV-positive partners (serodiscordant couples)

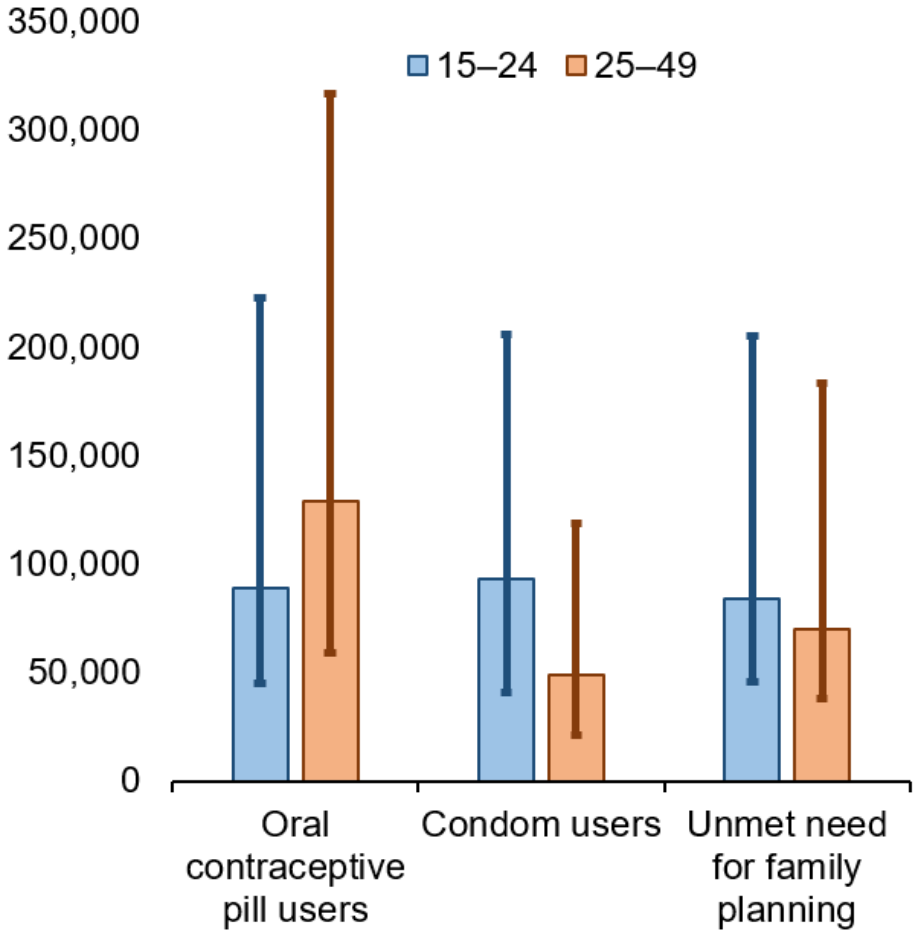
Family planning use

- Primary analysis: oral contraceptive pill (OCP) users
- Additional analyses:
  - Condom users
  - Women with unmet need for contraception

PrEP use

- Primary analysis: women not using PrEP
- Additional analyses:
  - PrEP users
  - Women receiving FP and PrEP in integrated delivery settings

Estimated DPP demand by age and method*



* Adapted from: Begg L, Brodsky R, Friedland B, et al. *BMJ Sexual & Reproductive Health* 2021;47:166-172.

Goal: Compare multiple DPP launch countries

Countries

- Primary analysis:
  - Nyanza region of Kenya
- Additional analyses:
  - South Africa
  - Zimbabwe

HIV epidemic control

- Primary analysis:
  - “95-95-95” achieved by 2030
- Additional analyses:
  - “95-95-95” achieved by 2025

Countries modeled for DPP launch selected by stakeholders based on:

- High need
- Potential demand
- Enabling policy and regulatory environments

Goal: Compare multiple outcomes

Primary outcome: incremental cost-effectiveness ratio (ICER) = incremental costs / health impact

- Numerator: Net cost = DPP cost – avoided OCP and/or PrEP cost – avoided ART cost due to averted infections
- Denominator: Disability-adjusted life-years (DALYs) averted due to HIV & pregnancy prevention

Additional outcomes:

- HIV infections averted
- Pregnancies averted

Timeframe for outcomes

- Primary analysis: 30 years, 3% annual discounting
- Additional analyses: 20 to 40 years, 0% to 6% annual discounting

Assumptions: Pregnancy and maternal mortality rates

Assumption	Value
Annual pregnancy rate among women with unmet need for contraception	35%
Percent of unintended pregnancies ending in abortions	31%
Percent of abortions resulting in mortality	0.185%
Maternal mortality rate	0.362%
Reduction in pregnancy rate with OCP	90%
Reduction in pregnancy rate with male condom	75.5%

Sources: Singh et al., *Pop and Dev Rev* 2017, https://onlinelibrary.wiley.com/doi/10.1111/padr.12027 Polis et al., Polis et al. https://www.guttmacher.org/report/contraceptive-failure-rates-in-developing-world https://thepalladiumgroup.com/news/Improving-Data-to-Save-Maternal-and-Newborn-Lives-in-Kenya

