Improving the Quality of PrEP Implementation for Adolescent Girls and Young Women in Eastern and Southern Africa

A Regional Think Tank

4th March 2021

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The Global Fund

2gether 4SRHR

Sweden Sverige

Aims and Objectives

The aim of the regional think tank and webinar series is to inform quality implementation and scale-up of PrEP Programming for AGYW in the ESA region as part of combination HIV prevention interventions.

Engage and convene diverse stakeholders

Generate implementation considerations

Document and disseminate key considerations

Share best practice, evidence, and lessons learned from implementation

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What We Heard Last Session: Healthcare system Considerations

Integration with family planning and SRH services

An integrated package which incorporates the spectrum of SRH and FP services required by AGYW and supports diverse delivery platforms, including community based, online, postal/courier and tele-health is important to cater to the needs of AGYW.

What is the minimum package?

PrEP provision should be integrated into existing AYFS models and based on global standards for quality health care services for adolescents. This includes ensuring technically competent providers and facility features that enhance accessibility i.e. one stop shop, fast track lines.

Risk Assessment

Risk assessment/ screening tools should be implemented as part of a prevention package to support a holistic approach to HIV prevention. It is important that risk assessment is used as a means to reach and identify those that are at risk and not as an exclusionary tool

Capacity building for providers

It is important to recognize that capacity building of providers extends beyond training of providers. There should be systems for mentorship, supervision, coaching and continued learning. It is also important to anticipate workforce changes and plan accordingly to maintain service continuity.

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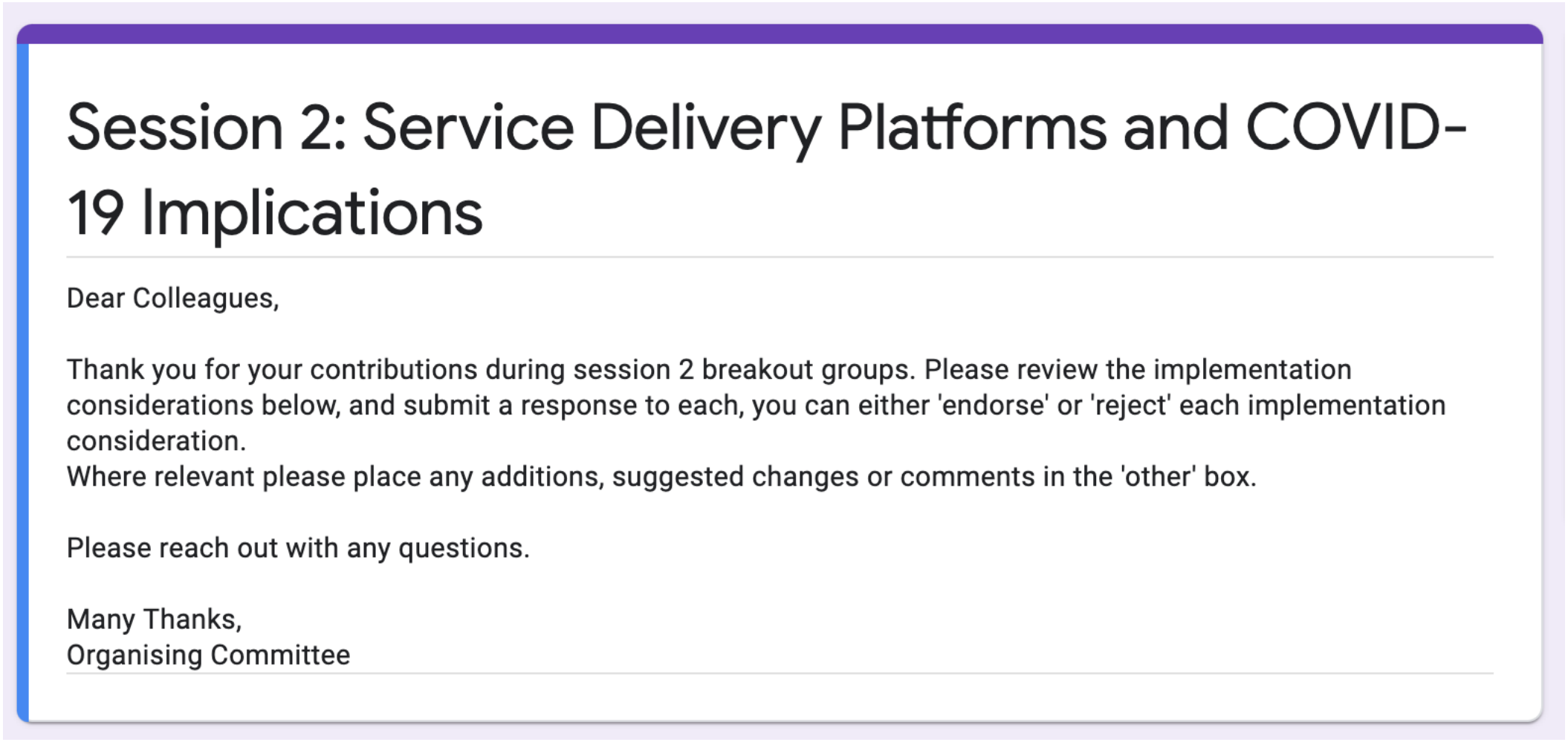
Delphi Survey for Consensus



Session 2: Service Delivery Platforms and COVID-19 Implications

Dear Colleagues,

Thank you for your contributions during session 2 breakout groups. Please review the implementation considerations below, and submit a response to each, you can either 'endorse' or 'reject' each implementation consideration.
Where relevant please place any additions, suggested changes or comments in the 'other' box.

Please reach out with any questions.

