Experiences from adolescent studies in Cape Town

HIV/SRH research for adolescents- making it a reality.

Linda-Gail Bekker
Desmond Tutu HIV Centre
21 June 2021

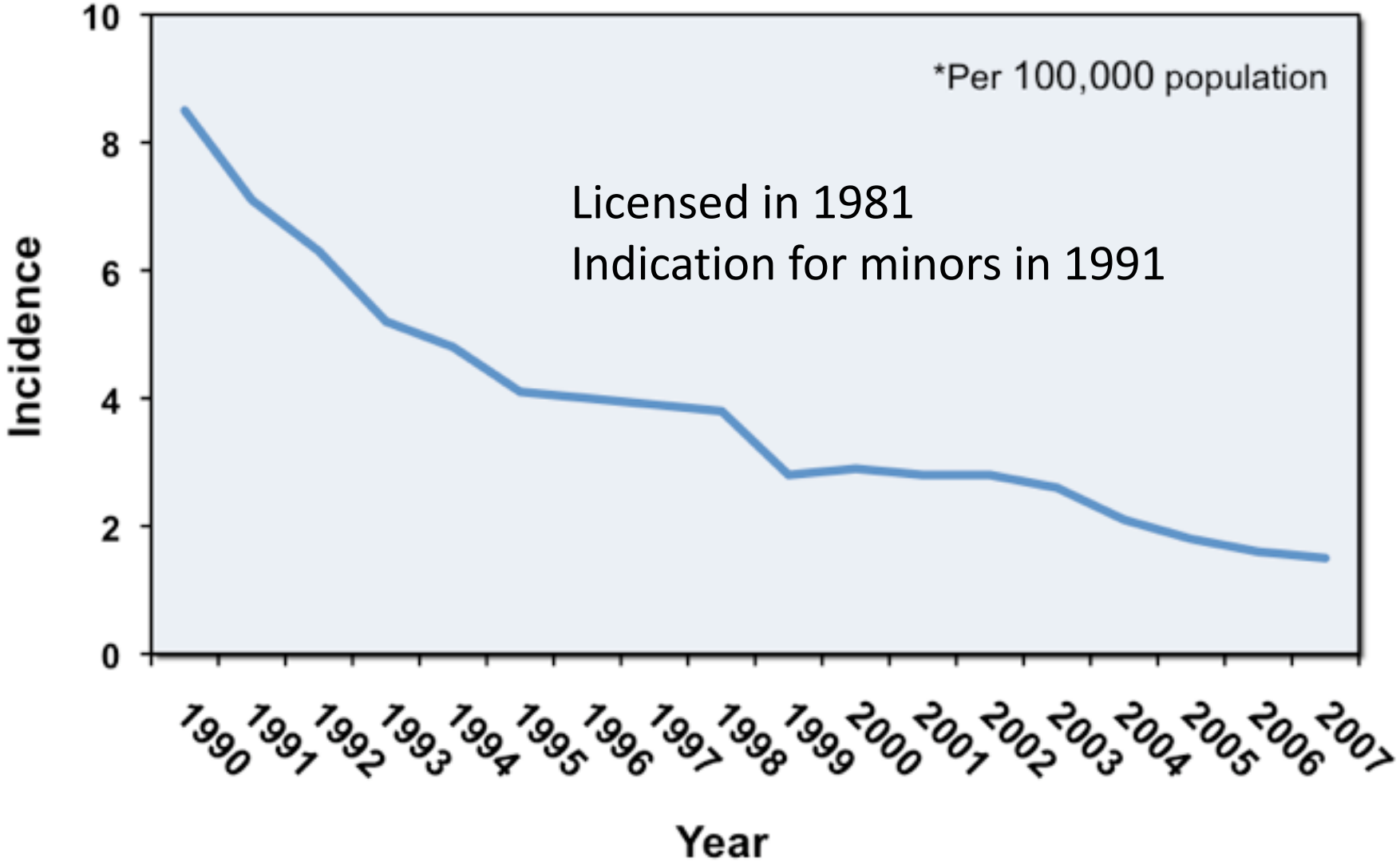
DESMOND TUTU HEALTH FOUNDATION

DESMOND TUTU HIV CENTRE

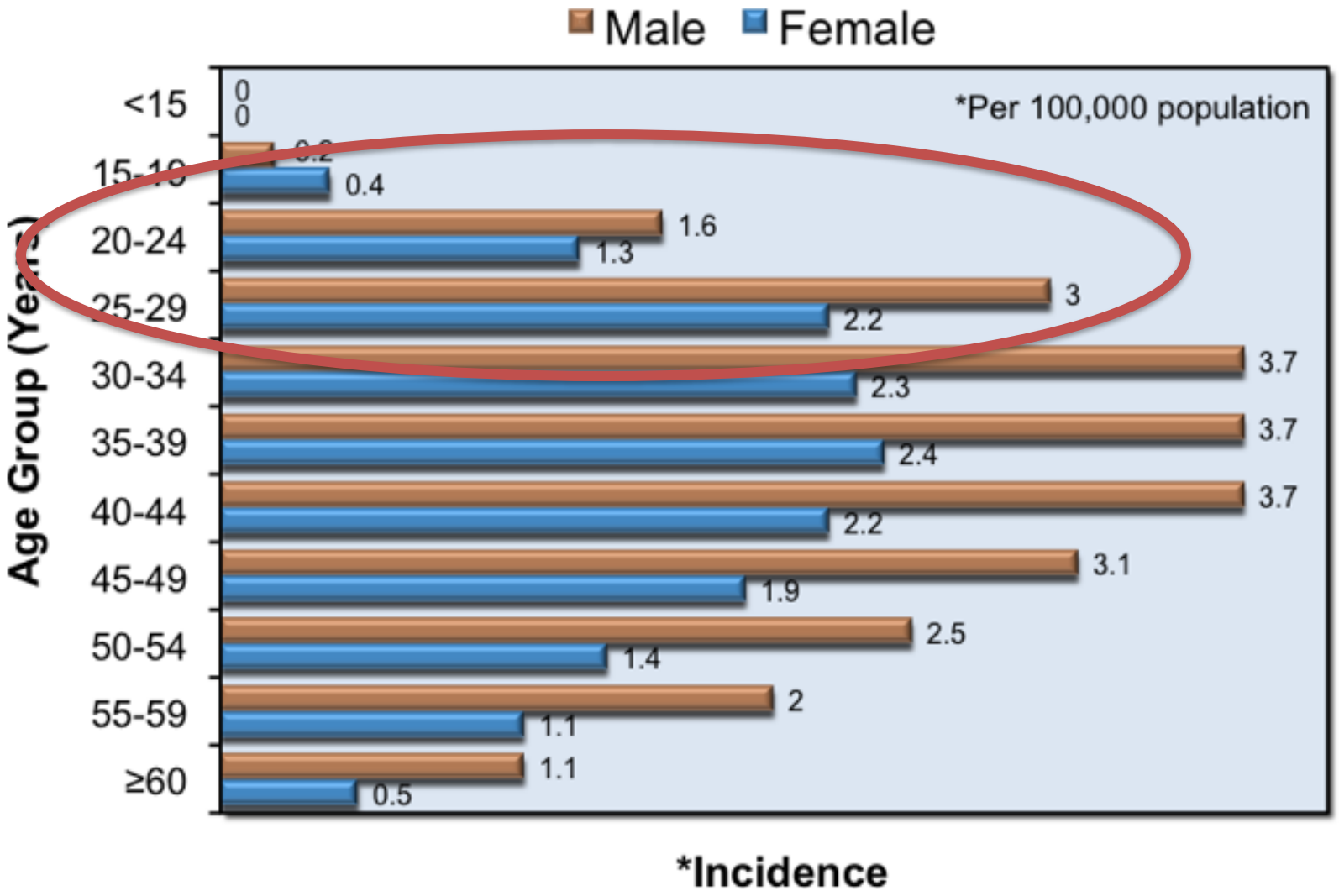
Therapeutics for minors

- Ocular medicines in children: the regulatory situation related to clinical research.
  - Filomena Fortinguerra*, Antonio Clavenna and Maurizio Bonati; BMC paediatrics 2012
- 197 ocular medications
- Approx 50% licensed for paediatric use
- Only 50% of those had an RCT

Hepatitis B vaccine experience



Hep B infection incidence



almost 2 billion

people are between the ages of 10 and 24 years

Source: Population Reference Bureau, 2006

Many are at risk for HIV and other STIs, many will have unintended pregnancies.....

Why the reluctance to involve adolescents?

