Adolescents: the forgotten cohort....

Linda-Gail Bekker
The Desmond Tutu HIV Centre
UCT
1 October 2010
Forgotten or -
Ignored??
almost 2 billion people are between the ages of 10 and 24 years

Source: Population Reference Bureau, 2006
1/4 of the world
1/3 of Africa
Most are at risk for HIV acquisition....

In fact,

1.2M of 2.7M new infections in 2007 occurred in 15-24 yo.
In 2006, 19,000 (34%) new infections in 13-29 yo.
10 million youth living with HIV

SOURCE: UNICEF/UNAIDS, 2004; youth age 15 - 24

Kicosehp NGO (support group for people living with HIV/AIDS). Kenya, Africa. © UNAIDS/G. Pirozzi
63% of HIV positive youth live in sub-Saharan Africa.

SOURCE: UNICEF/UNAIDS, 2004; youth age 15 – 24
Disproportionate impact on young girls

2.4 million young boys living with HIV

7.6 million young girls living with HIV

SOURCE: UNICEF/UNAIDS, 2004; young boys/ girls age 15 - 24
80% HIV infected in E Europe and Central Asia <30yrs.
Or is it simply cynicism?

I don’t believe it will happen…..

so why get all worked up about it?
“We are really groping in the dark”

Salim S. Abdool Karim
Quoted in the Washington Post upon notice of STEP vaccine futility
November 1, 2007
Adolescents are on the train when it gets to the station....
Much talk…and advocacy

- PACTG vaccine preparedness: Baltimore 2004
  - awards 2004/5 Soweto and Cape Town
- Botswana – AAVP and WHO -2005
- DAIDS White paper 2006/7
- FDA guidance document 2007
- NICHD/NIAID/NIMH/NIDA/OAR/Forum for collab Res 2009
- FDA: regulators/IRB consultation 2009
- JAIDS Suppl July 1 2010
WHO/AAVP recommendations:

• *Thus, it is recommended that adolescents be included in HIV/AIDS vaccine trials as soon as possible when a candidate has sufficient promise to be advanced into an efficacy trial(s) in adults.*
HIV vaccine - no correlate of protection

Phase I
- Tens

Phase II
- Hundreds

Phase I

Phase IIb
- Safety pause

Phase III
- Thousands
- Adolescents 12*-15
- Adolescents 16-17
- Adults

Adolescents preparedness

Ten of thousands

Time (years)
• Broadening inclusion of vulnerable populations in HIV vaccine clinical trials.

• Expert Review Vaccines 7(2) 259-268.

• Chuen Yen Lau, Massimo Cardinale, Paul Sato, Alan Fix and Jorge Flores.
Guidance for Industry: Development of Preventive HIV Vaccines for Use in Pediatric Populations

To provide recommendations to sponsors regarding data to support the:

• 1) Initiation of pediatric studies of a preventive HIV vaccine under a United States (U.S.) investigational new drug application (IND); and

• 2) licensure of a preventive HIV vaccine for pediatric use.
Inclusion of Adolescents and Young Adults in Biomedical HIV Prevention Research

- Introduction: Paving the Way for Biomedical HIV Prevention Interventions in Youth
  Guest Editors: Bill G. Kaplan and Monica S. Diaz, MD, MPH, Ed Mandleman, MD, and Susan Lee, PhD
- Ethical and Regulatory Considerations for the Inclusion of Adolescents in Biomedical Prevention Research
- Behavioral Considerations for Engaging Youth in HIV Clinical Research
- Population-Level Considerations: The Development of Prevention Programs
RECOMMENDATIONS

• The need for Adolescent specific data in clinical trials
  – Safety and toxicity data in microbicides, PrEP and vaccines- dose
  – Sufficient numbers of adols in trials
  – Acceptability/tolerability/feasibility
  – Extrapolation and bridging studies
other recommendations

