Adherence in Adolescents: An HIV Treatment and Prevention Challenge

Linda-Gail Bekker
Desmond Tutu HIV Centre, UCT | International AIDS Society
Who is the Modern Adolescent?

Gen Z
Born after 1997
Age in 2017: 20 and younger

GENERATIONAL COMPOSITION

DTHF Youth Centre 2017
Adolescents now are not the adolescents of old:

- **Instant communication** is not exciting, it’s a **basic right**
- **Transparency** in the system – political, corporate, organisational – is **expected**
- **Collaboration** and **VOICE** is expected and **obvious**
- **Web-based self-learning approach**: for school, for recipes, for work, for anything.
- **Comfortable within a diverse society**
- **EXPECT innovation** and solutions to today’s problems
The coming Youth Bulge

I in every 4 youth will live in Africa in next 20 years.
Emergence of youth treatment bulge

AIDS leading cause of death among RSA youth
AIDS is the no. 1 cause of death of adolescents in Africa, and the 2nd leading cause of adolescent death worldwide. 85% of young people living with HIV live in sub-Saharan Africa. Young women and adolescent girls account for 75% of new HIV infections in sub-Saharan Africa.

Adolescent Mortality

*Unicef 2012*
Effective Prevention is urgently needed in adolescents.

610,000 people aged 15-24 years were infected with HIV in 2016.

1,700 were young women in South Africa in just last week alone.

32% of new infections occurred outside Africa.
Adolescence is a Developmental Transition: Biological and behavioural vulnerabilities

- Greater Risk Taking
- Present Bias
- Poor knowledge and application
- Lack of abstract thought
- Disregard for rules
- Poor health seeking
- Prejudicial and inadequate health services
- Lack of privacy

Pre-adolescence
10-13 years

Middle Adolescence
14-16 years

Late Adolescence
17-20 years

Emerging Adulthood
21-25 years
Adherence......challenges us all!
Youth Vulnerabilities

- Biological
- Psychological
- Behavioural
- Social
- Structural
Adherence: The extent to which the patient continues the agreed-upon mode of treatment under limited supervision when faced with conflicting demands, as distinguished from compliance or maintenance.
Biologic Basis for Risk

- Early maturation of the Limbic system
  - Impulsive
  - Reactive
  - Moody
  - Emotionally labile
  - Immediate gratification
  - More sensitive to rewards
  - Sensitive to social cues
  - Vulnerable to peer pressure

- Later maturation of Prefrontal Cortex
  - Attention
  - Organizing/Planning
  - Weighing risks & rewards
  - Self-regulation
  - Decision making

- Increased connections between prefrontal & subcortical areas
- Increased modulation of social & emotional inclinations

Barriers to services and care

**Individual**
- Poor Education
- Poor Knowledge
- Poor risk perception
- Social isolation
- Stigma
- Mental health
- Financial Resources

**Health care system**
- Designed for adults/Children
- Discrimination
- Poor knowledge
- Judgmental attitudes
- Lack of privacy
- Lack of confidentiality
- Lack of peer involvement
- Overcrowding
- Fragmentation
- Transport
- Clinic hours

**Other structural barriers**
- Legal consent issues
- Criminalization
- Discriminatory laws or practices

There is a need for HEALTH CARE TRANSITION from child to adult services.

Through adolescence

Blum RW, JAH 1995,
Callahan, et al COP 2001
Separations and Autonomy

Transition in adolescence from teen to adulthood

Separations and Autonomy

Transition in adolescence from teen to adulthood

Transition in Health care from Paediatric to Adult care

Complex interactions.....
Impact of HC Transition on HIV care

Health System.
Different venue
Transportation
Inadequate cover
Inadequate communication

Adult Clinic
Poor mental health support
Non youth friendly SRHs, LGBTs, SUs.

Adolescent
Social isolation
Fear of Disclosure
Decreased adherence
Reluctance to “retell” history
Paediatric service is “family”

Fair C, et al AIDS CARE 2011
Adolescents with chronic disease...

- Developmental delays
  - Psychosocial, emotional, physical
- More social isolation, suicide and depression
  - Blum RW, JAH 1995
- More likely to take risks that impact health
- Poor adherence to have greater impact
  - Brown et al JCPP 2000; Watson Paed Neph 2000; Timms BrJN 1999
- Concerns about body image overshadowed/exaggerated
- Feelings of isolation when all adult focus on condition.
Engage – to promote adherence?

Adherence to chronic medication in adolescence: not just an HIV problem

Insulin adherence in adolescents with Diabetes:
- Adolescents have poorer glycaemic control and higher rates of acute complications than adults. Snyder, 2014
- Recommendations incl. positive psychological interventions

Adherence to and continuum of hormonal contraceptives:
- Breakdown social stigmas - 11% of all births worldwide come from adolescent girls. WHO, 2016
- Enhanced counselling & intensive reminder systems, including phone call follow up and daily text messages Halpern et al., 2014
Additional issues with HIV infection.