Assumptions: Annualized total healthcare costs for different products

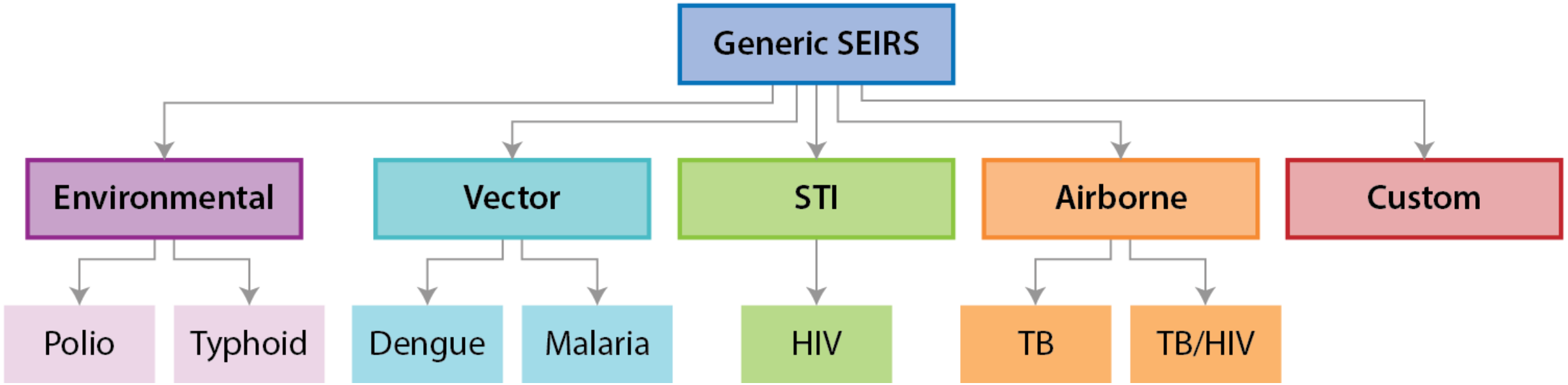
Annualized total costs, 2021 USD (inclusive of delivery costs)	**DPP***	**PrEP**	**OCP***	**Male condom**	**ART**
First year of use, 2025-2027	$202.35	$176.88	$12.49	$2.38	$251.39
Subsequent years of use, 2025-2027	$181.67	$156.20**			
First year of use, 2028+	$181.50	$171.29			
Subsequent years of use, 2028+	$160.82	$150.61**			

* Accounts for wastage due to choosing to skip menstruation or consecutive missed pills (which necessitate starting a new monthly pack)

**Assumes PrEP drug cost will decline by same proportion as DPP drug cost. Without this assumption, DPP would become less expensive than PrEP in 2028.

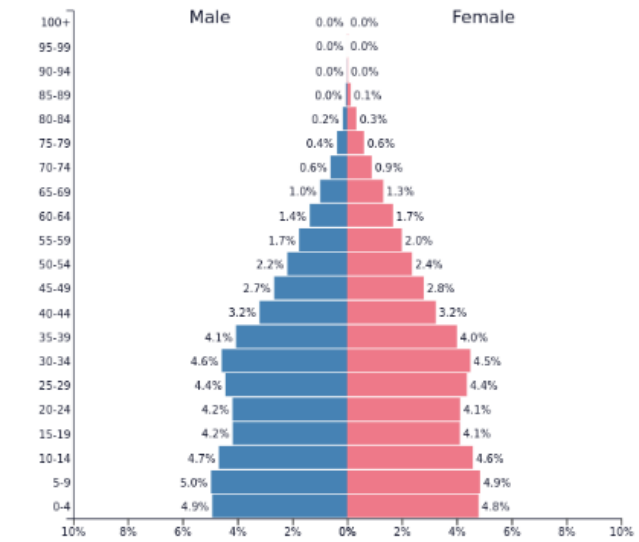
Model: Epidemiological MODeling (EMOD) disease modeling framework

- Agent-based epidemiological modeling framework
- Developed and maintained by Institute for Disease Modeling (part of BMGF)
- Built into a larger codebase, EMOD, which supports several disease types
- Model source code available: https://github.com/InstituteforDiseaseModeling/EMOD
- Documentation & user guide available: https://docs.idmod.org/projects/emod-hiv/en/latest/index.html