Perceived vulnerability:

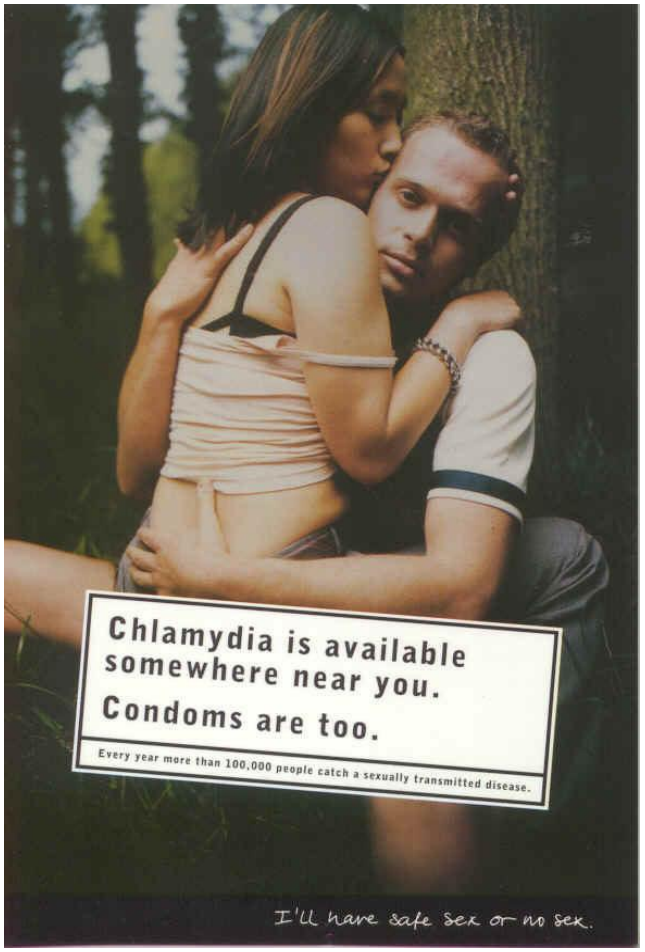
- Ethicoregulatory (minors)
- Cognitive development
- Psychosocial
- Logistical

Pre-Adolescence to Early Adolescence (10-13 years):

- Bodily changes, pre-occupation with self image and normality
- Same sex peer-group pressure dominates
- High levels of mood swings
- Concrete operational stage (Piaget)

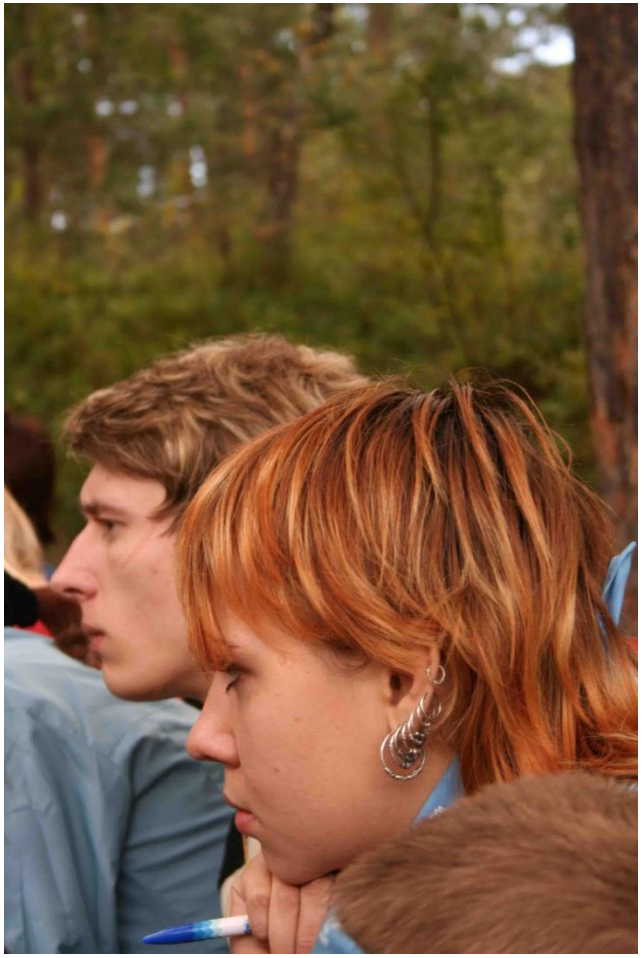
Middle Adolescence (14 -16 years):

- Asserting independence is a priority
- Lingering concerns over attractiveness
- Increased risk taking and sexual experimentation
- Formal operational stage

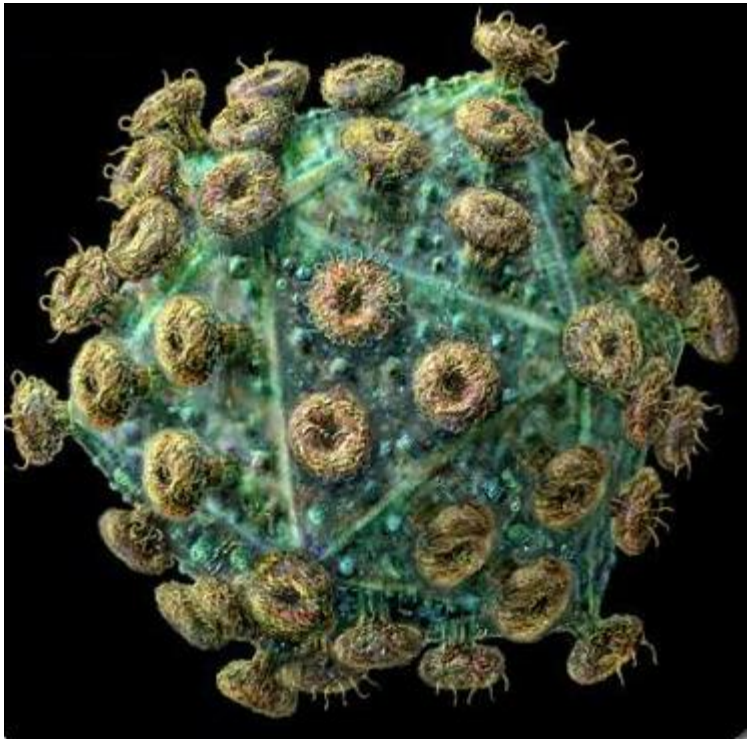


Late Adolescence (17-20 years):

- Major concerns about career, lifestyle and relationships
- Degree of independence established
- Realistic body image and sexual identification established



HIV, Sexual and Reproductive, Mental Health and prevention research….