- Cognitive, physical, emotional delays
- Increased perceptions of stigma and discrimination
- Issues with disclosure to HCW, partners, others
- Issues with sexuality, fertility intent.
- Parental loss, family sickness.
Treatment outcomes in HIV-infected adolescents attending a community-based antiretroviral therapy clinic in South Africa

Antiretroviral Therapy Adherence, Virologic and Immunologic Outcomes in Adolescents Compared With Adults in Southern Africa

Antiretroviral medication adherence among the REACH HIV-infected adolescent cohort in the USA
Adherence in the context of HIV

- Care + Support
  - Pill pick ups
  - Viral load suppression

- Prevention + PrEP
- Adolescent Adherence
- ART + Monitoring

- SRHs + Contraception
  - HIV testing
  - Couples counselling
  - Pill pick ups
  - Drug level monitoring
  - Condom pick ups

- Keeping appointments
- Attending support groups

Pill counts
Pill pick ups
Appointments
Double Helix Cascade

COUNSELING AND TESTING

UNINFECTED

INFECTED

Link

ADHERENCE

SRHs Uptake

ART Uptake

SRHs Persistence

ART Persistence

HIV/Preg/STI Free

VIRAL SUPPRESSION

ADHERENCE

Hosek, Bekker 2015 JIAS

Contraceptives

Condoms

PrEP

MMC

STI screening

Harm reduction

Harm reduction

Contraceptives

PrEP

MMC

STI screening

Harm reduction
Retention: HC Transition.
Loss to follow up of HIV+ adolescents on ART, before and after transition to next age band

<table>
<thead>
<tr>
<th>Age at ART start</th>
<th>Rate before transition to next age-band (per 100 person years), (95% CI)</th>
<th>Rate after transition to next age-band (per 100 person years), (95% CI)</th>
<th>RR (95% CI), p-value</th>
<th>Adjusted* RR (95% CI), p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Older children (5–9 years)</td>
<td>5.07 (4.10, 6.26)</td>
<td>2.27 (1.48, 3.48)</td>
<td>0.45 (0.28, 0.72), p = 0.001</td>
<td>0.63 (0.37, 1.08), p = 0.094</td>
</tr>
<tr>
<td>Young adolescents (10–14 years)</td>
<td>3.39 (2.59, 4.43)</td>
<td>4.95 (3.44, 7.12)</td>
<td>1.46 (0.93, 2.30), p = 0.100</td>
<td>1.54 (0.94, 2.55), p = 0.089</td>
</tr>
<tr>
<td>Older adolescents (15–19 years)</td>
<td>9.54 (7.47, 12.19)</td>
<td>16.26 (10.49, 25.20)</td>
<td>1.70 (1.03, 2.81), p = 0.038</td>
<td>1.79 (1.05, 3.07), p = 0.033</td>
</tr>
</tbody>
</table>

*adjusted for time on ART, sex and calendar year. LTFU = loss-to-follow-up.

Kranzer et al., JIAS, 2017
Retention: Age Matters.
Loss to follow up rate of HIV+ adolescents in different age groups according to when they started on ART

<table>
<thead>
<tr>
<th>Current age</th>
<th>Rate in those who started ART in this age group (per 100 person years)</th>
<th>Rate in those who started ART in a younger age group (per 100 person years)</th>
<th>RR (95% CI), p-value</th>
<th>Adjusted* RR (95% CI), p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Young adolescents</td>
<td>3.39 (2.59, 4.43)</td>
<td>2.27 (1.48, 3.48)</td>
<td>1.49 (0.90, 2.47), p = 0.121</td>
<td>1.33 (0.76, 2.32), p = 0.315</td>
</tr>
<tr>
<td>(10–14 years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Older adolescents</td>
<td>9.54 (7.47, 12.19)</td>
<td>4.95 (3.44, 7.12)</td>
<td>1.93 (1.24, 2.99), p = 0.003</td>
<td>1.70 (1.05, 2.77), p = 0.032</td>
</tr>
<tr>
<td>(15–19 years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*adjusted for time on ART, sex and calendar year. 
ART = antiretroviral therapy.

Older adolescents have higher rates of loss to follow up generally, but early starters on ART have lower rates of loss to follow up in both age categories.