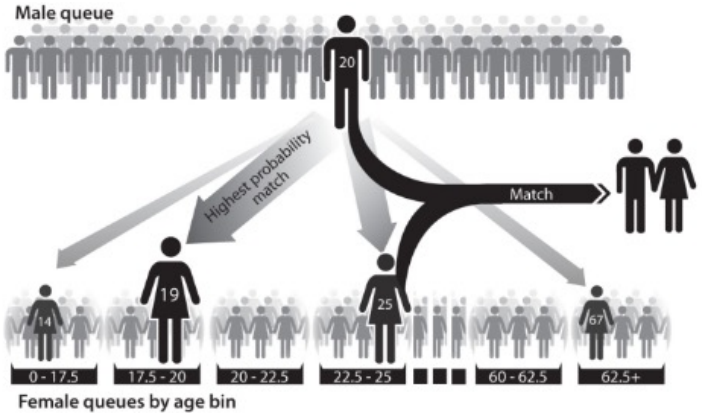


Model: Key components of EMOD-HIV

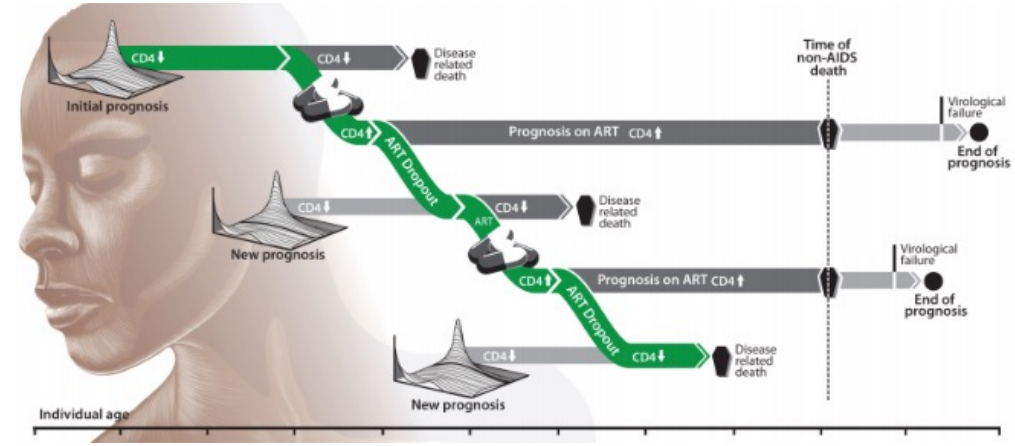
Demographics (fertility, non-HIV mortality)



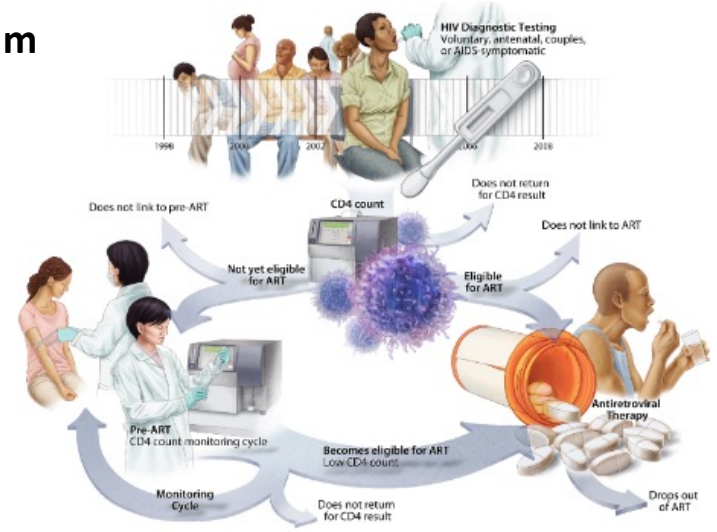
Transmission network (sexual, mother-to-child) & HIV prevention interventions