“non therapeutic……”

Our Early Work:

- Preparatory work with SAAVI and HAVEG
- Looking at feasibility and acceptability:
  - Can we recruit/retain adolescents?
  - What is HIV incidence/ SRB in this group?
  - How can we best collect SRB data from adolescents?
  - What are attitudes towards ethico-legal issues; WTP?

DESMOND TUTU HIV FOUNDATION

Early work (Continued):

Issues raised and recommendations made:

- –Botswana AAVP 2006: position paper for WHO
- –DAIDS White paper 2007
- –FDA guidance document 2006

•At what point do we include adolescents in trials?

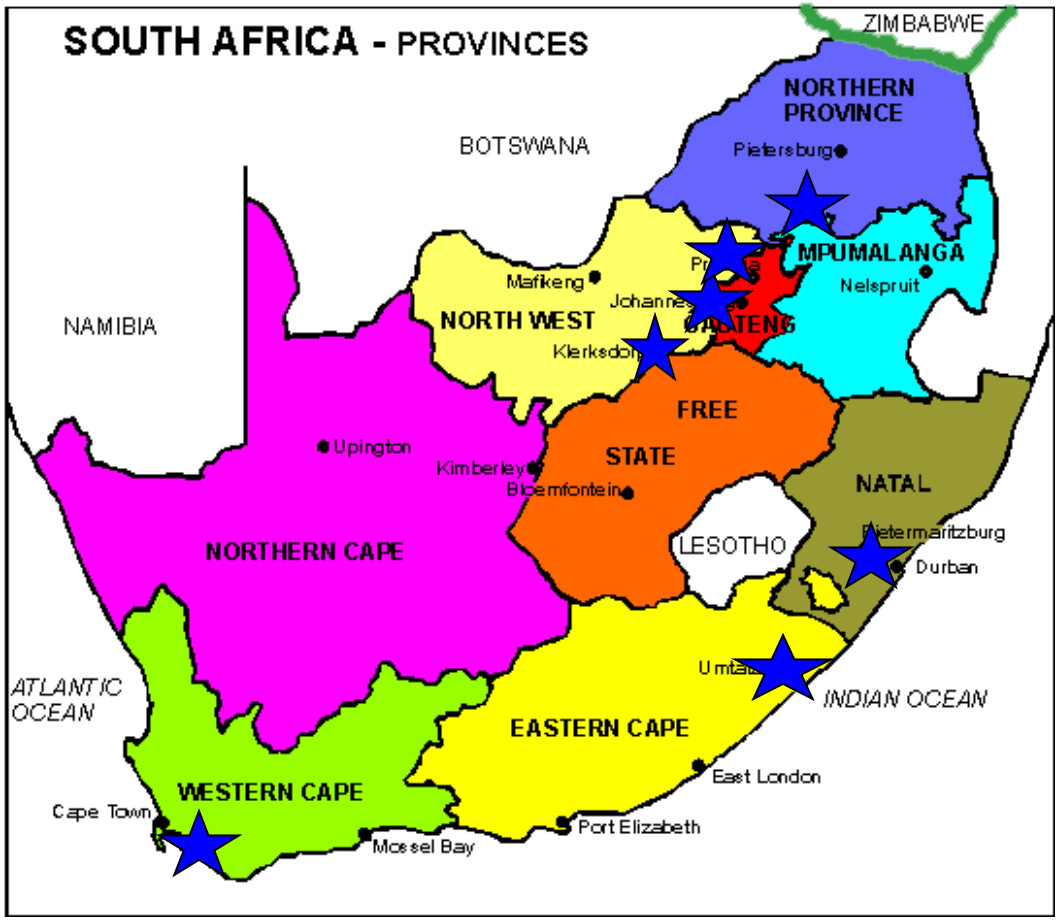
•Concerns around sexual disinhibition; social harms; retention; legal issues

DESMOND TUTU HIV FOUNDATION

Preparing for adolescent HIV vaccine trials in South Africa

to explore the feasibility of running adolescent HIV vaccine trials in South Africa, address some of the challenges identified, and build capacity for this purpose

South African multi-site project…..
Core site at Desmond Tutu HIV Centre, CT



Mpumalanga/ Ndlela

Pretoria/ Medunsa

Soweto/ PHRU

Klerksdorp/ KOSH

Durban /CAPRISA

Mthatha /WSU

Cape Town/DTHC

SASHA study:
building capacity and testing systems for a trial

- Extensive community engagement
- Identifying and addressing logistical, SB and EL barriers to including adolescents
- Emulating an HIV vaccine trial using HPV vaccine
- Lowering age range: 12 – 17 years