- Risk compensation research
- Acceptability/utilisation research
- Eligibility criteria- sexual activity
- More guidance from regulators
- Community engagement
- Youth participation
- Standard of care and prevention
- GOAL: to ensure licensure
Domestic Adolescent HIV Prevention Efforts through the ATN

- Conducts trials related to both HIV treatment and HIV prevention among youth aged 13-24

- Three ongoing ATN trials highlight the active prevention research

- ATN 076, 040, and 082
ATN 076-”The Behavioral Disinhibition Study”

–enrolled 120 youth to evaluate the effectiveness of brochures (theory based, professionally created with youth involvement) to be used for specific education about trial design to reduce the risk of preventive misconception in a trial
ATN 040-”The Connect to Protect Project”

• Phase III, Connect-to-Protect (C2P) site staff, their official community partners established in Phase I, and newly invited community sector representatives (i.e., individuals from various key parts of the community) will form a coalition that will work toward achieving local action plan to ultimately reduce HIV acquisition and transmission.

• ATN 040b is the evaluation protocol.
ATN 082-”Project PrEPare”

– 18-22 yo MSM (99)
– feasibility and acceptability of combining an effective behavioral (3MV) intervention with the potentially effective biomedical intervention of PrEP at 2 sites in Chicago.
– Roll down to 16-17 yo for qualitative FGs.
– The trial is currently 50% enrolled, with strong minority representation.
Consortium of Adolescent Clinical Trial Sites in South Africa
Core site at Desmond Tutu – co-ordinating and overseeing other sites

Pretoria/ Medunsa
Soweto/ PHRU
Klerksdorp/ KOSH
Durban /CAPRISA
Mthatha /WS
Cape Town/DTHC
SASHA 1 and 2

- Aims 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
  - Community engagement and interrogation
  - HIV vaccine simulated clinical trial in 12-17yo with HPV vaccine as a surrogate.
SASHA 1 :Community

• Community engagement
• Focus groups:
  – With stakeholders, parents and adolescents separately
  – Explore community attitudes toward adolescent participation
  – Attitudes towards some of the ethical issues associated with this
  – Explore requirements for providing an adolescent-friendly sexual health service including factors such as birth control provision, risk reduction counseling and circumcision
  – Explore perceptions of risk behaviour in adolescents
SASHA 2: Simulated HIV Vaccine trial

• 1400 adolescents (12-17 years) self-select (with parental consent) to receive or not receive the vaccine

• **Inclusion Criteria:**
  – For 12-15 year olds – no sexual risk criteria
  – For 16-17 year olds sexually active (ever had sexual intercourse)
  – Willing to participate in HIV testing and counseling
  – Willing and able to assent to study
  – Parent or legal guardian willing to provide written consent
  – HIV-negative serostatus
  – Not pregnant or breastfeeding

• Adolescents: 5 visits over 9 months (screening, enrolment (0mths), 2mths, 6mths and 9mths)

• Parents: one visit at screening
SASHA STUDY SCHEMA

Recruitment

- Demographics
- Intention to participate in VDGs

Vaccine discussion groups

- Demographics intention to participate in screening
- Pre and post VDG assessment
- Knowledge and attitudes towards HPV and HPV vaccine trial

Screening

- Demographic information
- Assessment of understanding
- How/where they were recruited
- Motivation for participation/consent to adolescent participation
- Attitudes towards current legal age of informed consent for participation in research
- Attitudes towards confidentiality for adolescent test results and sexual risk behaviour
- Attitudes towards circumcision as a risk reduction method for adolescents
- Attitudes towards HIV, HIV vaccine trials, HPV and the HPV vaccine
- Parent/adolescent sexual communication measure (Miller et al; 1998)
- Parent/adolescent process of communication measure (Miller et al; 1998)
SASHA STUDY SCHEMA

Enrolment

- Motivations for participation
- Sexual activity and sexual risk behaviour
- Correlates of sexual risk and protective behaviours (condom use, delaying sexual debut, number of partners, partner status, types of sex) – perceived benefits, susceptibility, barriers, outcomes, normative beliefs, self-efficacy
- Attitudes toward age of informed consent for participation in research
- Attitudes toward confidentiality for adolescent test results and sexual risk behaviour