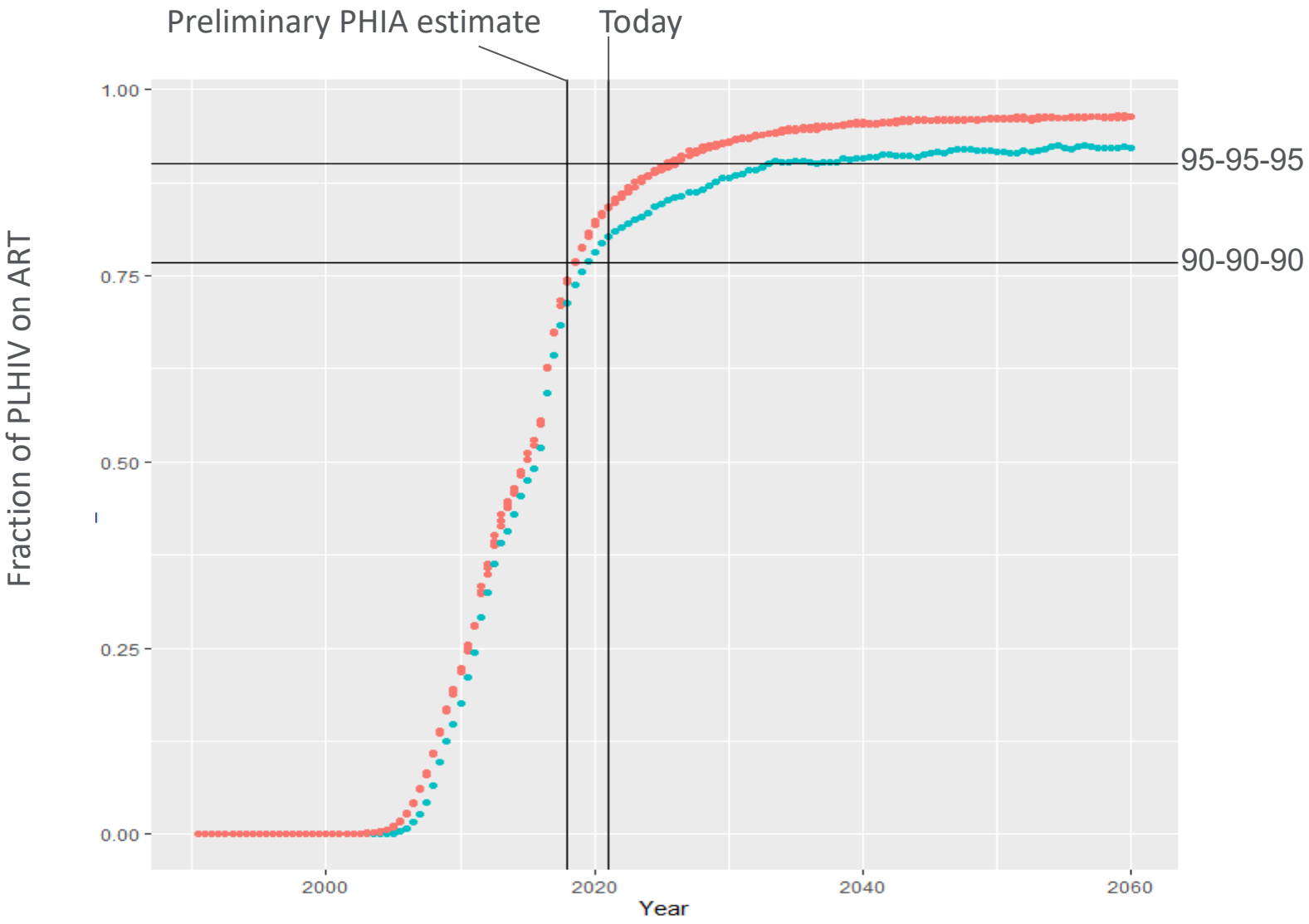
HIV disease progression & HIV treatment



Care continuum



Model: Assumptions about ART coverage (Nyanza, Kenya)