SASHA
South African Studies on HIV in Adolescents

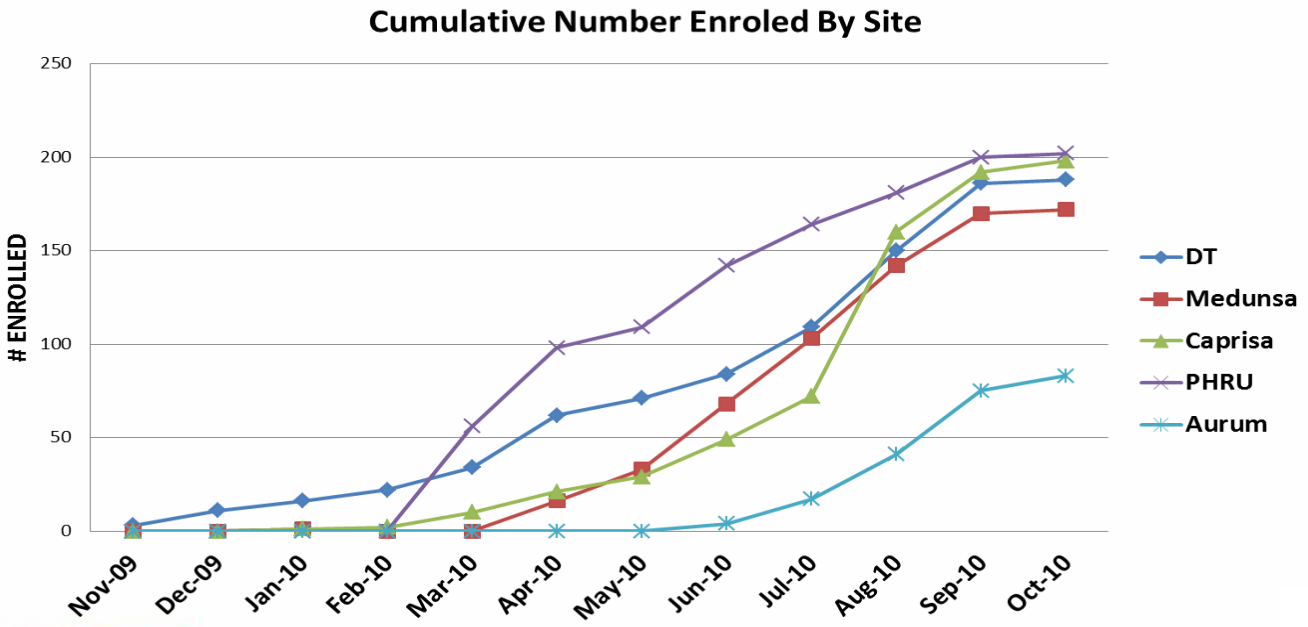

knowledge is power
get tested
?

Capacity building and community engagement

- Development of youth CABs
- Mapping of adolescent support services
- Staff training
- Study sites made adolescent-friendly
- Focus groups with adolescents, parents, stakeholders
- Communities supportive of adolescent work

Feasibility: Enrolment

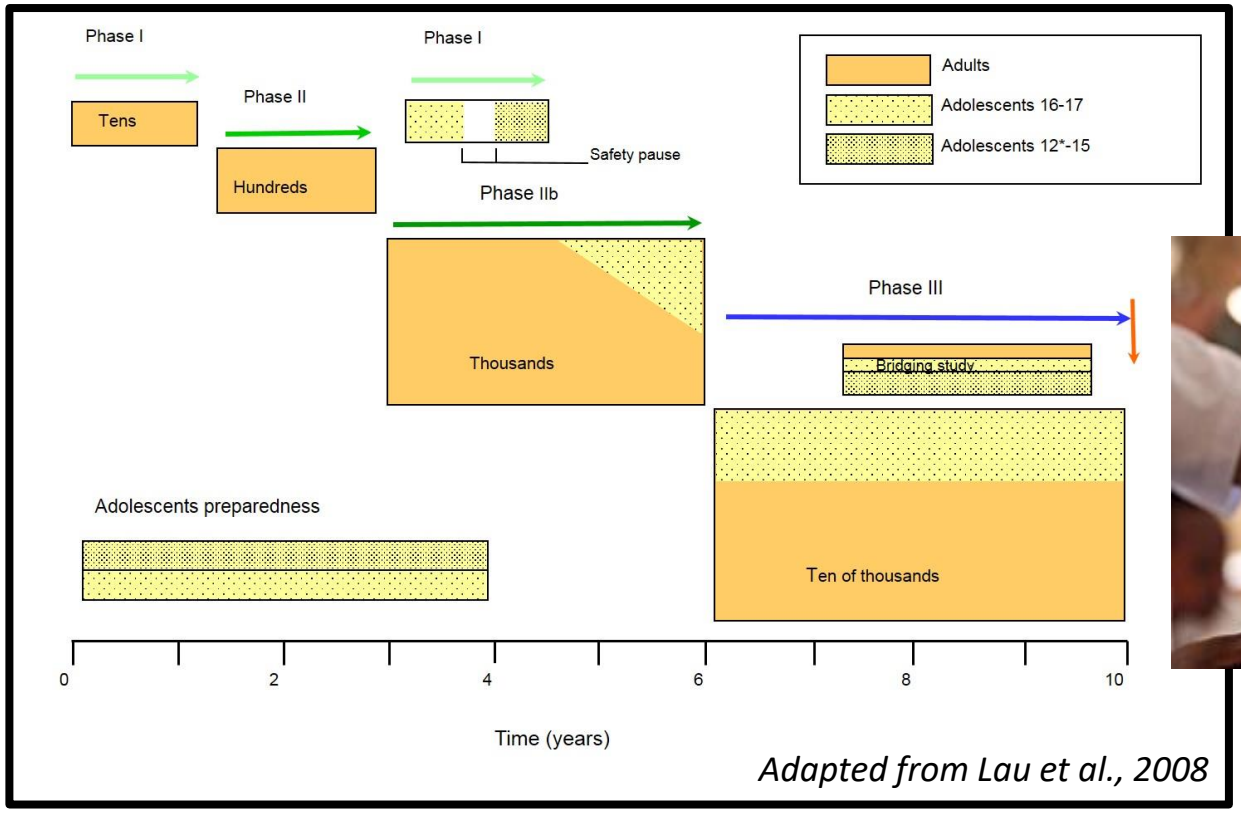
•Staggered site initiation: each site recruited an average of 168 participants over an average of 8.4 months = 20 participants/mth



South African Studies on HIV in Adolescents

Adolescent Vaccine Trials & Preparedness:

Example: Adolescents, Phasing in of Adolescent Clinical Trials



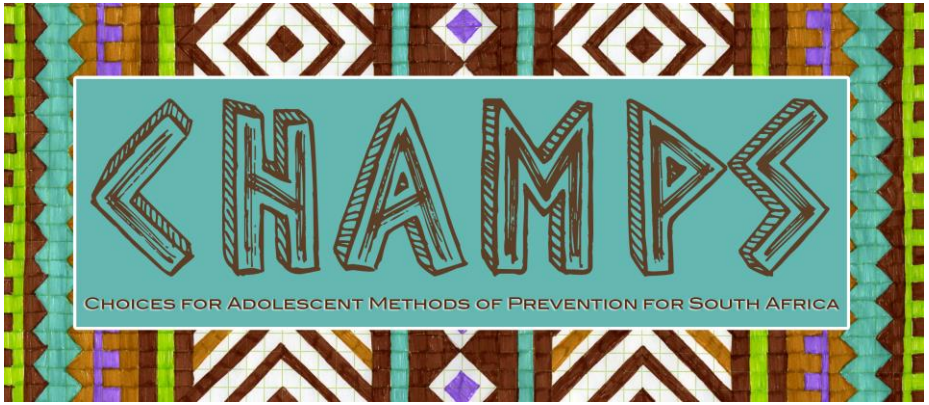
Adapted from Lau et al., 2008

A feasibility and acceptability trial in (SASHA) South Africa across 5 sites found good uptake of a vaccine to combat sexual infection diseases – **but that it could be higher amongst those at high risk if parental consent for older adolescents was waived.**

(Wallace et al., 2018, SAMJ)

Step 2- CHAMPS: 4 PHASES

1. Literature Review of what was out there.
2. Pilot studies of biomedical technologies.
3. Modelling exercise to see impact.
4. Further thought to design of clinical trials.