Month 2

- Social harms and benefits of participation in the HPV vaccine study
- Knowledge of and attitudes towards circumcision as a method of risk reduction and anticipated impact on sexual risk behaviour
- Attitudes toward and experience of VCT
- Parent/adolescent sexual communication measure (Miller et al.; 1998)
- Parent/adolescent process of communication measure (Miller et al.; 1998)
SASHA STUDY SCHEMA

Month 6
- Demographics intention to participate in screening
- Social harms and benefits of participation in HPV vaccine study
- Preferred method of birth control and motivation for response
- Social support
- Substance abuse

Month 9
- Current sexual activity and sexual risk behaviour (interviewer-administered)
- Evaluation of method of collecting sexual risk behaviour data
- Evaluation of risk reduction counselling received
- Motivation for remaining in study
- Self evaluation of sexual risk behaviour change
- Social harms and benefits
- **Assessment of understanding**
Data to be collected:

Psychosocial:
• Sexual risk behaviour
• Parent-adolescent communication
• The link between thoughts/beliefs and sexual risk behaviour including self-esteem, risk perception
• Circumcision
• Social support
• Social harms/ benefits
• Substance abuse

Biomedical:
• HIV testing
• Syphilis and HSV2 testing
• Pregnancy testing
• Circumcision
Capacity building

• Staff: training and research experience with adolescents including
  – Protocol training
  – Ethico-legal training
  – Focus group training
  – FP, STI management, risk reduction counselling
  – Adolescent development

• Development of adolescent-friendly sexual health services at all sites

• Development of adolescent community advisory boards (CAB) to form a link between adolescent community and researchers at all sites
CAB development:

- Adolescent CABs established at all 7 sites
- Training CABs on
  - HIV prevention and management
  - Research methods and clinical trials
  - Advocacy and networking
  - SASHA project
- Conference calls held regularly between CABs nationally
- Camps held to facilitate training and build relationships
- CABs have been active throughout
Ethico-legal issues

Laws impacting on research with adolescents:
- Working with HIV/AIDS Vaccine Ethics Group
- Developed guidelines/memo detailing how we will act in accordance with these laws
- Guided by what is ethical rather than legal in certain cases
- Aiming to do what is in the best interests of the child/adolescent
- Working closely with REC’s to achieve this
WHO CAN TAKE PART IN THE STUDY?

Adolescents between the ages of 12 and 17 whose parents are willing to give consent for them to take part.

Parents / guardians of adolescents aged 12 to 17 years.

Members of the community who work with or care about young people and their sexual health.

We are going to speak to separate groups of young people, their parents and members of the community.

You are invited to have a confidential group discussion with about seven other people.

We will ask you questions on your thoughts and feelings about HIV vaccine trials, as well other ways of protecting young people’s sexual health. There are no right or wrong answers to the questions. We are trying to find out more about what you think and feel.
HVTN 913

- Follow on study in 600 SASHA enrollees
- Extend follow up from 9 mnths to 18 mnths
- HIV, HSV, Pregnancy incidence
- Retention
- Sexual debut incidence
- Risk over time
- Other parameters
Almost 800 youth enrolled

Cumulative number enrolled by site

# enrolled

Nov-09 Dec-09 Jan-10 Feb-10 Mar-10 Apr-10 May-10 Jun-10 Jul-10 Aug-10 Sep-10 Oct-10