Kranzer et al., JIAS, 2017
Pill taking in the HIV Context:
Treatment ↔ Prevention

ONE ARV PILL A DAY
Fixed Dose Combination ARV

A PILL TO PREVENT HIV

3 ARV pills in 1. Taken once a day.
Factors associated with self-reported adherence among adolescents on ART in Zimbabwe, Gross et al., 2015, AIDS Care
Clinic-level factors & adherence

Factors associated with self-reported adherence among adolescents on ART in Zimbabwe, Gross et al., 2015, AIDS Care

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Overall (n=262)</th>
<th>Excellent Adherence (n=101)</th>
<th>Suboptimal Adherence (n=161)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Visit frequency</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 4x/year</td>
<td>31 (12%)</td>
<td>12 (12%)</td>
<td>19 (12%)</td>
<td>0.35</td>
</tr>
<tr>
<td>4x/year</td>
<td>36 (14%)</td>
<td>10 (10%)</td>
<td>26 (16%)</td>
<td></td>
</tr>
<tr>
<td>&gt;4x/year</td>
<td>192 (74%)</td>
<td>78 (78%)</td>
<td>114 (71%)</td>
<td></td>
</tr>
<tr>
<td><strong>Action Taken for Missed Visit</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.04</td>
</tr>
<tr>
<td>None</td>
<td>146 (56%)</td>
<td>49 (49%)</td>
<td>97 (61%)</td>
<td></td>
</tr>
<tr>
<td>Telephone call or SMS to patient</td>
<td>37 (14%)</td>
<td>21 (21%)</td>
<td>16 (10%)</td>
<td></td>
</tr>
<tr>
<td>Contact parent/guardian</td>
<td>67 (26%)</td>
<td>28 (28%)</td>
<td>39 (24%)</td>
<td></td>
</tr>
<tr>
<td>Home visit</td>
<td>10 (4%)</td>
<td>2 (2%)</td>
<td>8 (5%)</td>
<td></td>
</tr>
<tr>
<td>Parent/guardian in room for clinic visit</td>
<td>117 (45%)</td>
<td>56 (58%)</td>
<td>61 (38%)</td>
<td></td>
</tr>
<tr>
<td><strong>Always</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Participate in group meetings for HIV+ children run by professional</td>
<td>145 (56%)</td>
<td>64 (65%)</td>
<td>81 (51%)</td>
<td>0.02</td>
</tr>
<tr>
<td>Participate in group activities for HIV+ children</td>
<td>146 (56%)</td>
<td>62 (62%)</td>
<td>84 (53%)</td>
<td>0.15</td>
</tr>
<tr>
<td>Participate in peer run support group</td>
<td>128 (49%)</td>
<td>47 (47%)</td>
<td>81 (52%)</td>
<td>&gt;0.5</td>
</tr>
<tr>
<td>Received individual counseling/mentoring</td>
<td>138 (53%)</td>
<td>54 (53%)</td>
<td>84 (53%)</td>
<td>&gt;0.5</td>
</tr>
</tbody>
</table>

- More frequent contact
- Rapid follow up if missed
- Optimal adherence when no action was taken for a missed visit
- Support of caregiver
- Adolescent involved in own care

**Significantly associated with excellent adherence**
Antiretrovirals for HIV prevention: pre-exposure prophylaxis (PrEP)

The same medications that revolutionized HIV treatment be harnessed to prevent new infections – in parallel ways as treatment and chemoprophylaxis.

To use PrEP, a person must be:

• HIV-negative
• STI-free
• Able to take pills daily whilst potentially exposed to HIV.
Correlates of low adherence in oral PrEP trials

- Younger age (Partners PrEP, VOICE)
- Not partnered (VOICE, FEM-PrEP)
- Low perception of risk? Stigma? (FEM-PrEP, others?)
- Less sex (Partners PrEP, iPrEx)
- Alcohol use (Partners PrEP)
- Not attending appointments (Partners PrEP, VOICE, others?)

Key factors diminish adherence to daily preventative therapy (or to optimal clinical trial participation).
Adherence to daily oral PrEP is a challenge to adolescents:

**Individual level challenges:**
- **Non-familiarity** with ARV-based prevention
- **Stigma** – need for normalisation of HV prevention
- **Social Support** – parents, peer and partner
- Current lack of **alternatives** to an oral daily formulation – although multiple are in the pipeline

**Structural Challenges**
- **Cost** of PrEP – targeted PrEP is most feasible if gov. provided
- Limited **adolescent-friendly healthcare** systems

Source: Hosek et al., 2015
If we offer it - will adolescents take it?

Adherence

Efficacy

Age

RCTs of pre-exposure prophylaxis with antiviral agents in HIV negative
Lack of Efficacy Restricted to Adolescent Age Group

Baeten J et al. NEJM 2016;375:2121-32

### Association of Adherence with Age

Adherence was significantly lower among young women aged 18-21 yrs

→ compared to women 18-21 years, women 22-26 yrs had 1.6-fold higher adherence and women 27-45 yrs had 4.1-fold higher adherence

**Definition “Good Adherence”**:  
- High plasma DPV >95 pg/mL  
- Low ring DPV <23.5 mg

---

Source slide: Lynne M. Mofenson, M.D.
Open Label PrEP: Age and Adherence

• There was no difference in adherence as measured by TFV detection in plasma by randomized group by age <25 years vs > 25 years