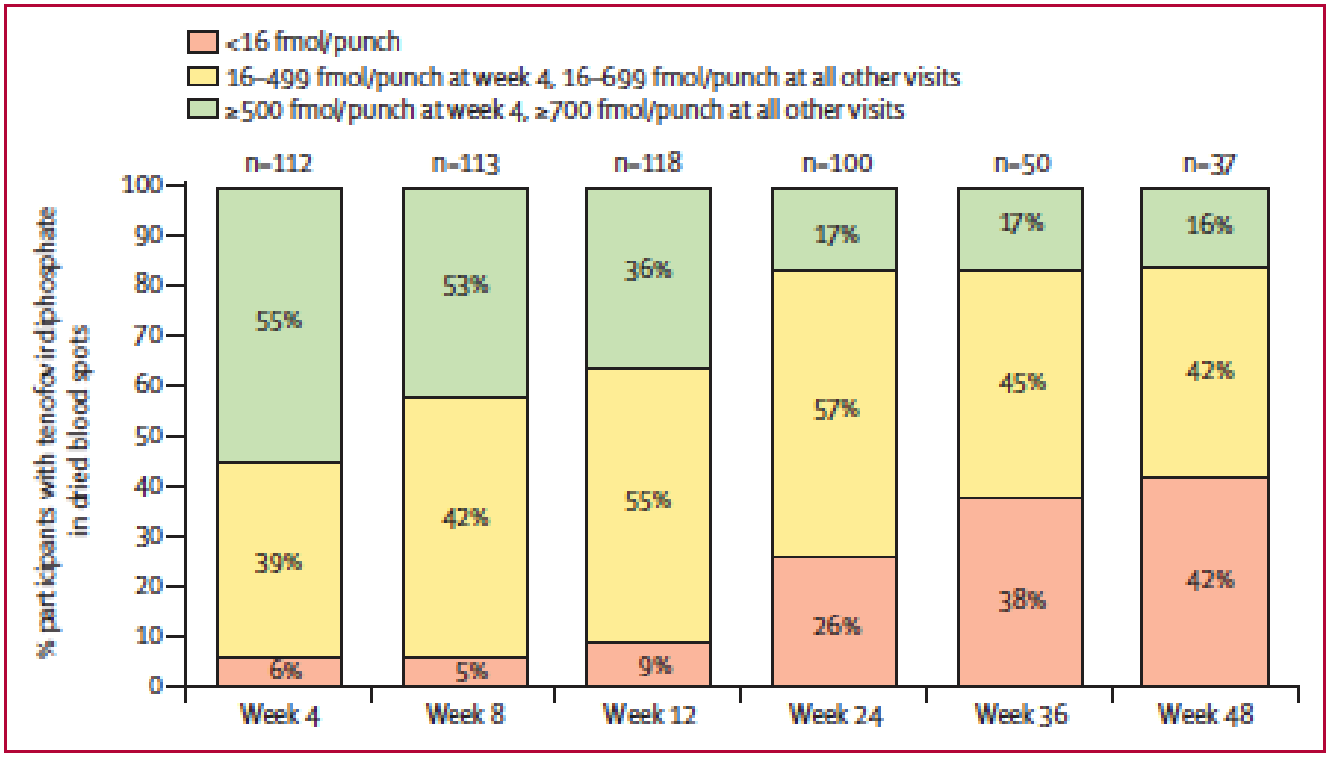


Pilot-Pluspills: Acceptability, safety, and patterns of use of oral PrEP in SA adolescents:

open-label single-arm phase 2 trial (Parental consent)

148 adolescents (15-19 years) in 2 RSA cities

- Monthly visits until week 12 and then quarterly visits until week 48
- As visit frequency decreased, so did adherence
- 55% had FTV-DP levels consistent with >4 pills/week in week 4 – dropping to only 16% in week 48

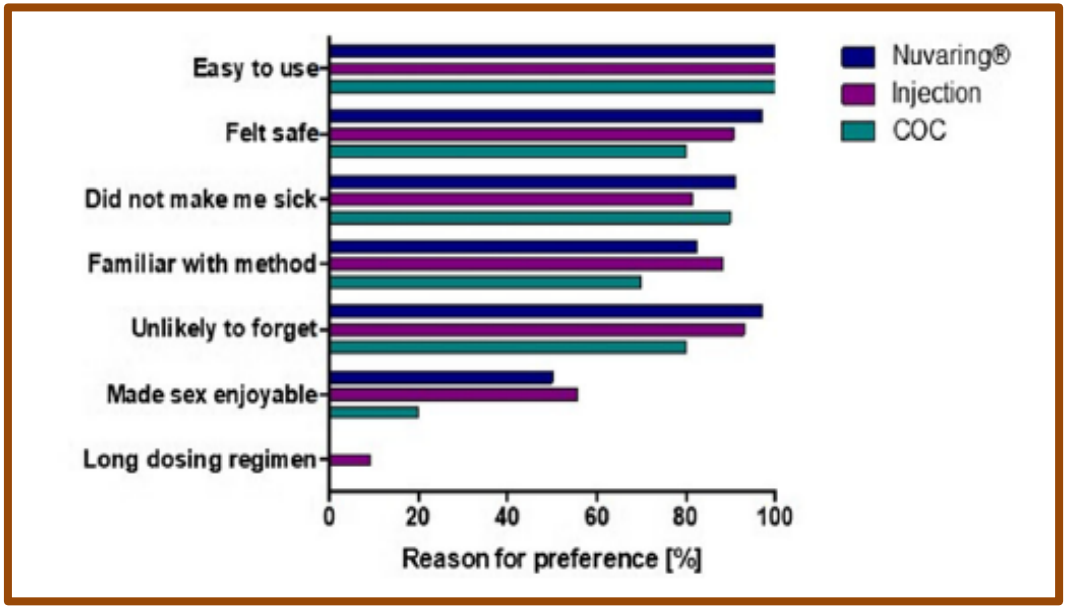


Gill K, et al Lancet child adol 2020

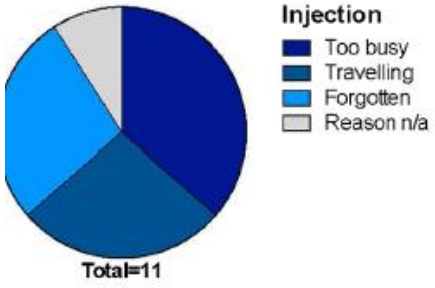
UChoose: An open-label, randomized crossover study to evaluate the **acceptability and preference** for contraceptive options in female adolescents (15 to 19 yo) in Cape Town, as a **proxy for HIV prevention methods**. **(Parental consent waiver)**

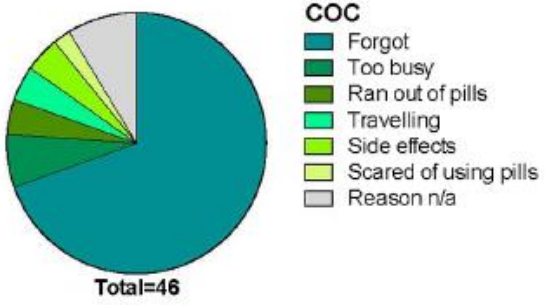
- 180 participants randomised to receive:
  - Monthly vaginal Nuvaring
  - Daily combined oral contraceptive (COC)
  - Bi-monthly injectable contraceptive
- At 16 weeks, participants crossed-over to another modality (all tried the Nuvaring – least familiar contraceptive)

Reasons For



Reasons Against





Adolescent programmes at Emavundleni Research Centre

MTN 034 – REACH STUDY

Adolescent Girls Study - (16 – 21 years of Age)

- Phase 2a cross-over trial
- Comparing oral PrEP to a Vaginal Ring containing Dapivirine
- Daily tablet vs monthly ring
- Started in Sep 2019
- 60 participants

BCG REVAX

To investigate the efficacy of BCG Revaccination against sustained TB infection versus placebo, in previously vaccinated, QFT negative, healthy adolescents.