MEDUNSA  PHRU  AURUM  CAPRISA  DTHF
## Screen : enrollment

### Overall Screenings and Enrolment by site

<table>
<thead>
<tr>
<th>Site</th>
<th># Screened</th>
<th># Enrolled</th>
<th>% Enrolled</th>
</tr>
</thead>
<tbody>
<tr>
<td>MEDUNSA</td>
<td>175</td>
<td>149</td>
<td>85.14</td>
</tr>
<tr>
<td>PHRU</td>
<td>228</td>
<td>189</td>
<td>82.89</td>
</tr>
<tr>
<td>AURUM</td>
<td>81</td>
<td>48</td>
<td>59.26</td>
</tr>
<tr>
<td>CAPRISA</td>
<td>252</td>
<td>165</td>
<td>65.48</td>
</tr>
<tr>
<td>DTHF</td>
<td>177</td>
<td>144</td>
<td>81.36</td>
</tr>
<tr>
<td><strong>Totals</strong></td>
<td><strong>913</strong></td>
<td><strong>695</strong></td>
<td><strong>76.12</strong></td>
</tr>
<tr>
<td>Reason</td>
<td>n</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>---------------------------------------------</td>
<td>-----</td>
<td>------</td>
<td></td>
</tr>
<tr>
<td>Parent withdrew child</td>
<td>2</td>
<td>1.69</td>
<td></td>
</tr>
<tr>
<td>Consent Issues</td>
<td>13</td>
<td>11.02</td>
<td></td>
</tr>
<tr>
<td>Not sexually active</td>
<td>53</td>
<td>44.54</td>
<td></td>
</tr>
<tr>
<td>HIV positive</td>
<td>13</td>
<td>11.02</td>
<td></td>
</tr>
<tr>
<td>Referred to hospital</td>
<td>2</td>
<td>1.69</td>
<td></td>
</tr>
<tr>
<td>Pregnant/Breastfeeding</td>
<td>4</td>
<td>3.39</td>
<td></td>
</tr>
<tr>
<td>Sexually active but not on contraceptives</td>
<td>4</td>
<td>3.39</td>
<td></td>
</tr>
<tr>
<td>Other Medical Problem</td>
<td>6</td>
<td>5.08</td>
<td></td>
</tr>
<tr>
<td>Not Interested</td>
<td>6</td>
<td>5.08</td>
<td></td>
</tr>
<tr>
<td>21 Days</td>
<td>5</td>
<td>4.24</td>
<td></td>
</tr>
<tr>
<td>Unspecified Withdrawl/Failure</td>
<td>10</td>
<td>8.47</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>118</strong></td>
<td><strong>100</strong></td>
<td></td>
</tr>
</tbody>
</table>
Enrolment by sex

- MEDUNSA
- PHRU
- AURUM
- CAPRISA
- DTHF

Females
Males
<table>
<thead>
<tr>
<th>HPV Vaccination Utilization</th>
<th>Enrolment</th>
<th>2-month visit</th>
<th>6-month visit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consented to the vaccination</td>
<td>530/531</td>
<td>223/223</td>
<td>39/39</td>
</tr>
<tr>
<td>Medically eligible</td>
<td>528/529</td>
<td>221/222</td>
<td>39/39</td>
</tr>
<tr>
<td>Vaccine given</td>
<td>527/528</td>
<td>219/221</td>
<td>39/39</td>
</tr>
</tbody>
</table>
HIV incidence

- Of the 13 adolescents who screened out for HIV positivity
- The mean age was 15
- 12/13 were girls

- There has been one seroconversion on study to date.
So WHERE are our challenges?

- Ethico-legal
- Regulatory
- Logistics
- Products-sponsors
Ethico-legal

• Minors are considered a vulnerable population requiring additional protections as research subjects.
• Prevention research : non-therapeutic
• Address justification
• Grade risk:
  – minimal
  – More than minimal
Risk/Benefit ratio

- Vulnerable populations

BUT

- A population also extraordinarily vulnerable to HIV
Adolescent cross sectional prevalence: 2005

Sexual debut

Mean prevalence

13-15
14-16
17-19
Survey: 23% HIV Prevalence
(orasure anonymous –10% pop)

Age strata

15-19
20-29
30-39
40-49
50+

males
females
## HIV prevalence in pregnant women in rural Vulindlela, South Africa (2005-2008)