Many Thanks,
Organising Committee

https://forms.gle/h4VJb49vxZDmSDrn6

Google Drive

My Drive > AGYW PrEP Implementation for AGYW Think Tank

Name	Owner	Last modified	File size
Session 1	me	Feb 18, 2021 me	–
Session 2	me	Feb 18, 2021 me	–
Session 3	me	Feb 18, 2021 me	–
Session 4	me	Feb 18, 2021 me	–
Session 5	me	Feb 18, 2021 me	–
Supplementary Material	me	12:54 PM me	–

Agenda

Research Car Park

Literature Compendium

https://docs.google.com/document/d/1fTKicCVmzbQK9JHspO8NzHz8fCpCtnRQ3m0bH2I9-wA/edit?usp=sharing

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Todays Agenda

Session 4: Emerging Areas of Interest

10:00 – 10:15	10:15 – 10:50	10:50 – 11:25	11:25 – 11:30
Welcome and Introductions	Presentations and Q&A	Consensus Building via Jam Board	Next Steps and Close

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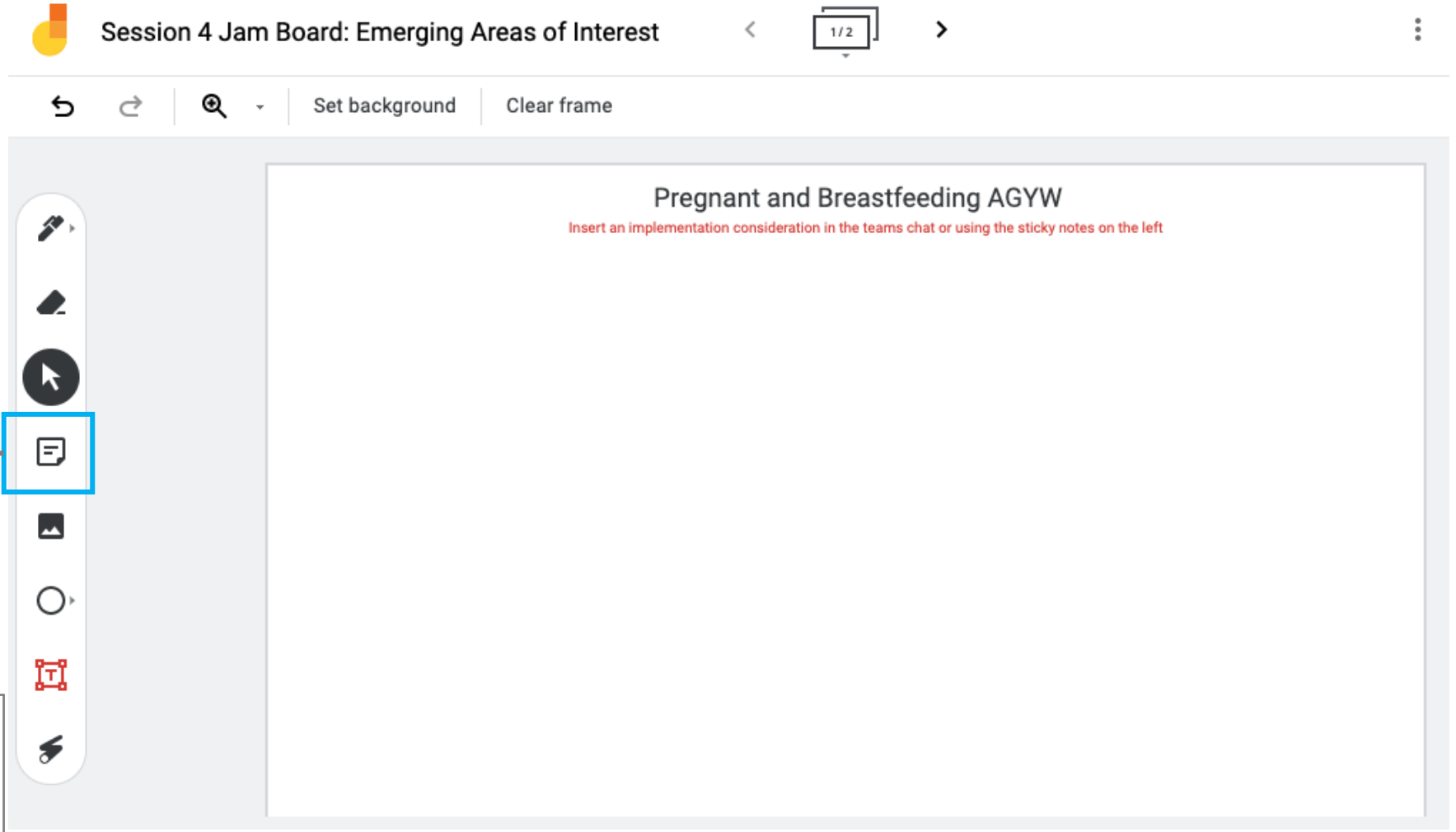
Jam Board Introduction

Note: If you cannot access the Jam Board use the Teams meeting chat

Access the Jam Board using the **link in the chat or below**

Add implementation considerations using the **Sticky Notes**



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Presentations: Emerging Areas of Interest

PrEP for Pregnant and Breastfeeding AGYW

Daya Moodley, The University of KwaZulu-Natal

New Biomedical Delivery Modalities

Sinead Delany-Moretlwe, Wits Reproductive Health Institute

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PrEP for Pregnant and Breastfeeding Adolescent Girls and Young Women

Daya Moodley, PhD
Associate Professor, Dept of Obstetrics and Gynaecology
School of Clinical Medicine
Research Associate, CAPRISA
University of KwaZulu-Natal

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Improving the Quality of PrEP Implementation for Adolescent Girls and Young Women in Eastern and Southern Africa