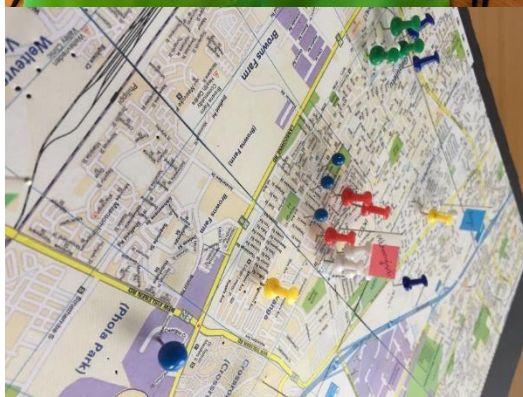
- Adolescent girls and boys (10 – ≤18 years of age)
- First enrolment Feb 2020
- Paused in March 2020, for a few months (Covid-19)
- Recruiting again, accrual period closing Sep 2021
- 172 participants (target is 288)

BCG revax

Trial of Vitamin D Supplementation in Cape Town Primary Schoolchildren

Phase III Double-Blind Randomised Placebo-Controlled Trial of Vitamin D Supplementation for the Prevention of Latent Tuberculosis Infection in Cape Town Primary Schoolchildren

Differences to many other studies:
- School based medical intervention study
- Young children



Lessons Learnt

- Flexibility and adaptability
- Community and school engagement
  - Proactive, regular updates and contact with school leaders
  - Long interval between team rotations
- Ppt Recruitment
  - Logistics of team spread
- Ppt Retention
- Staffing: Attracting and holding onto good staff
  - Community challenges; salary
- COVID
  - Close relationship and engagement with collaborator (chief investigator)
  - Good relationship with ethics committee

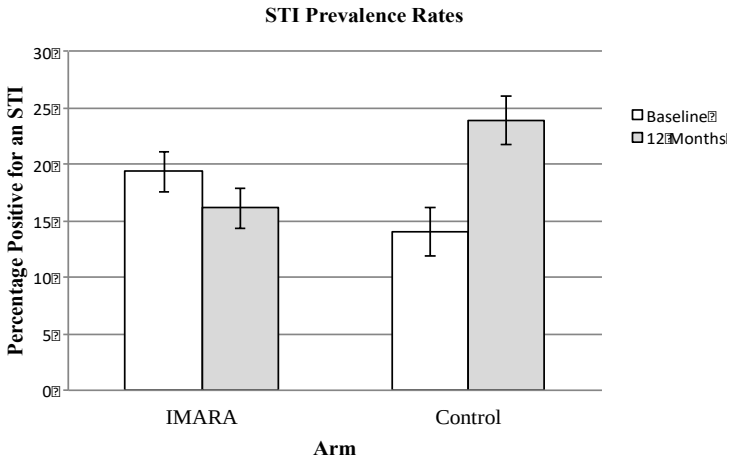
A Multilevel Comprehensive HIV Prevention Package for South African Adolescent Girls and Young Women: IMARA

Goal: Evaluate a comprehensive HIV prevention package that utilizes IMARA a promising family-based behavioral intervention (IMARA) to reduce incident HIV and STI infections, increase PrEP and HTC uptake, and reduce risky sexual activity among SA-AGYW.

TARGET POPULATION
AGYW 15-19 years-old: Sexually and non-sexually active
Female Caregivers

What is IMARA?

- A family based intervention
- Derived from SISTA, SIHLE, and Project STYLE
- Strengthen mother-daughter relationships and communication
- Increase knowledge and improve attitudes and beliefs about HIV prevention
- Build skills for prevention (assertive communication, condom use)
- Improve parental monitoring
- Recognize healthy peer and partner relationships



- 43% lower among girls who received the intervention than control, $p = .013$

- A significant reduction in depressive symptoms by 6 months in girls who received IMARA versus the control

Goals for Girls

A cluster RCT amongst 40 secondary schools in Mitchells Plain/ Klipfontein to evaluate the *feasibility, acceptability and impact* of integrating an in-school SRH education with an after-school sports-based programme (SKILLZ) amongst adolescent female

- Highly acceptable programme - particular appreciation for the girls only safe space and the use of near-peer coach mentors

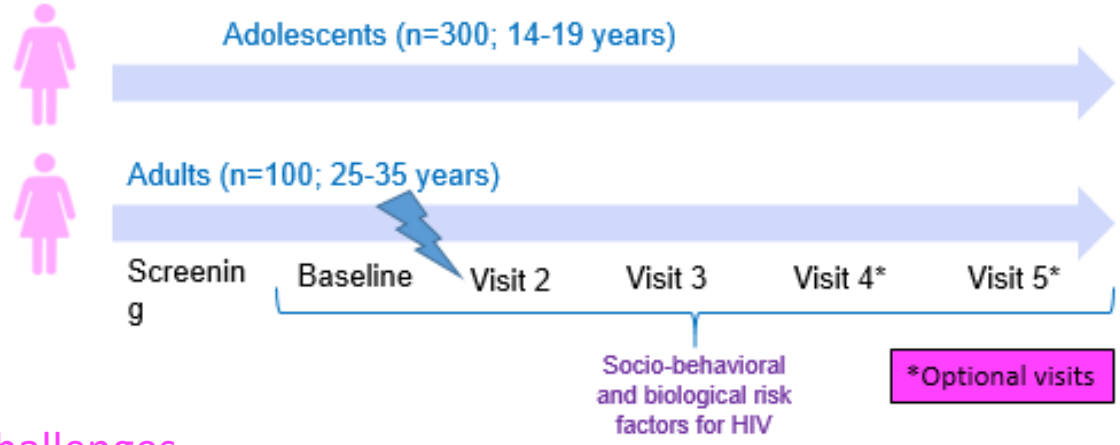
- High acceptability ≠ consistent attendance or implementation support at the school level, with a wide variety of barriers and enablers to implementation observed across schools.

Flexible designs that allow schools to self-organise and adapt to the programme were found to be supportive of implementation. E.g. Allowing schools to opt for sessions during school rather than after your school.

- High attenders were more likely to shown signs of biomedical and behavioural impact, including lesser reductions in STI incidence and increased likelihood to report more gender-equitable responses.