<table>
<thead>
<tr>
<th>Age Group (Years)</th>
<th>HIV Prevalence (N=1237)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤16</td>
<td>10.6%</td>
</tr>
<tr>
<td>17-18</td>
<td>21.3%</td>
</tr>
<tr>
<td>19-20</td>
<td>33.0%</td>
</tr>
<tr>
<td>21-22</td>
<td>44.3%</td>
</tr>
<tr>
<td>23-24</td>
<td>51.1%</td>
</tr>
</tbody>
</table>
Risk assessment

16-21yo
Mean age of sexual debut: 15.4 yrs
Mean number of sexual partners ever 3 (1-16)
Condom use ever: 71%
Condom use last sexual encounter: 0%
Transactional sex 25%
Transgenerational sex: 25%
Coercive sex: 10%
STD ever: 36%
Discharge/ulcer last 6 mths: 27%
Perceives self at risk for HIV: 49%
Perceives sexual partner at risk for infection: 51%
HIV pos partner in the last 6 mths: 81% don’t know.

- **Youth risk behaviour surveillance system**
- 47.8% of high school students: sexual debut
- Approx 35% were currently sexually active
- In sexually active: 15% >4 partners
- 7% SA before age 13
- 60% used condom at last SA.
- **Monitoring the future study:**
- 30%, 53%, 66% of 8, 10, 12th graders- alcohol
- Drugs assoc with HIV reported for all age groups
Youth and then there’s youth…

- Youth vulnerable to HIV are a heterogenous group
- Contextual factors play a role…

= RISK PROFILE

Environmental
Individual
Structural
Rural Zimbabwe study: women aged 15-18, youth whose mother had died, young women with infected mother had greater HIV rate, more STI and more likely to be pregnant.
Estimated 10,000 children live/work on the streets in South Africa; 100,000 in India. Worldwide 100-250 M. Some as young as 8yrs. (UNICEF/UNAIDS/UNFPA, 2002)

Washington: N = 288 homeless youth (age 14 – 21)/ Interviews. Relationship between sexual risk behaviour and homelessness (Ennett, 1999)

Study from Phnom Penh, HIV rates in street children doubled from 12-28% from 2004 to 2005. (Mills 2005)

13 year old Yana, Ukraine. Her father, an alcoholic, died early; her mother was sent to jail when Yana was 8 yrs old. Since, she has been living on the street. By injecting drugs, she gets infected with HIV. During Christmas 2004, she crawls into a hole and dies in the winter cold. © David Gillanders
Recreational DRUG USE / ALCOHOL

- Dependency Units in SA are treating children as young as 13 years for crystal meth ‘TIK’ addiction.
- Huge explosion of ‘Tik’ abuse in our previously ‘drug free’ communities.
- Adolescence time of general risk-taking; drug use impairs judgment and leads to increased sexual risk behaviour.

- **Alcohol:** Rwandan study showed that adolescents 15-24yrs who consumed alcohol were less likely to abstain from sex.
Concentrated Epidemics

Men who have Sex with Men:
A social and behavioural phenomenon
Unprotected anal sex = increased HIV risk
MSM are often young….

- Central America: 34% are < 24 yrs
- Peru: 50% are < 25 yrs

Young MSM are more at risk….

- Central Asia: 14-20 % HIV in 15-24 yr
- E Europe: 14-20 % HIV in 15-24 yr
- W Europe: 10 % HIV in 15-24 yr

More likely to take risks: ‘bare backing’, crystal meth usage, etc

J. Elford, Current Opinion in Infectious Diseases 2006, 19:26–3
CDC: 2008: One in 5 men

- 8000 MSM
- 21 cities
- Half don’t know it
- Young
- Sexually active
- Minority
- 38% Baltimore

Washington Post Sept 2010
Sexual debut in MSM younger:

- Cambodia 17.7yrs in MSM vs 22yrs

More male CSWs are youth:

- Russia: 40% of male CSW are <19 yrs
Concentrated Epidemics

IVDU:
Most effective way to transmit HIV
IVDU occurs in youth

- IVDU <20 yrs

<table>
<thead>
<tr>
<th>country</th>
<th>% IVDU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Russian Fed</td>
<td>33</td>
</tr>
<tr>
<td>Ukraine</td>
<td>20</td>
</tr>
<tr>
<td>India</td>
<td>24</td>
</tr>
<tr>
<td>Indonesia</td>
<td>70</td>
</tr>
<tr>
<td>Kazakhstan</td>
<td>54</td>
</tr>
</tbody>
</table>

1.5-8% of All Russian men <30 years have injected at some time
Young IVDU at risk for HIV:

• More likely to share needles
• More likely to inject in groups
• More likely to have increased sexual risks.

Poor HIV Knowledge
  – Karachi: 1:4 never heard of AIDS.
    • (WHO 2006)

• A drug user who shares needles is certain to contract AIDS,

"It's not a question of if, but when."

Director of Asia Harm Reduction, Tom Smits.
IVDU Youth (<24) are HIV infected:

<table>
<thead>
<tr>
<th>Country</th>
<th>% HIV infected</th>
</tr>
</thead>
<tbody>
<tr>
<td>Russia</td>
<td>55</td>
</tr>
<tr>
<td>Brazil</td>
<td>56</td>
</tr>
<tr>
<td>Central Asia</td>
<td>48</td>
</tr>
<tr>
<td>E Europe</td>
<td>40</td>
</tr>
<tr>
<td>Belarus</td>
<td>60</td>
</tr>
</tbody>
</table>

*(WHO 2006)*
Concentrated Epidemics

Commercial sex work:
More sex, more partners, more risk
Majority CSW are <25 years

- Cambodia
- China
- Lao People Democratic Republic
- Myanmar
- Russian Federation
- Viet Nam

70-80%

In Thailand as many as 35,000 < 18 year old women engaged in sex trade.
Career starts young:

<table>
<thead>
<tr>
<th>Country</th>
<th>Commencement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viet Nam</td>
<td>30% &lt;18 years</td>
</tr>
<tr>
<td>Jamaica</td>
<td>50% &lt;18 years</td>
</tr>
<tr>
<td>Djibouti</td>
<td>63% &lt;20 years</td>
</tr>
</tbody>
</table>

And at great risk for HIV Infection:

- Eritrea: 12% in 15-19 y
- 24% in 20-24 y
- Myanmar: 41% in 15-19 y
Clients of CSW often are youth

- India/Nepal: up to 70% are 20-24 years
- Kosovo: 18% are <20 years
  20% are 20-24 years

(WHO 2006)
Concentrated Epidemics

“The Degree of Civilisation in Society can be judged by entering its prisons.”

(Dostoevsky)

Detained, incarcerated:

The first three groups often supply this group
Incubators of contagion

• 9 M in prison at any time
• 30M moving back and forth at any time.
• HIV, Hep C, TB. (OSI 2004)
• South African prisons estim: 41% HIV prev
• Russia Fed: prisoners >4x higher rate in men and 15X rate in females.
• IVDU without needles, MSM without condoms, Tattooing without sterility.
• Little information and no services.
Successful Studies

- REACH study (pos/neg youth MSM): 87% retention in 4 yrs
- EXPLORE study: YMSM more mental health, subst abuse and sexual risk than older.
- Familias Unidas
- STYLE study- enrolled youth with psychiatric disorders
Behavioural vulnerability of youth

• Curiosity/ experimentation
  Stage characterized by exploration, general risk-taking behaviour—incl sexual experimentation.

• Peer pressure
  Adolescents influenced by group norms, seek acceptance by peers, look to affirm identity, time of high social acceptability of risk behaviour.
• **Invincibility**
Perceived invulnerability, adolescents characteristically believe they are impervious to disease.