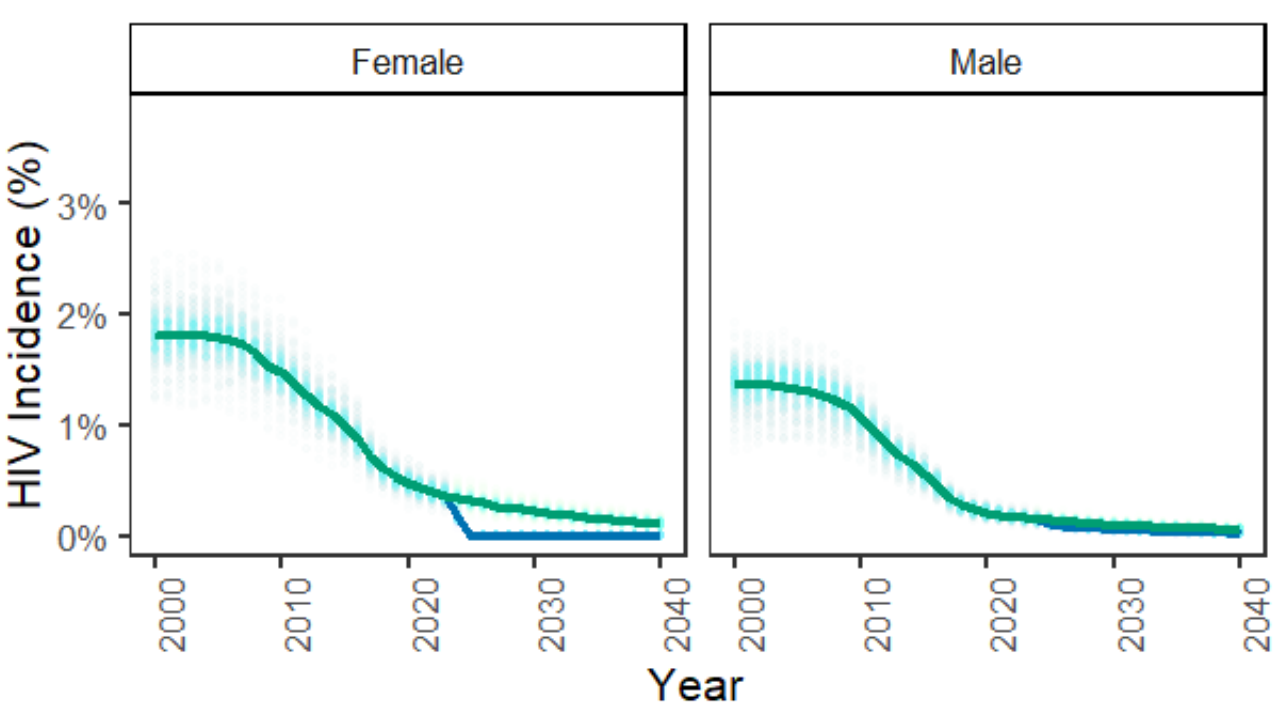


Primary analysis: "95-95-95" achieved by 2030

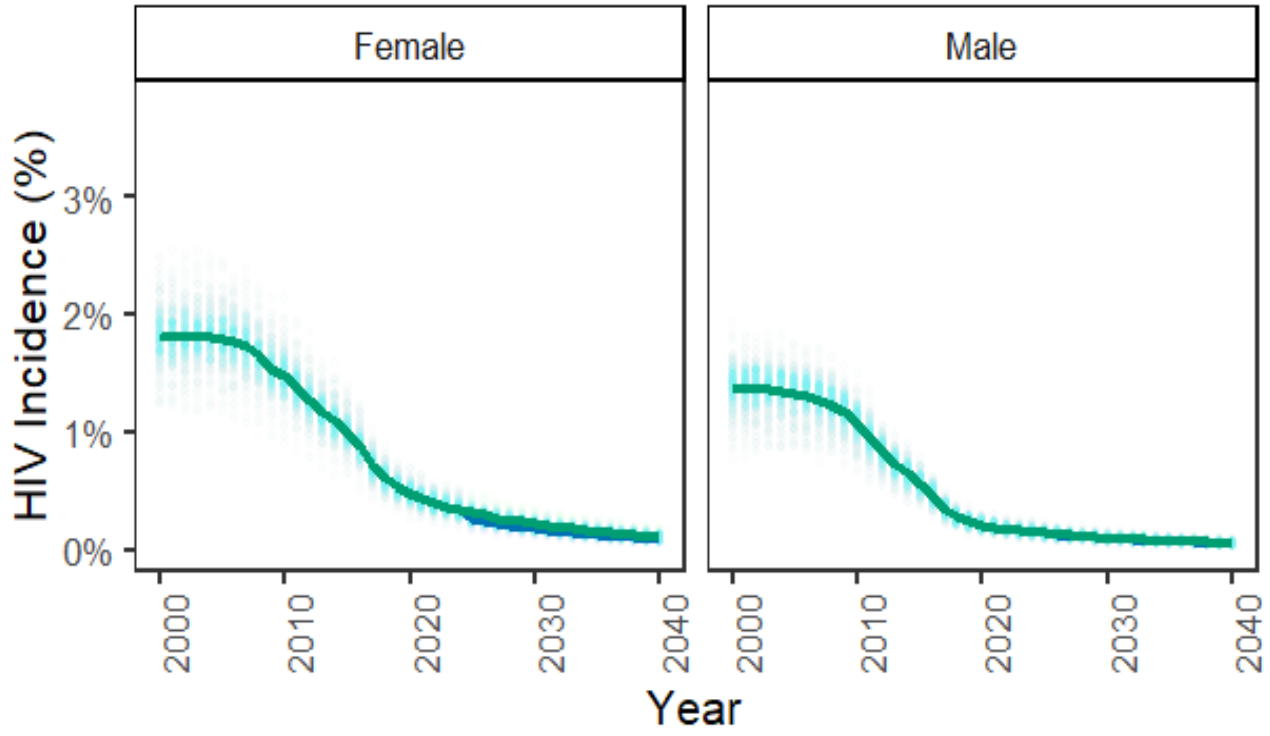
Additional analysis: "95-95-95" achieved by 2025