Mucosal injury from sexual contact

- To examine **anatomical and immunological** characteristics of the adolescent state that may contribute to **higher inflammation in the reproductive tract** - enhancing risk of HIV acquisition.
- To compare inflammatory responses to vaginal insertion products (VIPs) and consensual as well as non-consensual or coerced sexual intercourse in adolescent females and older women



Challenges

- **Ethical considerations with the age group**
- **School-going participants** are on a tight schedule
- Study visits are event-driven and unpredictable
- Adherence to study rules and visit schedule
- Small study team
- Safety in and around the PV area
- COVID restrictions, lockdowns, regulations, etc.

Samples collected:

- STI, BV, fungal hyphae, and HIV test results
- Urine for pregnancy tests
- Vaginal pH
- Physical examination & colposcopic imaging
- Cervicovaginal cytokine concentrations
- Cervical immune cell and microbial transcriptomics
- Vaginal microbiome and metaproteomics

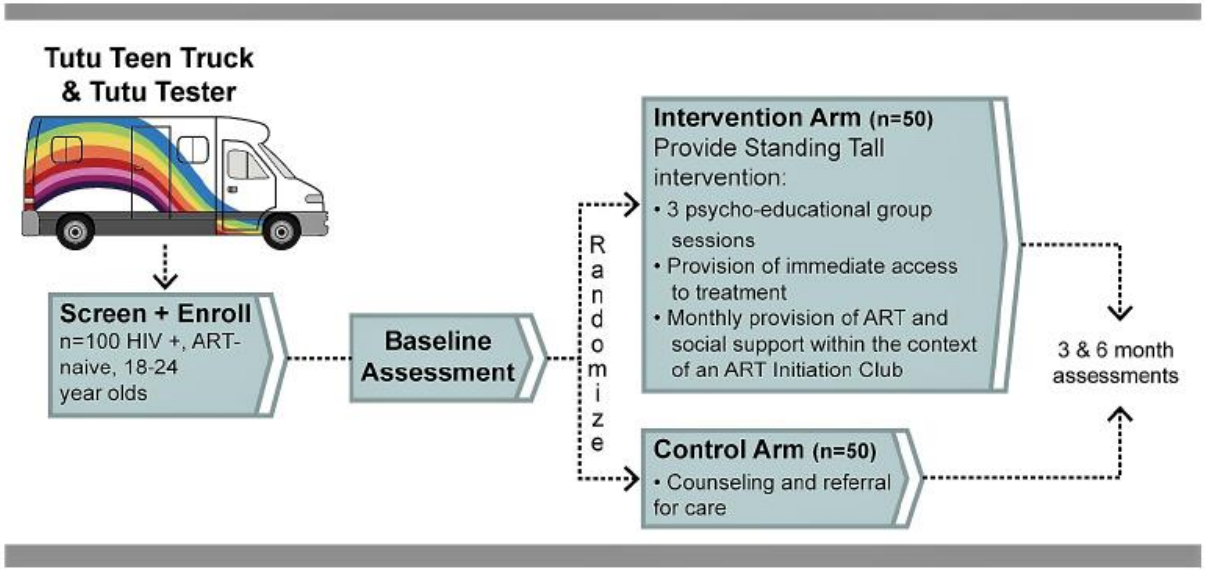
Standing Tall (Yima Nkqo)

Our *central hypothesis* is that newly diagnosed young adolescents and young adults (ages 18-24) avoid engaging in care due to a combination of: contextual factors, social-interaction processes, capabilities, attitudes and beliefs, and motivational appraisals (low self-efficacy).

(1) A three-session group intervention focused on treatment uptake, adherence, and health maintenance (addressing individual factors).

(2) Six months of ongoing treatment and social support (addressing social factors of adherence)

(3) Provision of immediate ART and refills in the context of an ART initiation club (addressing structural factors)



BUDDY: Bidirectional, Upbeat communication and Differentiated, Distanced care for Young people (15-24 yo)

Aim 1: To understand the *acceptability, feasibility, and effectiveness* of a *remote service delivery model* that will help young people living with HIV stay engaged with their HIV treatment during the COVID-19 pandemic

Aim 2: To look at the impact of *the lock-down orders on gender-based violence (GBV)* and other individual, socio-behavioral, structural risk factors over time among all young people living with and without HIV

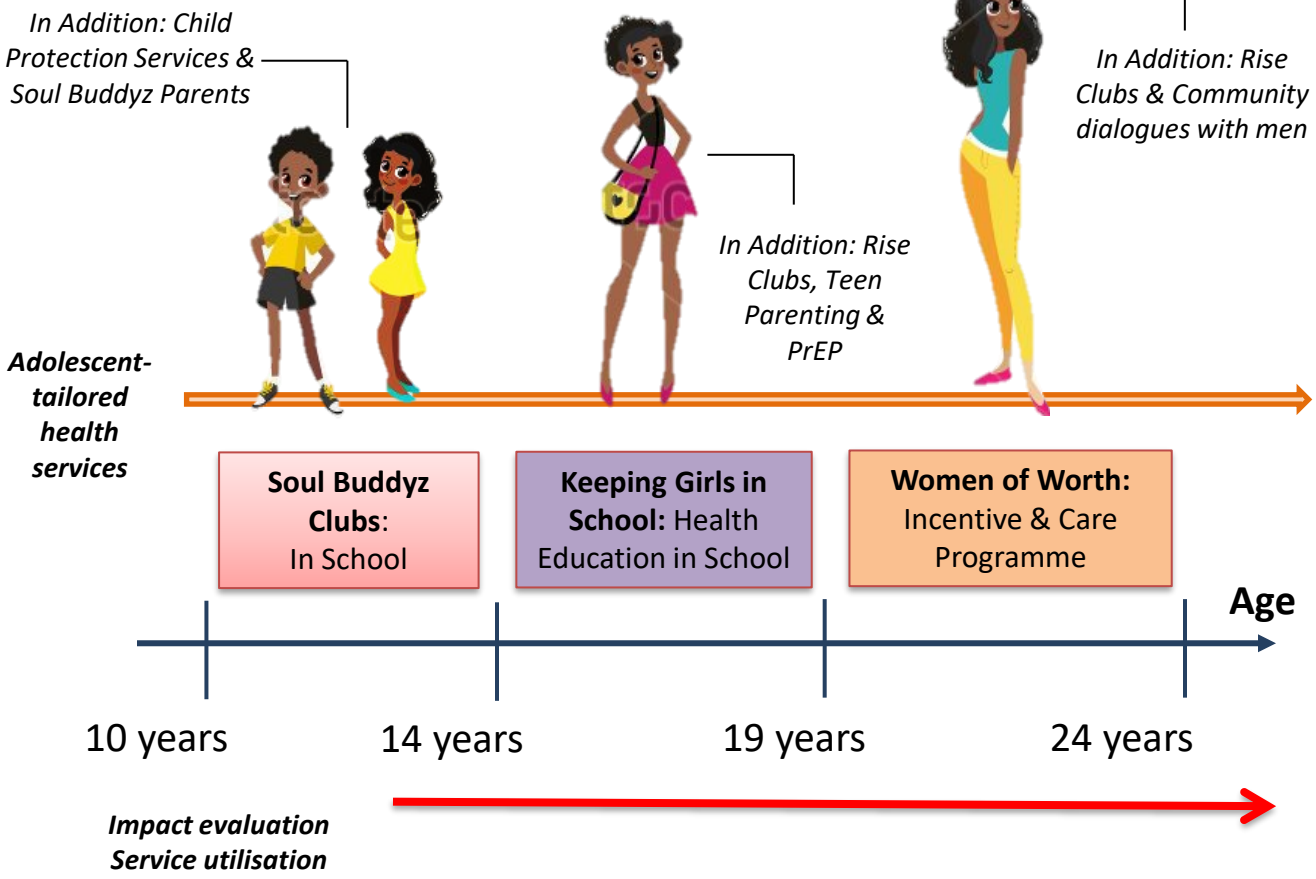
Lessons learnt (so far)