Pt Reporting Sex in Previous Week with Detectable TFV Levels by Age

<table>
<thead>
<tr>
<th>Weeks on study</th>
<th>Age (yrs)</th>
<th>Daily arm</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>&lt;25</td>
<td>87.0</td>
</tr>
<tr>
<td>30</td>
<td>&lt;25</td>
<td>81.3</td>
</tr>
<tr>
<td>10</td>
<td>&gt;25</td>
<td>100</td>
</tr>
<tr>
<td>30</td>
<td>&gt;25</td>
<td>76.9</td>
</tr>
</tbody>
</table>

>40 ng/ml in plasma means a tablet was taken in last 24 hours

Bekker LG Lancet HIV 2017
Synthesis- A model of Mutuality : ADAPT cohort

- The Naysayers
- The fence sitters
- Open minded- Need our help
- Prevention champions

Relationship- implies a good experience, with something to be gained


So.... less about AGE and more about relationship and engagement
Open label PrEP and young women  
**Prya M et al.**  *JAIDS* 2018;77:41-45

- 310 serodiscordant couples Kenya/Uganda on PrEP (Mems cap)

  - >90% efficacy of PrEP compared to expected number infections including in youngest women.

<table>
<thead>
<tr>
<th></th>
<th># infections/Incidence OBSERVED</th>
<th># infections Incidence EXPECTED</th>
<th>Efficacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>3/0.5 per 100p-y</td>
<td>41/7.6 per 100 p-y</td>
<td>93% (77-98)</td>
</tr>
<tr>
<td>&lt;25 yrs</td>
<td>1/0.7 per 100 p-y</td>
<td>11/7.8 per 100 p-y</td>
<td>91% (29-99)</td>
</tr>
</tbody>
</table>

Source slide: Lynne M. Mofenson, M.D.
Pluspills cohort: 150 (15-19 yo)

- “Self Selection” – adolescents who rated themselves at risk
- STI rates – 52% tested positive for at least 1 STI at screening
- 9% pregnant at screen
- 2% HIV infected at screen
- 44% reported condomless sex
- 27% concurrent partners
- 20% Intergenerational sex

Gill K, et al. IAS2017
One third of participants persisted with PrEP
Unknown if these were the most at risk participants

Gill K, IAS 2017
ATN 113 (Project PrEPare)

Designed to explore the safety, acceptability, and feasibility of PrEP among young MSM at risk for HIV infection (United States, 300 HIV-negative young MSM, aged 15-17 years).

Results released July 2016:

- The majority of participants achieved protective drug levels during monthly visits.
- BUT adherence decreased with quarterly visits.
- HIV incidence was still high despite PrEP provision, suggesting high background incidence.
- Regulatory approvals for youth under 18 years are required to foster support for youth-friendly settings that will optimize PrEP use.

Hosek S  AIDS Conf 2016
Solutions: what works, what could work?
HPTN 082: Design & PrEP uptake

HPTN 082: Evaluation of daily oral PrEP as a primary prevention strategy for young African women

Study Population
Uninfected women
Ages 16-25 yrs
Johannesburg & Cape Town, South Africa
Harare, Zimbabwe

Target Enrollment
• 400 women who accept PrEP at enrollment
• ≤ 200 women who decline PrEP at enrollment

Primary objectives:
Assess the proportion and characteristics of women who accept versus decline PrEP
Assess PrEP adherence using drug levels in young women

Figure 1: PrEP uptake overall and by site

<table>
<thead>
<tr>
<th>Location</th>
<th>PrEP accepted</th>
<th>PrEP not accepted</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>95%</td>
<td>5%</td>
</tr>
<tr>
<td>Harare</td>
<td>97%</td>
<td>3%</td>
</tr>
<tr>
<td>Cape Town</td>
<td>99%</td>
<td>1%</td>
</tr>
<tr>
<td>Johannesburg</td>
<td>88%</td>
<td>12%</td>
</tr>
</tbody>
</table>

PrEP accepted  PrEP not accepted
HIV Incidence: Pluspills

No HIV infections in 130 adolescent years of follow up.

Preliminary Data Oct 2016

HIV Incidence: 7.4 per 100 person years (95% CI: 4.3-12.8)

Pluspills: Motivators

- Perceived Risk
- Determination to remain HIV negative
- Desire
- Family/Friends
- Reimbursement

It was easy for me to participate because I know us teenagers are not perfect, we do things, we party and I thought I needed PrEP, so it was easy for me.

I said knowing that you are safe, even if you do a little mistake you know that you are safe.