Results: DPP incorporated into EMOD-HIV model

Sanity check: 100% DPP use with perfect adherence and efficacy → zero incidence

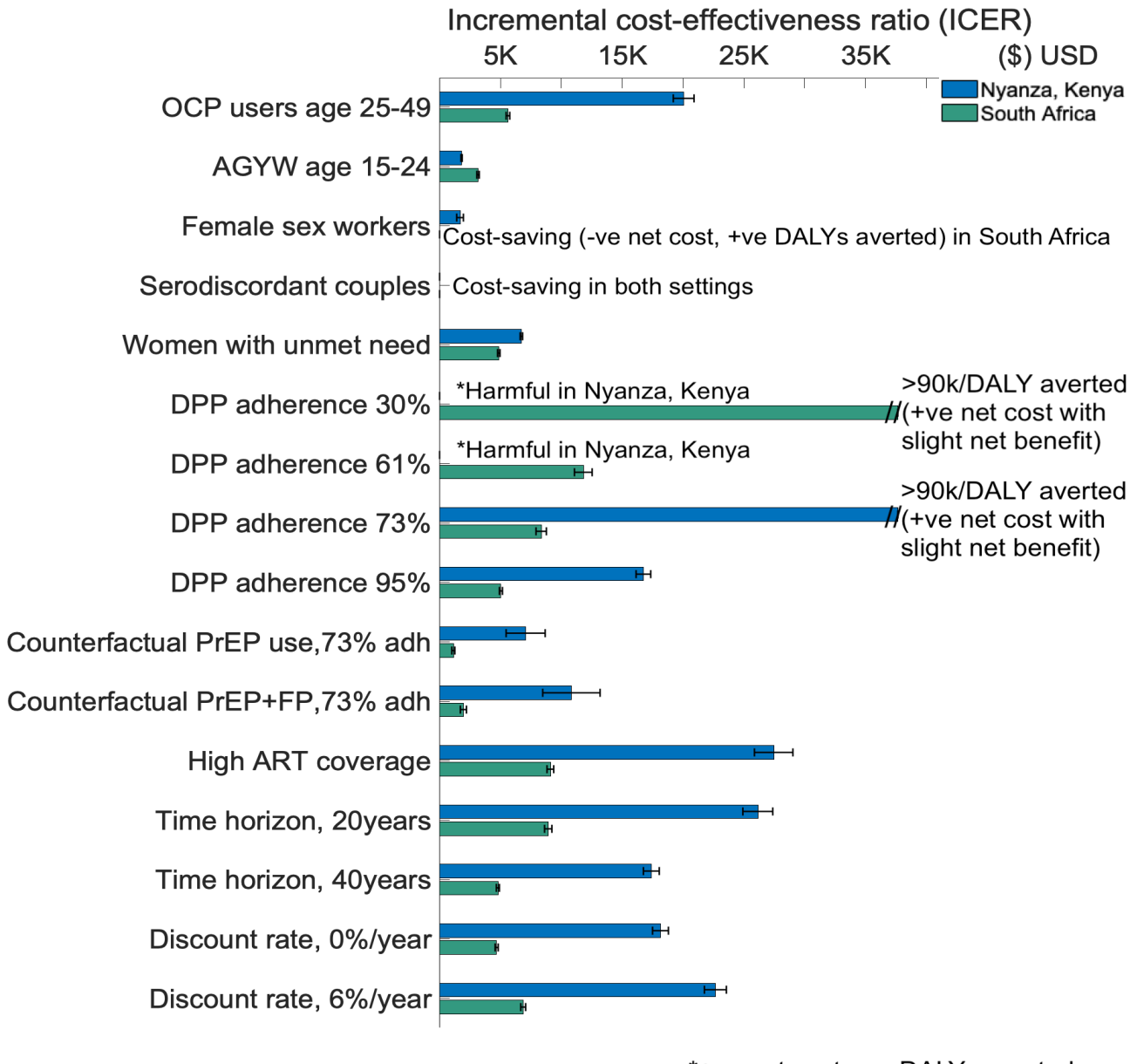


Primary analysis: Meet demand for DPP among OCP users ages 25-49



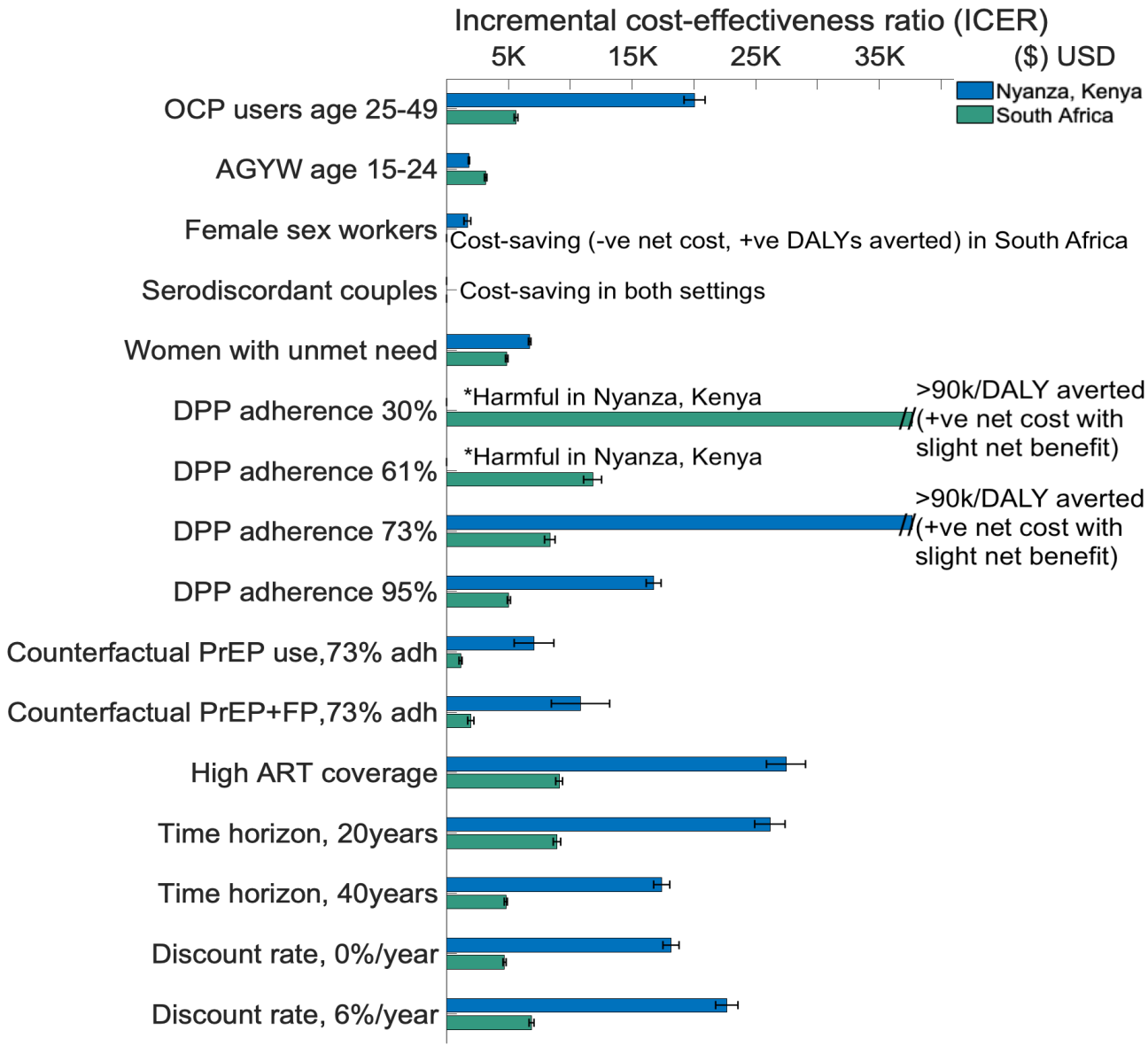
Results: Cost-effectiveness

- The DPP is <u>unlikely</u> to be cost-effective in OCP users ages 25-49 (population with highest demand)
- The DPP is <u>more likely</u> to be cost-effective in settings and populations with higher HIV incidence
- DPP is <u>likely to be cost-saving</u> in serodiscordant couples and female sex workers currently using OCP or with unmet need for contraception.
- The DPP <u>could be net harmful</u> if it reduces adherence among current OCP users.