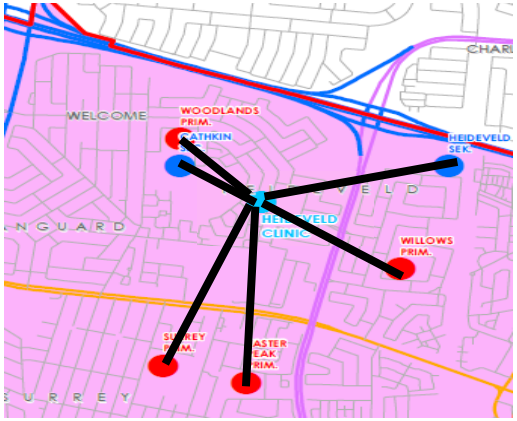
1. There has been a keen interest amongst YPLWH to enroll in BUDDY and to *opt-in* for ART courier service delivery.
2. However, amongst those who were randomized to receive weekly SMS messages, only 1 participant responded that they wanted further contact with our team thus far.
3. Three months into the study attrition has been minimal (no loss to follow up thus far).

ViiV Healthcare

The Zimele Project

The Programme: geared towards those in their 2nd decade of life





✓ **Operational Footprint:**

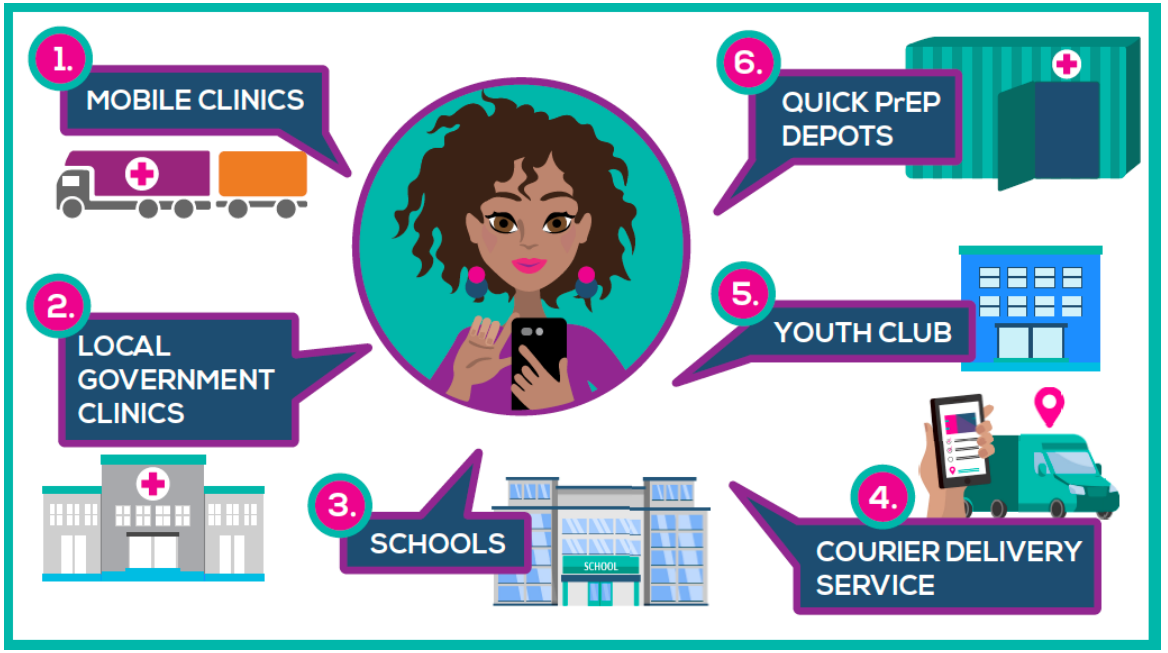
- 50 Primary Schools
- 45 Secondary schools
- 24 Health facilities
- 10 Community Venues

FastPrEP

Aim: **To understand AGYW's preferences for PrEP delivery and to optimize these PrEP delivery modalities for rapid uptake of current and new HIV prevention products**

Offer de-centralized service to AGYW through a Facility-MOBILE-Community model: placing mobile as the hub and a mixture of local clinics, community-based facilities/spaces, and homes (courier service) as the spokes

- Track individuals digitally and allows movement between various service points - flexibility and convenience, maximising opportunities to stay engaged!
- Address diverse needs of AGYW without fragmentation - the "one stop shop"
- Cut out extraneous services not needed by the youthful, largely healthy community
- Decongest and reduce waiting times and wasted time – realise efficiencies both in the service and for the clients.




EXIT
Desmond Tutu HIV Centre
Research Centre

Key lessons learned

- Adolescence is a challenging time for all stakeholders
- Adolescents are unique and fun – but also vulnerable and need special care and attention.
- Invest time – friendliness, confidentiality, patience, eye contact, speak to them (not down) and be non-judgmental.
- Staff continuity important, especially with counselling
- Adolescent friendly area is ideal:
    - Space to relax, music, TVs, computers, desks to do homework while waiting.
    - Don’t necessarily want to share space with adults/younger children
- Adolescent clubs/groups (Covid has been hard!)
- Often hungry……! Fun food -
- Adherence always challenging - need ongoing reminding – calls before and after visits, WhatsApp groups, retention officers visit homes if needed
- Ongoing encouragement (study fatigue) – milestone certificates
- Study specific interventions:
- Music for pelvic exams
- Models/pictures for explanations
- Try and schedule clinics after school/late & Saturdays

Community engagement

Desmond Tutu HIV Centre
Masibambane Ngezandla

- Development of youth CABs
- Staff training and sensitisation
- Study sites made adolescent-friendly
    - Confidentiality, flexibility, information, one stop
- Peer support often welcome
- Mapping of adolescent support services
- Parents/Communities should be included where possible

Desmond Tutu HIV Centre
Masibambane Ngezandla

Conclusions

- We are in the midst of a biomedical prevention revolution
- We are on the cusp of the next wave of vaccine efficacy research
- Adolescents CAN, SHOULD and MUST be part of clinical development plans
- There is NO reason why our new biomedical interventions should NOT include adolescents de novo or as soon as they are available to adults.

Acknowledgements:

Carey Pike
The DTHC and DTHF teams
The DTHF Youth CAB
HAVEG
Adolescents and their families
Other collaborators
Funders who trusted us
Our Ethics committees who have had faith in us!

DESMOND TUTU HIV FOUNDATION