148 adolescents 15-19 years – Parental proxy consent

Gill K, IAS 2017
Lessons learnt from getting adolescents onto contraceptives:

- 80 000 unplanned pregnancies annually in SA – but only 40% of adolescent girls are on contraception

- Adolescents do not plan social encounters
- The Imagined Audience – fear & embarrassment
- Need for the construction of an entry point into the health system
- Risk perception
- Influential relationships – excluding medical health professionals

Taking this into account, helping to build an evidence-base of what will work for PrEP

Source: Daley, 2014
Lessons from oral contraception: interventions to optimised adherence. A U.S. RCT evaluated two interventions to improve compliance amongst 1,155 adolescent (16-24 yrs) first-time oral contraception users:

- Standard of Care
- Once-off basic education and behavioural counselling
- Once off counselling + monthly phone calls

- The 2 intervention groups showed increased compliance compared to the standard of care group amongst first time users initially; with phone calls particularly helpful for younger participants (16-19 yrs) **but**
- Over time, clinic-based education, with or without phone call follow up, was not found to be effective in increasing accurate or long-term use.
- **The development of cues** (objects or actions that act as a reminders to take medication) **lead to improved compliance regardless of intervention.**

*Berenson, 2011 Dissertation*
Lessons from oral contraception: psychological determinants of adherence. A cross-sectional survey to determine modifiable psychological determinants of oral contraception adherence amongst 130 female university students.

The 2 strongest psychological predictors of good adherence were:

Perceived behavioural control
“I am capable of taking my contraception.”

Coping planning:
“I have a detailed plan on how to take my contraception”
“I have thought about possible setbacks and how to deal with them”

Molloy, Graham & McGuinness, 2012
3 Ps for Prevention: Partners, PrEP, and Payment.

Who is in your taxi?
Plans for pill taking
Provide a weekend pill box
Give drug level feedback
Incentivise if levels ok

>90% of women (median age 19yrs) have detectable tenofovir in the first 3 months.
For the first time in my life – I own my sexuality

Personal Control
Part of a movement

Its like a pregnancy pill- if you take a pill you don’t get pregnant......if you take PrEP you wont get HIV.
PrEP decision support tool

- PrEP is new to AGYW in our community
- Limited time with clients in busy clinic setting

WHAT ARE MY OPTIONS TO PREVENT HIV?

People who are HIV-negative can use HIV prevention methods to lower their chance of getting HIV. These may be best used in combination!

- Tap any method below to get more information.

**PrEP**: an HIV prevention medicine that I can take daily before and after sex

**PEP**: an HIV prevention medicine that I can take daily after sex for a month

**Condoms**
(Male & Female)

**Decreasing my sex partners**

**Knowing if my partner has HIV**

**If my partner has HIV, he takes HIV medicines**

Using HIV prevention and family planning helps us stay healthy and have loving, healthy relationships and families. We use these methods for one or many reasons. Here are some reasons why:

- "I am sexually active and don’t always use condoms, so I use HIV prevention."
- "I recently had a sexually transmitted infection, so I use HIV prevention."
- "I use alcohol or drugs before sex, so I use HIV prevention."
- "I have new partners, so I use HIV prevention."
- "I think my partner has other partners, so I use HIV prevention."
- "I don’t know my partner’s HIV status, so I use HIV prevention."
- "My partner is violent or controlling, so I use HIV prevention."
- "Many young women get HIV from partners who are 5 or more years older than them. My partner is older than me, so I use HIV prevention."
- "My partner has HIV but isn’t taking HIV medications as he has been taking medications for..."
Lessons from oral contraception: proposed strategies to improve compliance

- **Education and counselling** – with inclusion of graphic instructions on what to do when you miss a dose
- **The use of reminders** – with immediate enrolment onto an online reminder system after initiation onto treatment
- **Same day initiation** – found with oral contraception to improved short term continuation but no impact on the long term.
- **Longer medication supplies** – for oral contraception supplies are recommended up to one year where possible.

Choi & Dempsey, 2014
WHO ENROLLED IN THE STUDY?

A diverse group of women were enrolled in the CHOICE Program in the St. Louis region. Each age, education, and race group had women in each category.

WHAT METHOD DID WOMEN CHOOSE?

The majority of women chose a hormonal IUD as their method of contraception. Teens also chose LARC methods.

AGE (Years)

- 36-45
- 26-35
- 21-25
- 18-20
- 14-17

EDUCATION

- College degree
- Some college
- High school or less

RACE

- Black
- White
- Other

Numbers: 14-17 years (45.84% IUD, 14.44% Implant), 18-20 years (52.25% IUD, 22.43% Implant)

CHOICE Program, 2016, USA
UChoose study

An Open-Label, Randomized Crossover Study to Evaluate the Acceptability and Use of Contraceptive Options in Healthy HIV-Uninfected Female Adolescents, 16-22 Years of Age as a surrogate for HIV prevention intervention preferences.
100 Healthy 16 and 22 year old women