From Research and Demonstration Projects to Quality Implementation at Scale

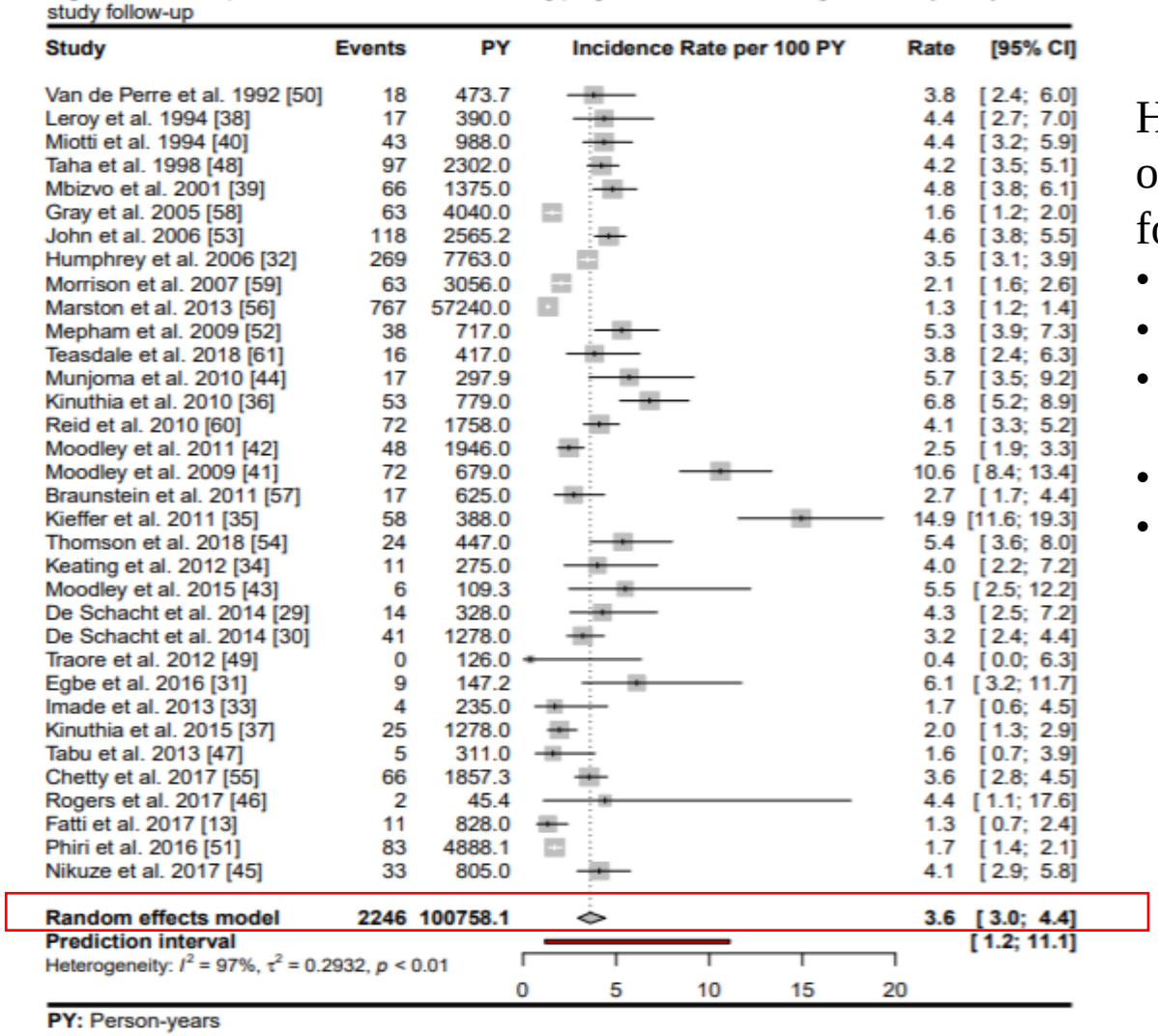
4 March 2021

Agenda

- HIV Incidence and Identifying PBFW for PreP
- Safety of PrEP in PBFW
- WHO PrEP Implementation Framework for PBFW
- Implementation Experience in ESA
  - PrEP Uptake, Adherence and Persistence
- Key Considerations

HIV incidence during pregnancy and breastfeeding

Figure S1. Forest plot of HIV incidence rates among pregnant and breastfeeding women, by mid-year of study follow-up



HIV incidence in meta analysis of 37 cohorts – 100 758 PY followup:

- Pregnancy=3.4/100 PY
- Breastfeeding=3.1/100 PY
- Combined=4.6/100 PY

- Pre-2010 = 4.1/100py (1.1-12.2)
- Post-2014 = 2.1/100py (0.7-6.5)

Source: Graybill, AIDS, 2020

Algorithm for Combination HIV Prevention Strategy for Moderate to High Risk Population within the PMTCT Programme

Antenatal Registration

Provider Initiated Counselling and Testing

HIV Seronegative

Primary HIV Prevention

HIV Seropositive

PMTCT, Treatment, Support

1. Risk Assessment
2. Clinical and Laboratory Assessments if at Substantial Risk
3. Risk Reduction Counselling
4. STI Screening and Treatment (Syndromic and syphilis)
5. Condom Promotion
6. Partner Invitation for HCT

Partner Accepts Invitation

1. Client Initiated Counselling and Testing or Couple Counselling

Partner Declines/Does Not Respond to Invitation

1. Re-Assess Risk of Pregnant Woman
2. Offer PrEP if at Substantial Risk
3. Emphasise importance of followup visits and repeat HIV Testing

Partner HIV Negative

8. Condom Promotion
9. Risk Reduction Counselling
10. Referral for VMMC

Partner HIV Positive

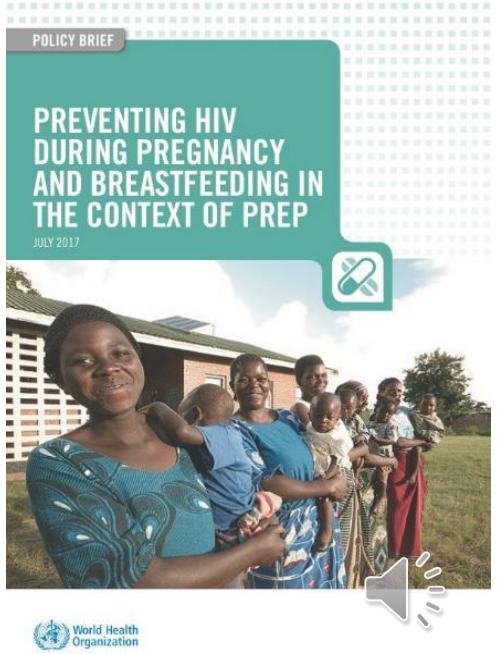
1. Condom Promotion
2. Referral for ART

HIV Unexposed Woman

6. Reassess HIV Risk 6 monthly
7. Continue Risk Reduction Counselling

HIV Exposed Woman

1. Offer PrEP and adherence counselling
2. Emphasise importance of followup visits and repeat HIV Testing



Safety of PrEP in Pregnancy

- There is significant exposure *in utero* as TDF in amniotic fluid and cord blood.
- Studies of TDF use in HIV-uninfected pregnant women are limited.
- Evidence of safety is reassuring.
- **However, it will be important to continue surveillance of maternal, pregnancy and infant outcomes to confirm the safety that reviews to date suggest.**

