



Celebrating 30 Years of HIV Research
Building on Excellence & Shaping the Future

Including Adolescents in HIV Prevention Clinical Trials in Africa

The Future of HIV Prevention Clinical Trials Summit
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Overview

- Importance of including adolescents in clinical trials
- Reasons for the exclusion of adolescents from clinical trials
- Lessons learnt from HIV prevention clinical trials in adolescents
- The future of adolescent HIV prevention clinical research



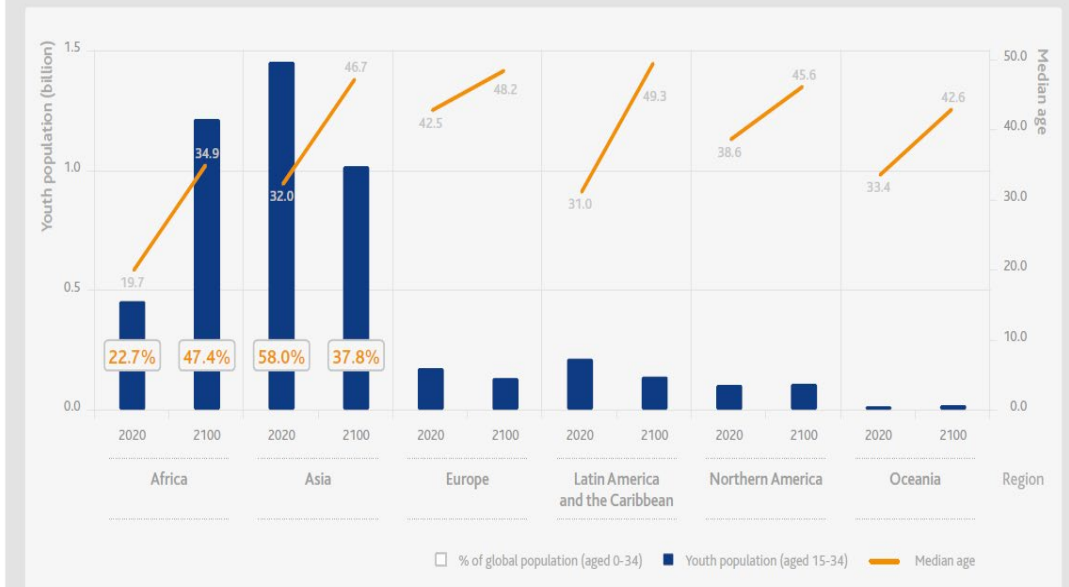
IMPORTANCE OF INCLUDING ADOLESCENTS IN CLINICAL TRIAL

Africa has the fastest-growing and youngest population

60% of Africa's population is younger than 25 years

By 2100, half of the world's youth will live in Africa

World regions: youth population (aged 15-34) & median age (2020 & 2100)



Source: MIF based on UNDESA

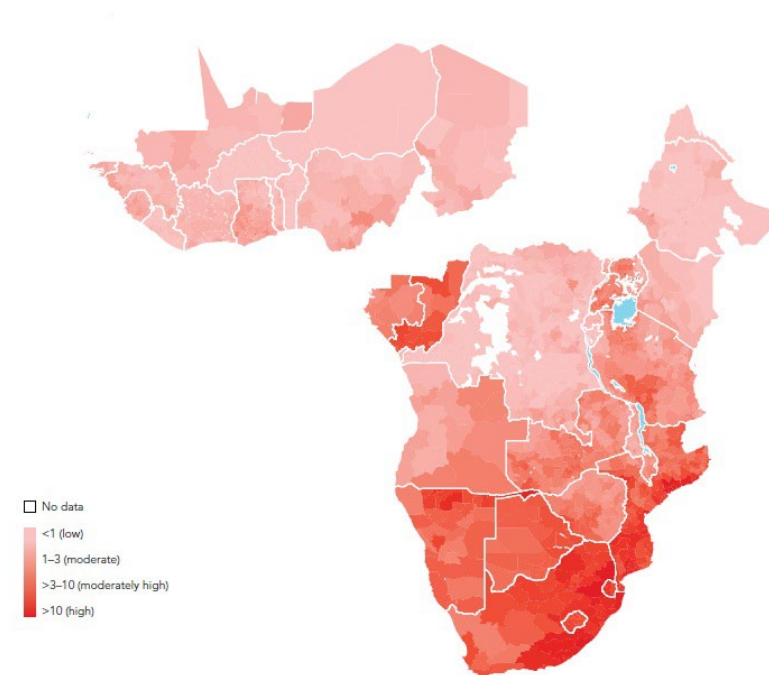
Adolescents and HIV

AGYW are still at disproportionate risk of HIV acquisition

HIV incidence is 3 times higher in AGYW compared to their male counterparts

Two thirds of new HIV infections in 2022 among AGYW occurred in Eastern and Southern Africa