Randomised 1:1:1

4 months follow up with 2 x 2 monthly scheduled visits

Dapivirine Ring

Oral PrEP

LA PrEP

50 young women

25 young women

25 young women

50 young women

25 y w

25 y w

50 young women

4 months follow up with 2 x 2 monthly scheduled visits

Uchoose Gill, K
Contraception History

Reported Contraception Use at Enrolment

<table>
<thead>
<tr>
<th>Contraception Type</th>
<th>Hypothesized Prevalence of Use</th>
<th>Actual Prevalence of Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral Pill</td>
<td>5%</td>
<td>8%</td>
</tr>
<tr>
<td>Injectable</td>
<td>60%</td>
<td>75%</td>
</tr>
<tr>
<td>Naïve to Hormonal Contraception</td>
<td>35%</td>
<td>17%</td>
</tr>
</tbody>
</table>

- BUT... 28% of participants had not used contraception within the last 2 months

STI Diagnoses at Screening-Gene Xpert

<table>
<thead>
<tr>
<th>STI</th>
<th>Prevalence (% of participants)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacterial vaginosis</td>
<td>42.3</td>
</tr>
<tr>
<td>HSV-2</td>
<td>29.2</td>
</tr>
<tr>
<td>Chlamydia</td>
<td>30.8</td>
</tr>
<tr>
<td>Gonorrhoea</td>
<td>10.8</td>
</tr>
<tr>
<td>Trichomonas vaginalis</td>
<td>9.2</td>
</tr>
</tbody>
</table>

(Prelimin) Uchoose Gill, K
Acceptability

Based on their experience with uChoose products, participants were asked which would be their preferred method of HIV prevention.

- Oral Pill: n=34
- Vaginal Ring: n=29
- Long-acting Injectable: n=8

Preliminary Uchoose Gill, K
Adherence:

• Percentage of pill and ring users reporting only 1 or fewer days of imperfect adherence in the last week

• 92% of those using long-acting injectable contraception received their injection on time

Preliminary Uchoose Gill, K
PrEP Adolescent network and demo studies

- HPTN 082: Randomised Biofeedback Oral TDF/FTC
- MTN 034: Randomised Vag. Ring vs Oral PrEP
- Power: FP/Youth clinic/Mobile same day oral PrEP
- 3P: Randomised CCT for detectable drug levels
- Community PrEP: Randomised on adherence club vs clinic vs CDU oral PrEP pick up.
- HPTN 086: Cabotegravir LA for youth
Can we find a BREATHER from ART for adolescents?

199 perinatally-infected adolescents (8-24 yrs) from 11 countries. Stable on an Efavirenz treatment regimen for at least 12 months at baseline.

**BREATHER Study:** Daily treatment vs. Short Cycle Treatment (2 days off)

Benefits:
- Reduce treatment fatigue
- Cost saving (reduced ART use)
- Acceptable amongst adolescents

Limitations:
- Requires counselling & understanding of patient
- Follow up time was short (12 months)
- All patients were stable on ART already (might not work for those who already have treatment failure)

Future: longer follow up, different drug regimens, resource-limited settings.

Short cycle treatment was non-inferior to daily treatment.
- The treatment group had 6% virological rebound vs. 7% of control.
- No difference in resistance mutations or adverse effects.

BREATHER Study, Ferrand & PENTA 16 group, 2016
So what CAN we do.....

Together......
Understand what adolescents want-
Specific adolescent preferences for sexual and reproductive health services

Adolescent Friendly Services
- Appropriate info and services tailored to them
- Confidentiality and privacy

Flexibility:
Opening times that suit them, is close to them & adapts around their school obligations

Comprehensive services of high quality
- Counselling & education
- Contraceptives
- Link to adoption services & pre/post-natal care

Phil Smith, SAMJ 2018
Engage – where?

- Non judgmental
- Staff know-how
- Less fragmentation
- Staff continuity
- Flexi hours
- Affordable
- Peer involvement
- Relaxed
- Psychosocial support
- Other services available

Smith P, et al SAMJ
Double Helix Cascade

COUNSELING AND TESTING

Positive
Negative

Adolescent centred
Adolescent friendly
Adolescent driven
Community based

Hosek, Bekker 2015 JIAS
Differentiated care is applicable across the HIV care continuum

Differentiated care

- **PREVENTION**
- **90%**
- **DIAGNOSED**
- **90%**
- **ON TREATMENT**
- **90%**
- **VIRALLY SUPPRESSED**

Children, adolescents, pregnant and breastfeeding women and members of key populations should not be excluded from clinically stable client care based on their population characteristics: age, pregnancy or breastfeeding status, drug use, occupation, sex, gender identity or sexual orientation. In principle, services should be tailored to keep families together as much as possible to simplify access and reduce cost.