Using a Risk Assessment Tool to Identify PBW for PrEP

HIV RISK ASSESSMENT TOOL

PID_____ **Initials:** _____

1. How old are you?

<25	2
≥25	0

2. Are you married or living with your partner?

No	2
Yes	0

3. How old is your current partner?

≥25	1
<25	0

4. Does your partner have other girlfriends?

Yes	1
I do not know	1
No	0

5. Does your partner provide you with financial support?

Yes	0
No	1

6. Have you had any alcohol in the last 3 months?

Yes	1
No	0

7. Have you had a STI in the last 3 months?

Yes	1
No	0

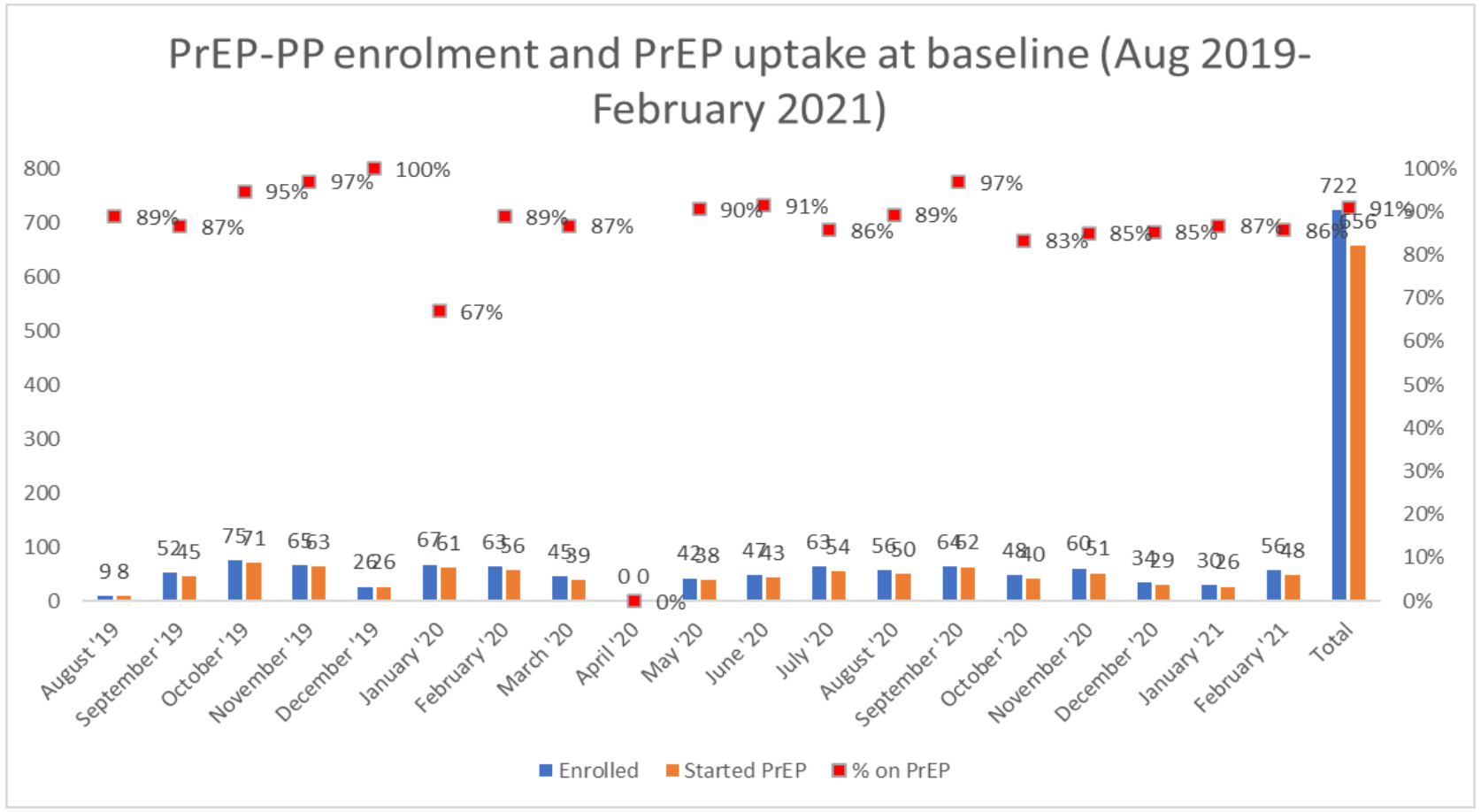
Final Score _____

High Risk	≥5
Moderate or Low Risk	<5

- 50% of the antenatal population could likely be identified at high risk vs 3% actual infection rate
- Sensitivity: This tool could accurately identify 75% of women who subsequently acquired HIV infection during pregnancy or postpartum and could benefit from PrEP.
- Specificity: The poor specificity (59%) however, would mean that up to 40% of antenatal attendees and their unborn babies may be unnecessarily exposed to PrEP.

Uptake of PrEP

Study enrollment & PrEP initiation



Overall, we enroll ~50 pregnant women/month of whom >90% of women initiate PrEP at baseline

PrEP persistence declines significantly across women in sub-Saharan Africa[1]

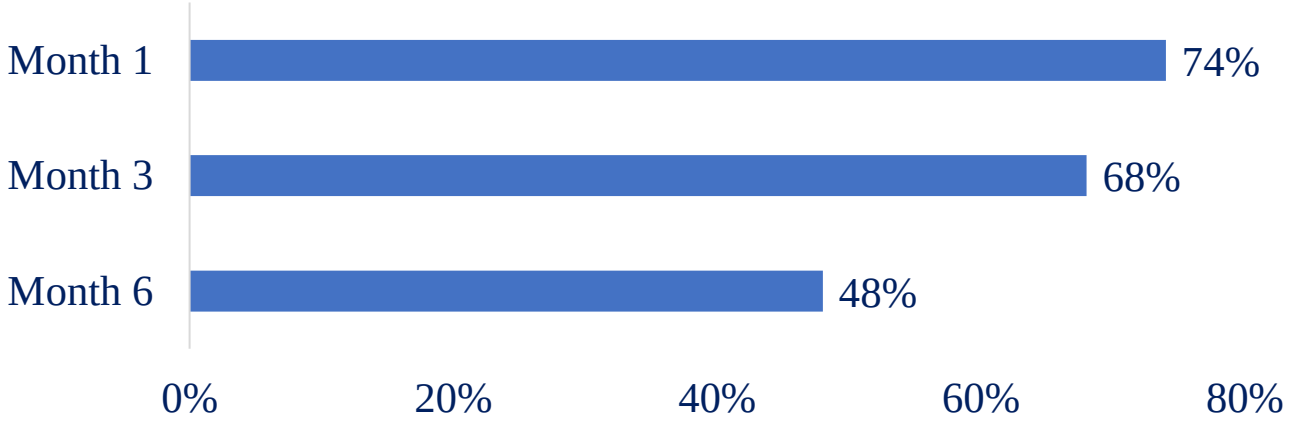
Study	Country	Persistence rates (M=month)
POWER[2]	Kenya, South Africa	43% (M1) 20% (M3)
PrIYA[3, 4]	Kenya	**MCH clinic:** 39% (M1); 12% (M6) **FP clinic:** 41% (M1)' 24% (M3);15% (M6) Pregnant women reported **side effects** more frequently than non-pregnant women & 36% of women discontinued PrEP
EMPOWER[1]	South Africa, Tanzania	73% (M1) 61% (M3) 34% (M6)

Source:

1. Rodrigues, et al. Starting and Staying on PrEP: a scoping review of strategies for supporting effective use of PrEP, HIV R4P (2021)
2. Rousseau-Jamewa et al, Early persistence of PrEP for African Adolescent Girls and Young Women from Kenya and South Africa, HIVR4P (2018)
3. Kinuthia, et al. PrEP uptake and early continuation among pregnant and postpartum women within maternal and child health clinics in Kenya: results from an implementation programme (2019); Mugwanya et al. Integrating PrEP in routine family planning clinics: A feasibility programmatic evaluation in Kenya (2018)
4. Pintye, et al. PrEP Side-effects and Discontinuation in Pregnant and Non-Pregnant Women, HIVR4P (2018)

PrEP persistence

- Persistence defined as returning for repeat PrEP prescription after baseline initiation



- PrEP continuation drops precipitously after COVID lockdown and after postpartum period
- **To improve persistence:** phone interviews & adherence counseling, weekend visits and after hours to accommodate women and COVID risk

PrEP Adherence

TFV-DP in DBS for pregnant/postpartum adolescent and young women on PrEP in Africa

0980

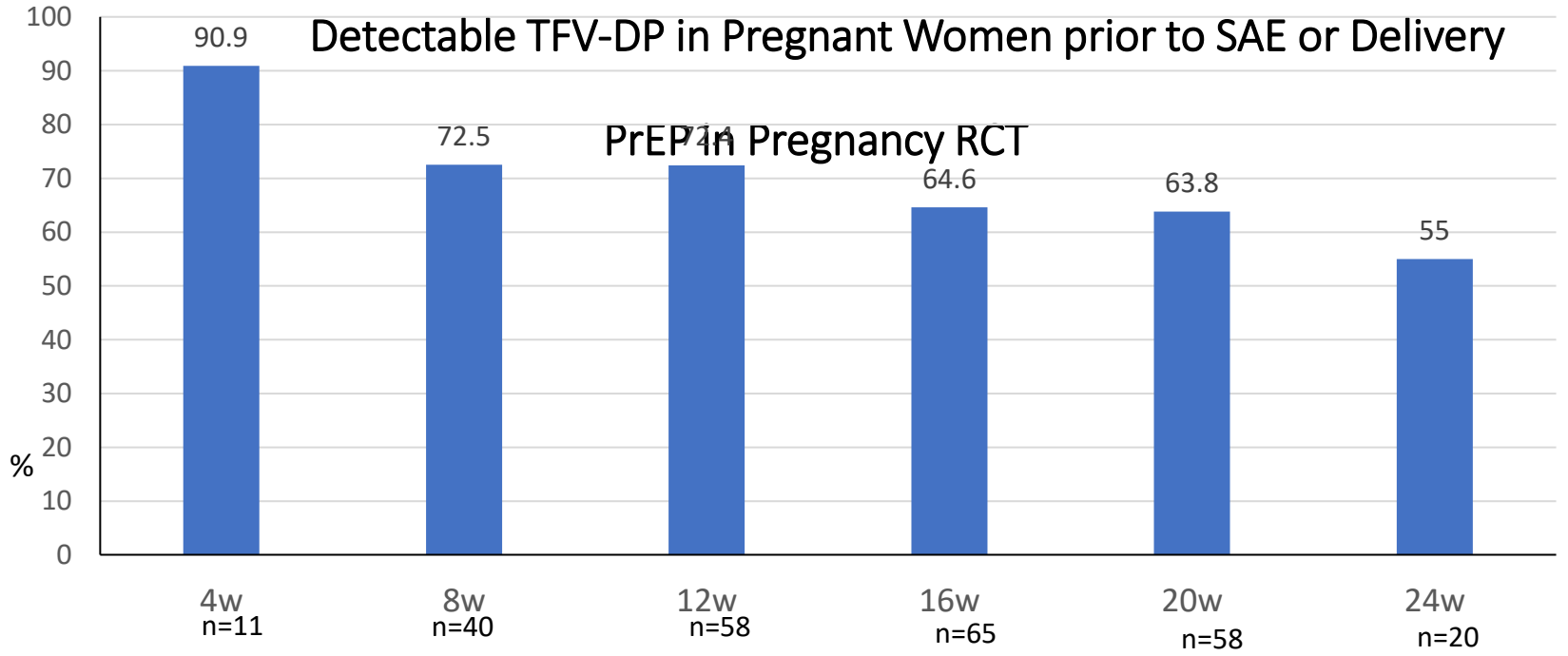
Peter L. Anderson[1], Lynda Stranix-Chibanda[2], Sharon Huang[3], Sybil Hosek[4], Deborah Kacanek[3], Teacler Nematadzira[2], Frank Taulo[5], Violet Korutaro[6], Clemensia Nakabiito[7], Masekole Masenya[8], Kathryn Lypen[9], Nahida Chakhtoura[10], Hans M. Spiegel[11], Benjamin H. Chi[12], on behalf of the IMPAACT 2009 team

Adherence benchmarks using TFV-DP in DBS were established for pregnant/postpartum African adolescents and young women

TFV-DP in DBS was 31%-37% lower in pregnancy compared with postpartum, in line with expectations. Strict adherence to PrEP is recommended during pregnancy.

	DBS TFV-DP fmol/punch	
Interpretation	Pregnant	Post-partum
~7 doses/wk	≥650	≥950
2–6 doses/wk	200–649	250-949
<2 doses/wk	<200	<250

PrEP Persistence and Adherence



CAP016

Doses per week	TFV-DP (fmol/punch)	Number (%; 95%CI)
7 doses/wk	>650	41 (23.6%; 17.5-30.6)
2-6 doses/wk	200-649	84 (48.3%: 40.7-71.8)
<2 doses/wk	<200	49 (28.2%; 21.6-35.5)

Key Considerations

- **Approaches to Offering PrEP to PBFW**
  - **Universal vs Targetted vs Demand**
- **Using Risk Assessment to Identifying PB AGYW for PrEP**
- **Adherence Monitoring and Support**
- **Monitoring Safety through Surveillance**
- **Optimizing PrEP Persistence and Retention**

Questions

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Novel PrEP delivery strategies