HIV incidence among all adolescent girls and young women (aged 15–24 years), subnational levels, sub-Saharan Africa, 2024



Source: UNAIDS epidemiological estimates, 2024 (<https://aidsinfo.unaids.org/>).
Note: HIV incidence estimated as new HIV infections per 1000 uninfected population.

HIV Prevention Program Coverage

- Access to life-saving HIV prevention products is still a challenge
- In 2023, less than half of the area in moderate and high incidence areas in SSA had a prevention program focused on AGYW



Joint United Nations Programme on HIV/AIDS;
2024

Importance of conducting clinical trials in adolescents

Clinical trials allow for:

- Access to investigational new drugs (IND)
- Controlled evaluation of the safety and efficacy of IND
- Age-appropriate products and dosing regimens
- Develop and test innovative service delivery models



REASONS FOR EXCLUSION OF ADOLESCENTS FROM CLINICAL TRIALS

Fear

- Safety
- Efficacy

Trial design and conduct

- Recruitment
- Outcomes
- Endpoints

Ethical considerations

- Informed consent
- Parental inclusion
- IRB

Sensitive issues

- Sexual behavior
- Sexually transmitted diseases

Results of exclusion

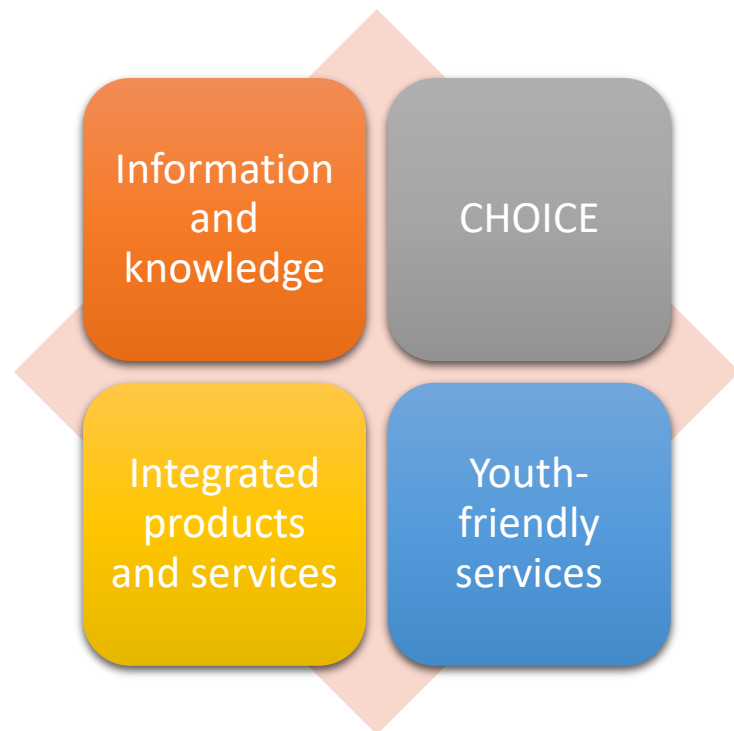
Delayed regulatory approval for IND

Lack of data on safety, efficacy, toxicity, risks and benefits

Prolonged off-label use

Limited treatment and prevention options

What do young women want when it comes to HIV prevention?