Anna Grismrud, IAS 2018
ART adherence clubs

Community ART groups (CAGs)

Health care worker-managed group

Client-managed group

Fast track ART refill collection at facility

• Mobile outreach
• Fixed community ART refill distribution
• Home ART delivery

Facility-based individual

Out-of-facility individual
Youth Clubs in South Africa

- Pilot data from MSF supported project in Khayelitsha, South Africa between March 2012-May 2015
- Clubs met monthly for the first 6-12 months, thereafter two monthly at the clinic
- ART refills, HIV clinical management and FP were integrated
- Youth Clubs included ART ineligible youth (21.7%), newly ART initiated youth (52.8%) and stable on ART youth (25.5%)
- School going and out of school Clubs
- 12-month retention was 81.7% (95% CI 76.4-86.0%)
  - 86.4% among newly initiated
  - 94.3% among stable on ART

Wilkinson et al, AIDS 2016, TUPEE490
Zvandiri and the CATS model in Zimbabwe

• Started in 2004 as one support group of ALHIV
  • “Zandiri” – “As I am” in Shona
• Provides differentiated care for children, adolescents and young people with HIV, 0-24 years of age
• Implemented by Community Adolescent Treatment Supports (CATS)
  • HIV positive 18-23 year olds
  • Trained and mentored to provide support across the HIV cascade
• Adopted by the Government of Zimbabwe
• Recommended for scale up by WHO, UNAIDS, AIDStar One, UNICEF, SADC
Coverage and scale up

- 1047 trained, mentored CATS in 51 districts of Zimbabwe
- Integrated within 456 health facilities
- DSD for 46,441 HIV positive children, adolescents and young people
- Estimated cost of $36USD/beneficiary (CHAI)
- Funded through: PEPFAR (USAID, CDC/ITECH), EGPAF (CIFF), UNICEF, Child Protection Fund, ELMA, CBM
- Through the Zvandiri Technical Support Unit support 85 CATS in Mozambique, Tanzania and Swaziland
Community-based support (CBS) for adolescent ART adherence: CBS associated with reduced patient attrition and reasonable cost-effectiveness.

South African study used clinic-linked, lay health workers to support adolescents receiving ART. CBS workers made home visits to determine challenges for adherence and subsequently provided counselling, appropriate interventions and referrals.

6706 participants enrolled in the study. Participants receiving CBS:
- Showed reduced mortality
- 40% lower loss to follow up
- After 5 years, 18.8% of CBS participants verses 37.2% of non-CBS participants failed to achieve viral suppression.
- The intervention was found to be cost-effective, US$600 per patient loss averted.

Efficacy in reducing attrition was 42.2% after 1 year and 35.9% after 5 years.

Fatti et al., 2017, JIAS
POWERS: an open-level cohort study to evaluate DSD for PrEP.....FP/YC clinic/Mobile

1000 HIV-uninfected women (16-25 years)

- Initiates PrEP – Why?
  - Cost
  - Relation to pregnancy, sexual exposure & contraceptive use

- Doesn’t initiate PrEP - Why?
  (Participants retained in study regardless of PrEP choice)

- PrEP Use
  - Patterns of use & Adherence
  - Delivery Methods
  - Timing of & reasons for discontinuation

- HIV Incidence?
- HIV Resistance?
PrEP Accessibility.....

PrEP - the pill that protects you from HIV

PrEP + CONDOMS = Safe sex

PrEP. Delivered to you.

The fastest 4 Steps to PrEP treatment:
1. Register
2. Pathology test
3. We deliver
4. Follow up care

about the pill that protects you from HIV. Information visit www.prepclub.co.za

Iyeza Health

tutu teen truck

POWER
Prevention Options for Women Evaluation Research

USAID
FROM THE AMERICAN PEOPLE

PEPFAR
Engage – How?

• Gain-and loss-framed messages are differently persuasive.
• If a behavior leads to a certain outcome, gain-framed messages work well.
• If a behavior leads to a more uncertain outcome, then loss-framed messages more effective.
• Gain-framed messages can be more persuasive than loss-framed messages.
• In general, adolescents prefer certain alternatives to uncertain alternatives.

Adapted Rothman and Salovey, 1997; 2006
A harm reduction approach ..... Normalises behaviour (without medicalisation) whilst reducing risk.

This ?

Or this ?
Most important ingredients of young person engagement.....

- **Relationships** are key – peers, trusted adults, staff
- **Support** from home or intimate partner helps a lot
- **Accessibility**, speed
- **Ease of use** – no time wasting, no PT,
- **Tailored**, relevant information with trusted guidance on choices
- **Choice**- but presented with clarity
- **Fun** and Innovation
- **No stigma or bad feeling .....leading to suspicion**
- **Gain**-framed messages are great - if accompanied with good experience
“In control and in a movement.....”