Sinead Delany-Moretlwe, MBBCh PhD DTM&H
UNAIDS ESA PrEP in AGYW
February 2021

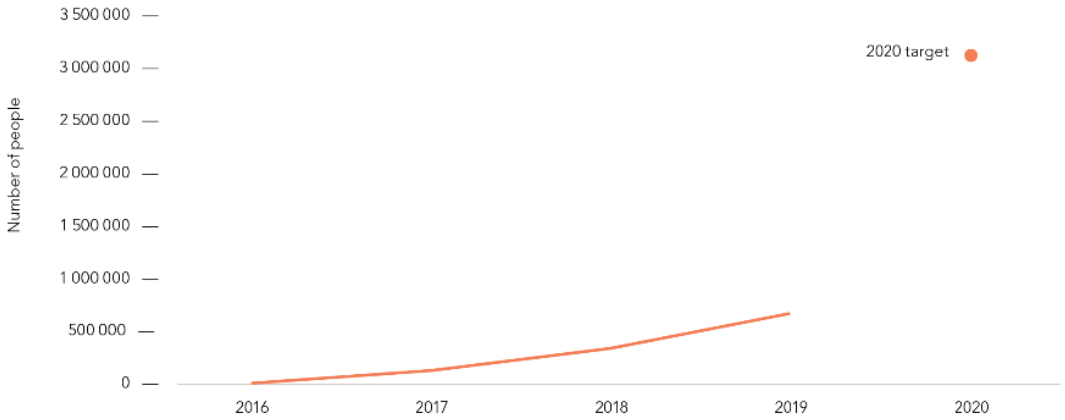
Overview

- Why do we need a range of PrEP options?
- What new options are likely to be available?
- What does this mean for implementation?

Tracking global oral PrEP access

By Q4 2020, **928,750** people on PrEP world wide

Number of people who received PrEP at least once during the reporting period, global, 2016–2019



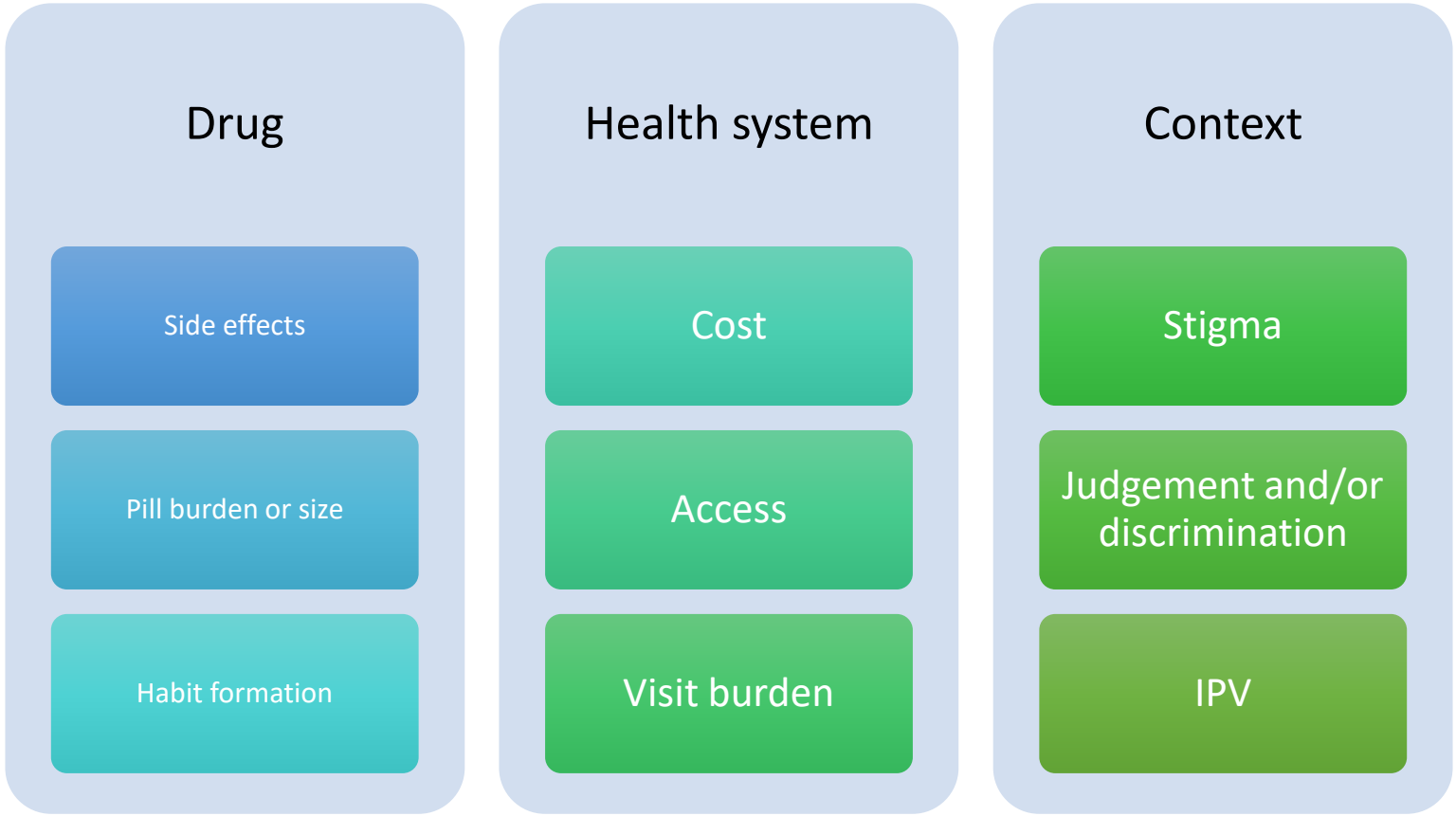
Source: UNAIDS Global AIDS Monitoring, 2017–2020 (see https://aidsinfo.unaids.org/); Country Updates. In: PrEPWatch [Internet]. AVAC; c2020 (https://www.prepwatch.org/in-practice/country-updates/); amfAR: PEPFAR Monitoring, Evaluation and Reporting Database [Internet]. amfAR; c2020 (https://mer.amfar.org/Manual/PrEP_NEW); Hayes R, Schmidt AJ, Pharris A, Azad Y, Brown AE, Weatherburn P et al. Estimating the "PrEP Gap": how implementation and access to PrEP differ between countries in Europe and central Asia in 2019. Eurosurveillance. 2019;24(41); and country documents and meeting reports (available on request).