**Rule-breaking**
Desire to develop autonomy from parents and society, test authority figures, struggle for individual autonomy
Neurobiological research

- Impulsivity: immature prefrontal cortex
- Risk processing: development of subcortical systems
- Combination of increased responsiveness to rewards and immaturity in behaviour control
- Bias youth to seek immediate gains

Casey, et al J Neurosc 2002
Reduce Riskiness

- Community engagement
- Youth and significant adults
- Informed consent process
  - Thorough, authentic, sustained
  - Parental consent
  - Adolescent Consent
  - Adolescent Assent
  - Adolescent Privacy
The tension of sexual activity eligibility and parental consent needed to conduct and efficacy evaluation
Adolescent Voices

• “I would really have a problem for my parent to know that I am sexually active.” AF

• “It will affect me if my parent find this out, because she know that every time that I don’t sleep at home, she will know that I’m with this women or girlfriend of mine. So I will not join the study.” AM

• “It won’t be a problem for my mother now, she was so stubborn in the beginning and not wanting to hear anything about relationships -but now she’s fine with it even the day she came for VDG’S for community study, the things she mentioned I was so surprised.” AF
Parents’ struggle

• “We need to push and force to communicate with our children especially nowadays with so many diseases, children get sick and die. This is not the time to continue hiding, it is tough we need straight talk.”

• “We need to tell our children the truth, lets us look at the whites they tell their children the truth. Why is it that blacks cannot tell our children the truth. “
Kaplan-Meier survival estimates, by adol

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

9.3 per 100py
Regulatory thinking…

- CARROT and STICK:
- for a new active ingredient, new indication, new dosage form, new dosing regimen, or new route of administration are to contain a pediatric assessment unless the sponsor has obtained a waiver or deferral from FDA.
- encourage the submission of pediatric development plans to FDA as early as possible in the vaccine development process.
What data from adults?

• Depends on:
  – The strength of the adult safety and immunogenicity data generated;
  – what is known about the investigational vaccine in terms of its relationship to well-characterized vaccines or novel vectors or production methods; and
  – the relationship of documented immune responses to protection.

• It is very important to have adult safety and activity data prior to the initiation of pediatric clinical studies of an HIV vaccine.
Extrapolation

• Adult efficacy data can be extrapolated to the pediatric population when it is likely that the disease and response to treatment in adults and children are reasonably similar.

• In such cases, efficacy in prevention of new HIV infections in adults supported by immunogenicity and safety data in children may be sufficient to support pediatric use of a preventive HIV vaccine.

• Correlate of protection would facilitate.
So what’s the plan?

- To not let the adolescent agenda be forgotten
- To entrée the adolescent involvement at the point that we have “promise”
- Microbicide 😊
- PrEP 🤔
- Vaccines 😊
- Design of studies: safety 😊? efficacy
Ongoing research

- Informed consent
- Adherence
- Sexual risk
- Risk compensation
- Preventive misconception
  - I have been assigned to the experimental condition
  - The unproven intervention has some significant efficacy for me
Address social harm

- Youth engagement
- Community engagement
- Youth friendly services
- Good referral systems
- Ready access to social support
- Confidentiality and transparency
- Standard of prevention
- Standard of care
logistical bottlenecks:

- more clinic hours- non traditional
- More resources- staff and money
- Finding guardians/parents
- Legal proof of guardianship
Tenofovir Jellies

• FACTS 001
• 2400 women in 6 sites : BAT 24
• 15% 16 and 17 yo
• identical eligibility and follow up
• 60-120/360 – more intense safety :
• 1 month 3x per week gel insertion
• 3 blood/genital PK, genital safety for 1 month.
• Annual DEXA scanning.
Not forgotten, not neglected, not ignored

Be affirmed, acknowledged, engaged and utilised
“I feel proud because we are taking part in something that is really going to change our country or our lives as people......you know youth being in some things like this it is making us very proud, you know...because tomorrow belongs to us...our future belongs to us...we are holding the future...”

Adolescent RSA 2010
Thanks

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- SAAVI
- IMPAACT
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ALL THE AUTHORS OF THE JAIDS ADOLESCENT SUPPLEMENT