Behaviours Centred Design: Aunger R, et al, LSHTM

McCann Advertising

3P: Cellum, Bekker 2016/7
Promising Interventions

Further research is needed to validate these approaches, but small studies have shown promise for the following interventions amongst HIV-positive adolescents:

<table>
<thead>
<tr>
<th>LEVEL</th>
<th>INTERVENTIONS</th>
<th>STUDIES IN THIS REVIEW INFORMING RECOMMENDATION</th>
<th>ADOLESCENT GROUP</th>
</tr>
</thead>
<tbody>
<tr>
<td>PUBLIC HEALTH SYSTEM-LEVEL</td>
<td>Decentralisation</td>
<td>Davila(^{18})</td>
<td>Pre-ART clinic attenders</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ART clinic attenders</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ART failure/poor adherence</td>
</tr>
<tr>
<td>PROVIDER/HEALTH FACILITY-LEVEL</td>
<td>Adolescent/youth-friendly opening hours</td>
<td>Lamb(^{23})</td>
<td>Pre-ART clinic attenders</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ART clinic attenders</td>
</tr>
<tr>
<td></td>
<td>Adolescent-specific services</td>
<td>Davila(^{18}), Lamb(^{23})</td>
<td>Pre-ART clinic attenders</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ART clinic attenders</td>
</tr>
<tr>
<td>COMMUNITY-LEVEL</td>
<td>Peer-support</td>
<td>Funck-Brentano(^{20})</td>
<td>ART clinic attenders</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>ART failure/poor adherence</td>
</tr>
<tr>
<td>INDIVIDUAL-LEVEL</td>
<td>Education and counselling (including education</td>
<td>Lyon(^{26}), Berrian(^{16}), Letourneau(^{24}), Kailin(^{22}), Bhana(^{17}), Lamb(^{23})</td>
<td>Pre-ART clinic attenders</td>
</tr>
<tr>
<td></td>
<td>sessions, individual and group counselling,</td>
<td></td>
<td>ART clinic attenders</td>
</tr>
<tr>
<td></td>
<td>motivational interviewing and case management)</td>
<td></td>
<td>ART failure/poor adherence</td>
</tr>
<tr>
<td></td>
<td>Directly observed therapy</td>
<td>Glickman(^{21}), Parsons(^{26})</td>
<td>ART failure/poor adherence</td>
</tr>
<tr>
<td></td>
<td>Adherence support devices</td>
<td>Berrian(^{16}), Foster(^{19})</td>
<td>ART clinic attenders</td>
</tr>
<tr>
<td></td>
<td>Financial incentives</td>
<td>Foster(^{19})</td>
<td>ART failure/poor adherence</td>
</tr>
</tbody>
</table>

**Figure 2** Typology of interventions to improve adolescents’ linkage, retention and adherence to ART. Where studies evaluated interventions consisting of more than one component, or complex multifaceted interventions, they are listed more than once in the figure.

*Systematic Review, MacPherson et al., 2015*
So where to from here?

CASHING IN ON THE OPPORTUNITIES THIS TRANSITION AFFORDS US IS OUR NEXT GREAT COLLECTIVE CHALLENGE
Building blocks to better adherence

• Work on meaningful engagement
  • Relationships – youth, parents, communities
  • Instill confidence and accountability with support
  • Pay attention to concerns- education, future, employability,

• Work on environment
  • Tailored, fun, logistically adolescent friendly
  • Decentralised, cohesive, safe.
  • Supported and fun.

• Market health promotion with passion

• ”Mind the Gap” – manage transitions

• Address the barriers:
  • More tolerability
  • Less frequent dosing

• Then address the individual aspects:
  • Two way SMS (soon after missed visit)
  • Pill boxes
  • Blister packs
  • Viral load and drug level feedback
  • Incentivised behavioural responses
Youth Energy and Innovation:
The Future Fighters
The DTHF Youth Centre, Kommetjie
Beyond 90-90-90 to the triple dividend

- **Innovation** and creativity
- **Move out** of facilities
  - E and Mobile health
- **Engage** teen communities
  - Esp. younger teens
- **Integrate** and go beyond to health and wellbeing
- **Tailor** services
  - Confidential
  - Efficient
  - Relevant
  - Respectful
  - Client centred
  - Peer supported
“Youth are a wonderful gift. They have an extraordinary capacity to see into the heart of things and to expose sham and humbug for what they are.”

Desmond Tutu 2014
For more details visit: www.differentiatedcare.org
Follow us on Facebook:

@TutuTeenTruck

@Zimeleproject

@WomenOfWorth

"Here's to the women. May we know them. May we be them. May we raise them."
23-27 July 2018
AMSTERDAM, NETHERLANDS

22ND INTERNATIONAL AIDS CONFERENCE (AIDS 2018)

INTERNATIONAL CHAIR: LINDA-GAIL BEKKER, SOUTH AFRICA
LOCAL CHAIR: PETER REISS, NETHERLANDS
Acknowledgements

- Rashida, Mike, Nyaradzo, James and Zim team!
- Carey Pike
- Anna G and IAS
- DTHC centre of Adolescent Health
- Dante, The DT youth Centre
- Elzette, The Tutu Teen Truck
- Sinead Delaney-Moretlwa
- Connie Cellum, 3P team
- Sybil Hosek
- Katherine + Pluspills +UChoose
- Andrew Merino
- Future Fighter Youth CAB
- McCann and BMGF
- Young people and their families
- DTHF/DTHC Funders