Goal: 3 million on PrEP by 2020

…And 1/3 new initiations discontinue within one month
Higher rates of discontinuation in AGYW

www.prepwatch.org; www.unaids.org;Stankevitz, AIDS 2020;

Reasons for oral PrEP discontinuation



Much like contraception, we need a range of PrEP options that can overcome these barriers across the life course

Zarwell, AIDS Behav 2020; Bargnighausen, Culture Health Sex 2020; Pillay, PLoS One, 2020 Rutstein, Lancet HIV, 2020;

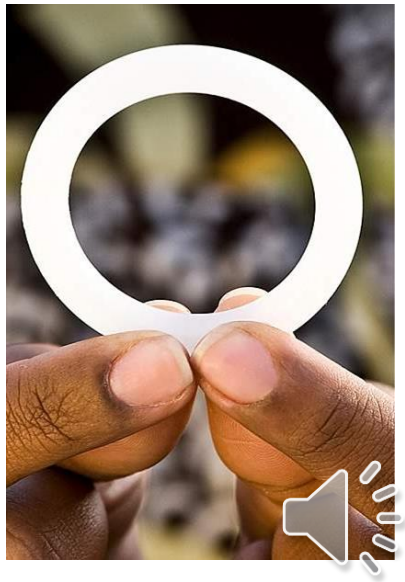
Monthly dapivirine ring

- Flexible silicone vaginal ring developed by IPM
  - Self-inserted monthly
  - Dapirivine released over 30 days
- Low systemic absorption
- Two Ph 3 trials showed well-tolerated and reduced HIV risk in women by **~30%**
- Open-label extension studies showed greater use with estimated **~50%** risk reduction
- Favourable side effect profile
- Favourable EMA opinion, July 2020
  - Recommended when women cannot use oral PrEP

Nel, NEJM 2016; Baeten, NEJM 2016; Baeten, IAS 2019; Nel, SA AIDS 2019

Monthly dapivirine ring – next steps

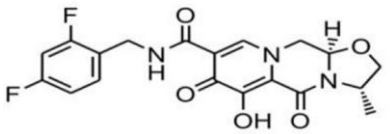
- WHO prequalification of DVR, Nov 2020
  - Included in guidelines, Feb 2021
- Paves the way for country-level approvals and implementation
- Additional studies
  - adolescents
  - Resistance in seroconverters
  - pregnant and breastfeeding women
- Future:
  - 90-day ring, dapivirine-contraceptive ring
  - 2 phase I studies using DPV



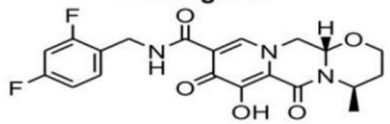
Long-acting injectable Cabotegravir

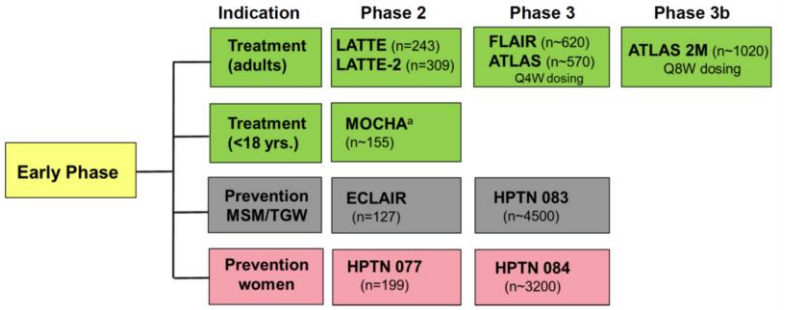
- Integrase inhibitor
- LA formulation is low solubility crystalline drug suspended in aqueous vehicle for intramuscular injection
- HIV treatment studies (with rilpivirine) demonstrate potent anti-HIV activity and high resistance barrier
- Developed for both HIV treatment and prevention

GSK1265744
(GSK744)