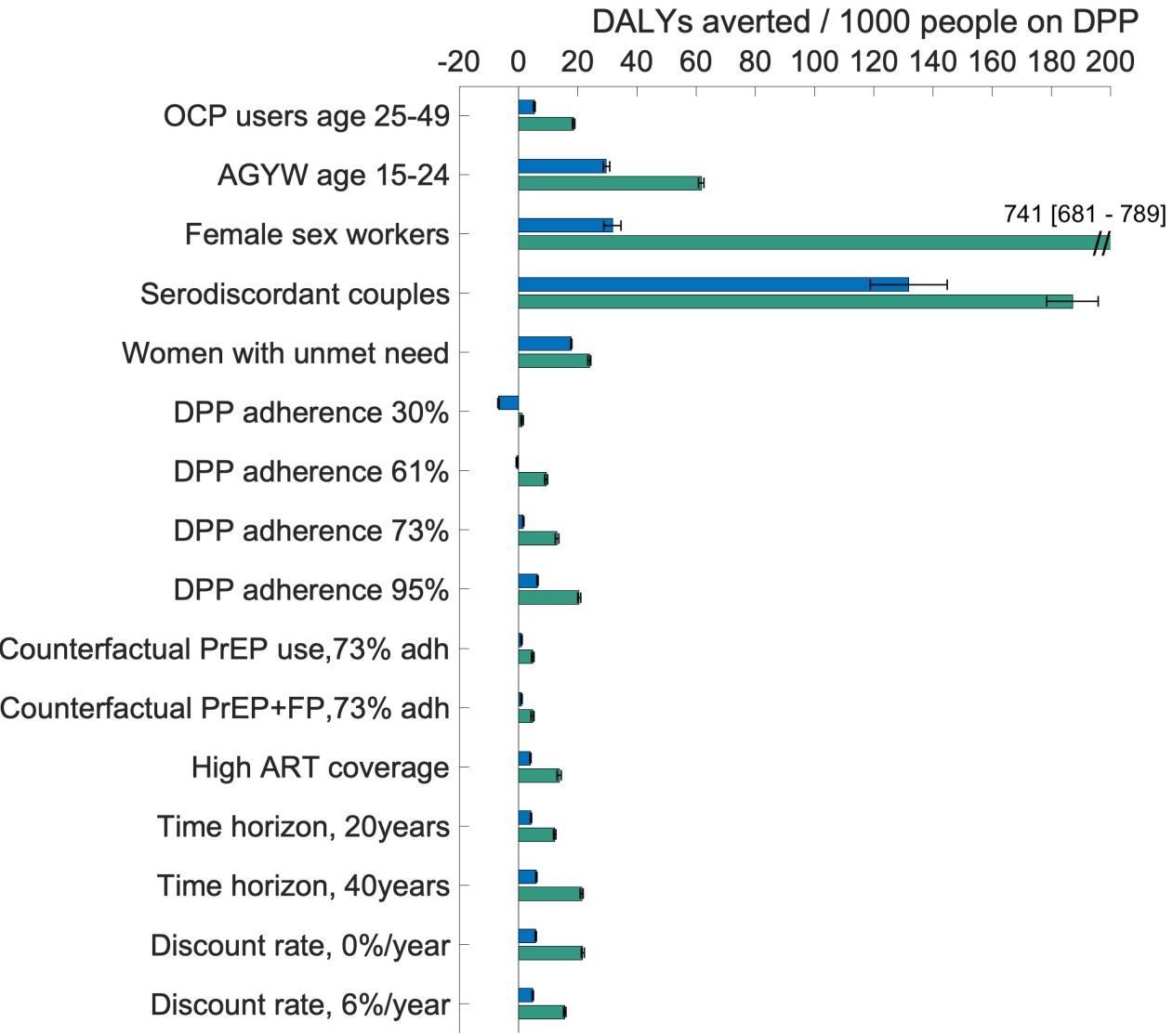
Results: Cost-effectiveness (cont'd)

- The DPP is more likely to be cost-effective for current oral PrEP users.
  - DPP could be cost-effective if it substantially increased PrEP adherence compared to separate PrEP & OCP pills.
  - Compared to separate PrEP & family planning services, incremental cost to deliver DPP is relatively small
  - Compared to integrated PrEP and family planning services, incremental cost of DPP is higher (no cost-savings from integration)
- Results were robust to:
  - HIV treatment scale-up
  - time horizon of analysis
  - economic discount rate