Dolutegravir

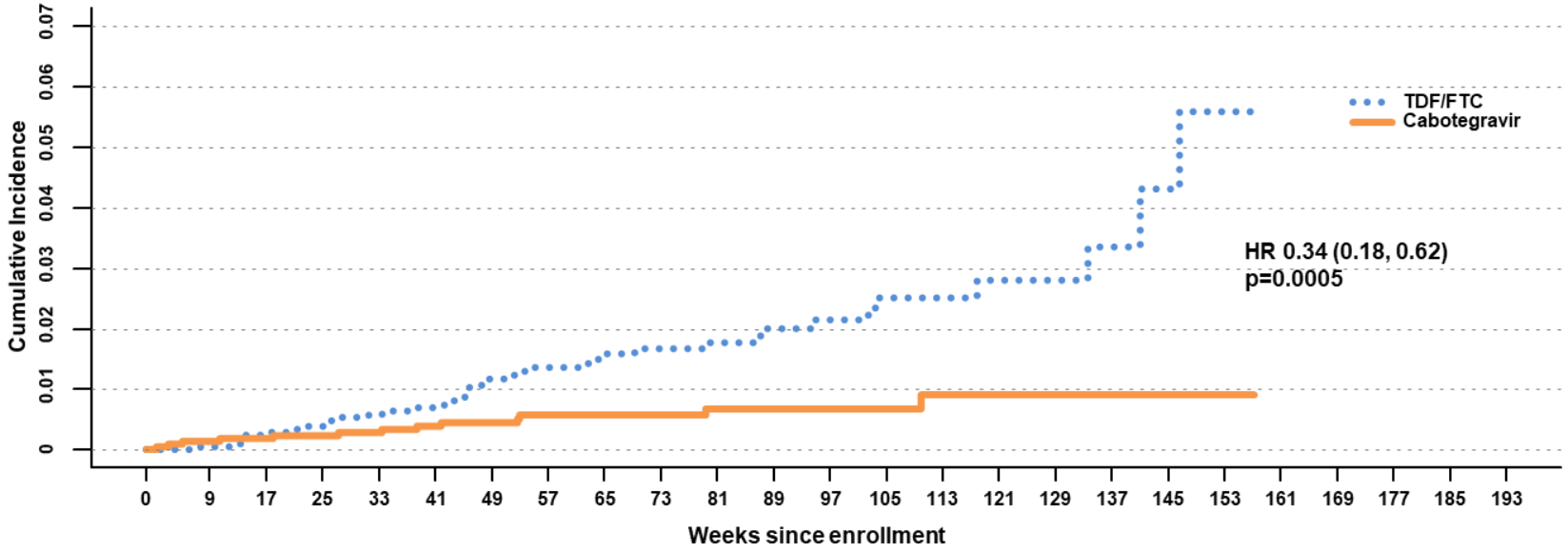




Source: Andrews, 2014; Radzio, 2015; Andrews, 2015; Andrews, 2017; Dobard, 2018

Long-acting injectable cabotegravir is safe and effective for PrEP

HIV incidence – ITT population

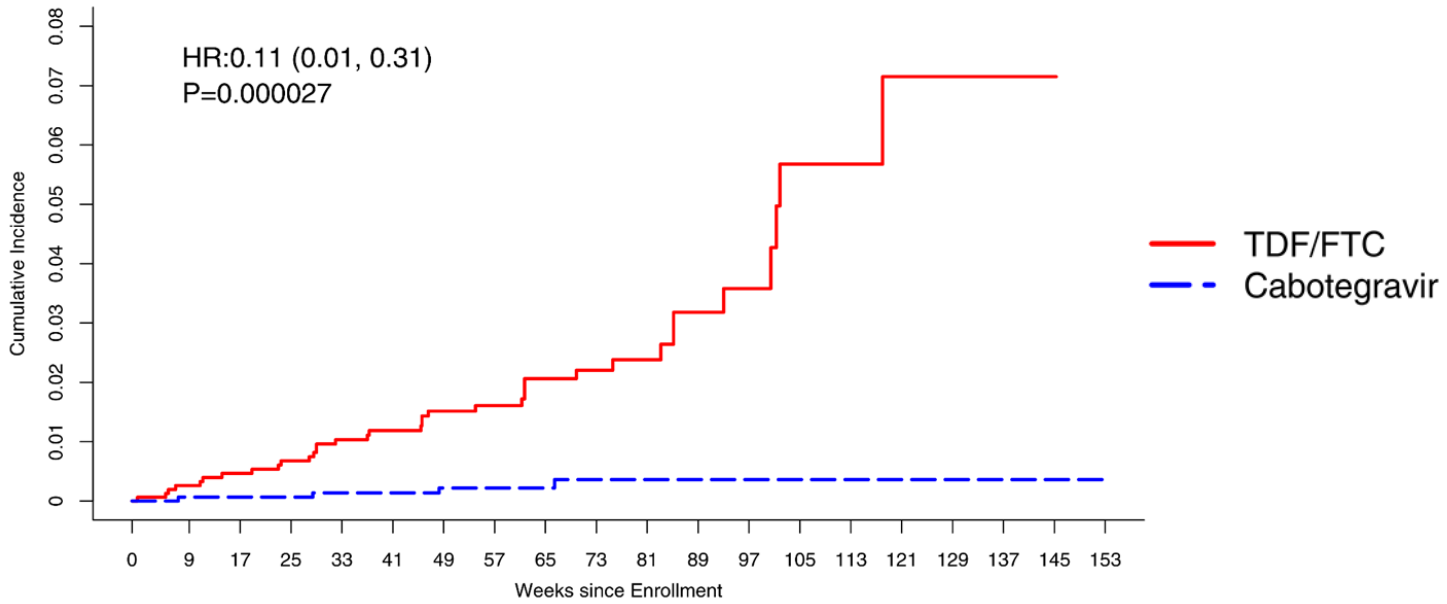


- N= 4566 cisgender men and transgender women
- Pooled incidence 0.81 (95%CI 0.61-1.07) per 100 PY

Landovitz RJ et al. AIDS 2020, #OAXLB0101

Long-acting injectable cabotegravir is safe and effective for PrEP

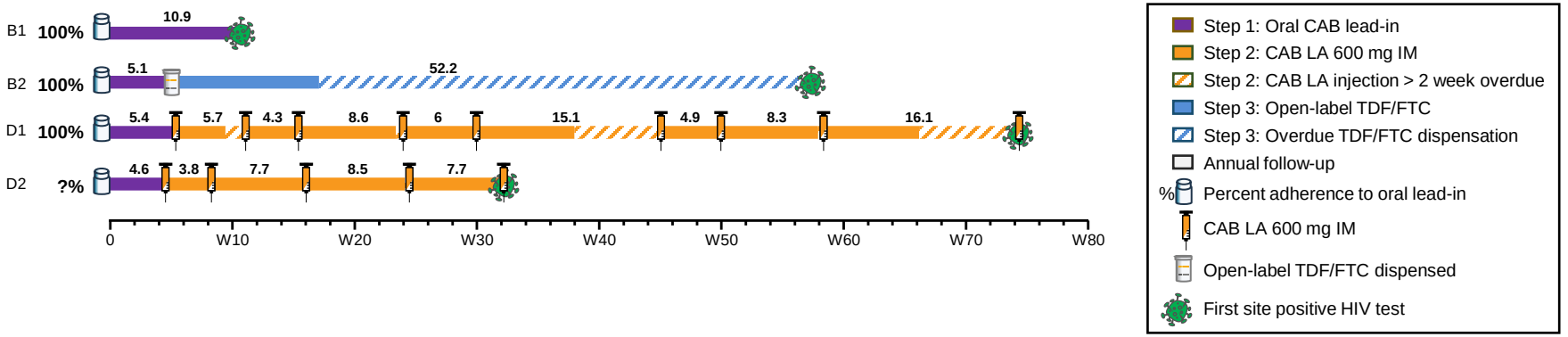
HIV incidence – ITT population



- N= 3224 cisgender women
- Pooled incidence 1.03 (0.73, 1.4) per 100 person-years
- Grade 2+ ISR CAB>TDF/FTC

Delany-Moretlwe al. HIV R4P 2021

Cabotegravir - 4 incident HIV Infections



Long acting injectable cabotegravir – next steps

- Blinded portion of studies stopped
- Additional HIV, PK and resistance testing of HIV infections ongoing
- Open-label extension with offer of CAB LA
  - Optional oral lead-in
- Additional studies in adolescents, pregnant and breastfeeding women
- The tail?

- MPT:
  - alignment with contraceptive visits, coadminstration or coformulation?
  - Future use in implants or micro-array patches

Flexner, IAS 2019

PrEP 2.0 – future long-acting products

- Monthly oral pill or implant – Islatravir
- 6-month sub-cutaneous injection – Lencapavir

- Phase III trial results expected 2024

Implications for implementation - opportunities

- Supporting product choice
  - Demand from men as well as women
  - Cost-effectiveness vs. affordability considerations
  - Health system – offer all or to those that fail oral PrEP
  - Provider training and support tools
    - Client preferences vs. product efficacy and safety profile

- Integration within sexual health services
  - Visit alignment
  - Multi-purpose products
  - Opportunities to increase uptake of range of services in a broad range of populations

Implications for implementation – more data needed

- Adapting to long-acting products
  - Delayed dosing and implications for resistance?
  - Implications for HIV diagnosis and rapid testing platforms?
  - Linkage to treatment
  - Provider skills and training
  - Messaging and decision support

- Strengthened surveillance
  - Strengthened pharmacovigilance for rare events in pregnancy
  - Resistance

Acknowledgements

Participants and communities taking part in these trials

Trial staff, sponsors and funders

Questions

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Next Steps

1 Complete the Delphi Survey

Consensus Building Exercise

You will receive a Delphi Survey via e-mail.

Please complete the survey by Monday 8th March

2 Join us for Session 5

Session 5:
Monitoring, Research Agenda and Finalisation

Tuesday 9th March

10:00 am – 11:45 am SAT

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