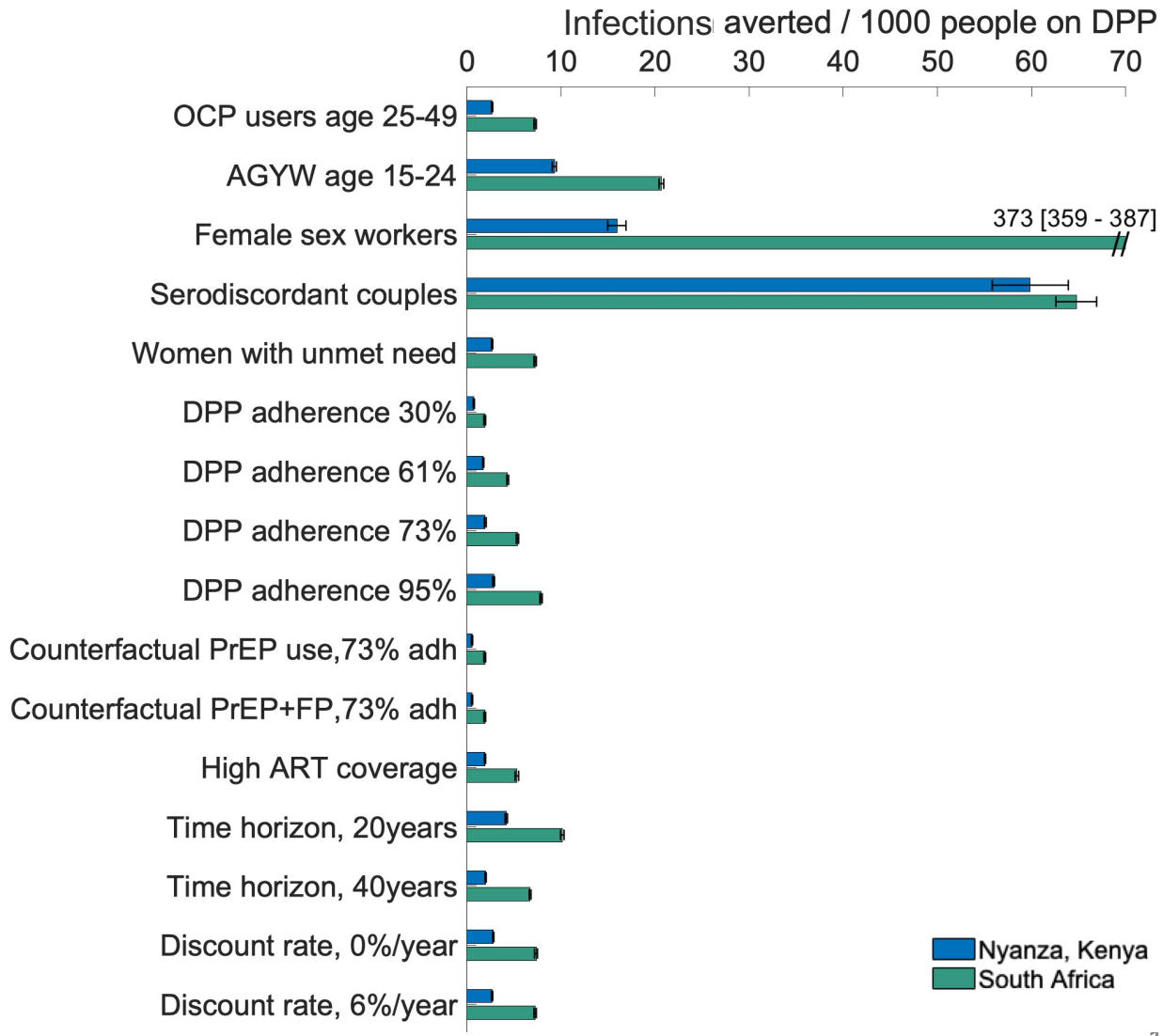


Results: Additional outcomes

Disability-adjusted life-years (DALYs) averted



HIV infections averted



Discussion: Key takeaways

For current oral contraceptive users: DPP may not be a cost-effective alternative to OCP in most populations, given declining HIV incidence and relatively high adherence to OCP.

For current PrEP users: The DPP may be cost-effective as an alternative to oral PrEP use with low adherence, assuming adherence on the DPP increases.

For people at high risk of HIV: The DPP is more likely to be cost-effective in populations & settings with higher HIV incidence. It may be cost-saving among female sex workers and serodiscordant couples.

Need for Effective Counseling: The DPP could be net-harmful if it reduces adherence among OCP users. Careful monitoring, appropriate messaging, and effective counseling strategies will be needed to support informed choice and effective use among potential users.

Discussion: Limitations

- Modeling did not comprehensively account for burdens related to unintended pregnancy:
  - Did not account for healthcare costs due to unintended pregnancy
    - Abortion costs, prenatal care costs, labor & delivery costs
  - Did not account for burdens of unintended pregnancy other than maternal mortality or abortion-related mortality
    - Unintended pregnancy has significant implications for women's health, well-being, and economic status
    - Unintended pregnancy is associated with ~ 40-60% increase neonatal and child mortality [1]
  - Did not account for ~2-3x increased risk of HIV acquisition during pregnancy [2]

- Modeling did not consider possible user self-selection to use DPP while at higher HIV risk:
  - PrEP users may self-select for having HIV-positive partners, multiple partners, condomless sex
  - Self-selection for PrEP use generally increases cost-effectiveness [3]
  - Self-selection with DPP may be different due simultaneous role as a contraceptive → need for further studies

Sources: [1] Cleland J, Conde-Agudelo A, Peterson H, Ross J, Tsui A. "Contraception and health." *Lancet* 380(9837), 149-156, 2012. [2] Thomson KA, Hughes J, et al. "Increased Risk of HIV Acquisition Among Women Throughout Pregnancy and During the Postpartum Period: A Prospective Per-Coital-Act Analysis Among Women With HIV-Infected Partners, *JID* 218(1), 16–25, 2018. [3] Phillips AN, Bershteyn A, et al. "Cost-effectiveness of easy-access, risk-informed oral pre-exposure prophylaxis in HIV epidemics in sub-Saharan Africa: a modelling study." *Lancet HIV 9*(5), e353-e362, 2012.

Acknowledgements

NYU Grossman School of Medicine

Masabho Milali

David Kaftan

Hae-Young Kim

Daniel Citron

Ingrida Platais

High Performance Computing Core

Clinton Health Access Initiative

Jenny Campbell

Sarah Jenkins

Danny Edwards

Dani Resar

Institute for Disease Modeling

Daniel Bridenbecker

Clark Kirkman

Philip Welkhoff, PhD

Daniel Klein, PhD

Adam Akullian, PhD

Christopher Lorton

DPP Consortium members