UNICEF Eastern and Southern Africa Regional Office, 2021

LESSONS LEARNT FROM PREVIOUS HIV PREVENTION TRIALS

- It is possible to recruit and retain adolescents in clinical trials
- Similar therapeutic response in adults compared to adolescents
- Long-acting PrEP choices can overcome challenges of adherence and persistence



Twice-Yearly Lenacapavir or Daily F/TAF for HIV Prevention in Cisgender Women

L.-G. Bekker, M. Das, Q. Abdool Karim, K. Ahmed, J. Batching, W. Brumskine, K. Gill, I. Harkoo, M. Jaggernath, G. Kigozi, N. Kiwanuka, P. Kotze, L. Lebina, C.E. Louw, M. Malahleha, M. Manentsa, L.E. Mansoor, D. Moodley, V. Naicker, L. Naidoo, M. Naidoo, G. Nair, N. Ndlovu, T. Palanee-Phillips, R. Panchia, S. Pillay, D. Potloane, P. Selepe, N. Singh, Y. Singh, E. Spooner, A.M. Ward, Z. Zwane, R. Ebrahimi, Y. Zhao, A. Kintu, C. Deaton, C.C. Carter, J.M. Baeten, and F. Matovu Kiweewa, for the PURPOSE 1 Study Team*

Articles



Safety, tolerability, and acceptability of long-acting injectable cabotegravir for HIV prevention in cisgender female adolescents (HPTN 084-01): a single-arm, open-label, phase 2b trial



Lynda Stranix-Chibanda, erica I hamilton, Julie Ngo, Yuqing Jiao, Brett Hanscom, Rahul Paul Choudhury, Yaw Agyei, Estelle Piwowar-Manning, Mark Marzinke, Sinead Delany-Moretlwe, Nyaradzo Mgodzi, Bekezela Siziba, Ishana Naidoo, Brenda Gati Miremba, Betty Kamira, Cynthia McCoig, Adeola Adeyeye, Hans M L Spiegel, Sybil Hosek, for the HPTN 084-01 Protocol Team*

HPTN 082

- Randomized open-label trial
- Adherence support strategies
 - Frequent clinic visits
 - Monthly adherence clubs
 - Social media platforms
 - WhatsApp groups
 - Youth-friendly clinics and staff
- High STI incidence

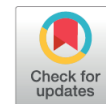
PLOS MEDICINE

RESEARCH ARTICLE

PrEP uptake, persistence, adherence, and effect of retrospective drug level feedback on PrEP adherence among young women in southern Africa: Results from HPTN 082, a randomized controlled trial


Connie Celum^{1*}, Sybil Hosek², Mandisa Tsholwana³, Sheetal Kassim⁴, Shorai Mukaka⁵, Bonnie J. Dye⁶, Subash Pathak⁷, Nyaradzo Mgodini⁸, Linda-Gail Bekker⁴, Deborah J. Donnell⁷, Ethan Wilson⁷, Krista Yuha⁷, Peter L. Anderson⁸, Yaw Agyei⁹, Heather Noble⁷, Scott M. Rose⁶, Jared M. Baeten¹, Jessica M. Fogel⁹, Adeola Adeyeye¹⁰, Lubbe Wiesner¹¹, James Rooney¹², Sinead Delany-Moretlwe³

¹ Departments of Global Health, Medicine, and Epidemiology, University of Washington, Seattle.



MTN 034

- Crossover study design
 - Allows for direct comparison of different products
- CHOICE
 - Menu of products
 - Adherence and persistence to a product during the choice phase was consistently high

Articles 

Adherence, safety, and choice of the monthly dapivirine vaginal ring or oral emtricitabine plus tenofovir disoproxil fumarate for HIV pre-exposure prophylaxis among African adolescent girls and young women: a randomised, open-label, crossover trial



Gonasagrie Nair, Connie Celum*, Daniel Szydlo, Elizabeth R Brown, Carolyne A Akello, Rita Nakalega, Pippa Macdonald, Gakiema Milan, Thesla Palanee-Phillips, Krishnaveni Reddy, Eunice Tahuringana, Felix Muhlana, Clemensia Nakabiito, Linda-Gail Bekker, Bekezela Siziba, Sharon L Hillier, Jared M Baeten, Morgan Garcia, Sherri Johnson, Tara McClure, Lisa Levy, Edward Livant, Cindy Jacobson, Lydia Soto-Torres, Ariane van der Straten, Sybil Hosek, James F Rooney, John Steytler, Katherine Bunge, Urvi Parikh, Craig Hendrix, Peter Anderson, Kenneth Ngure, on behalf of the REACH Protocol Team*

THE FUTURE OF HIV PREVENTION TRIALS

1. New biomedical PrEP modalities

- Co-designed approaches
- Discretion and privacy
- MPT (e.g., DPP)
- On-demand products



2. Differentiated PrEP service delivery

- Clear outcomes
- Trial endpoints
- Comparator
- Clear protocol procedures

Noel GJ, 2021



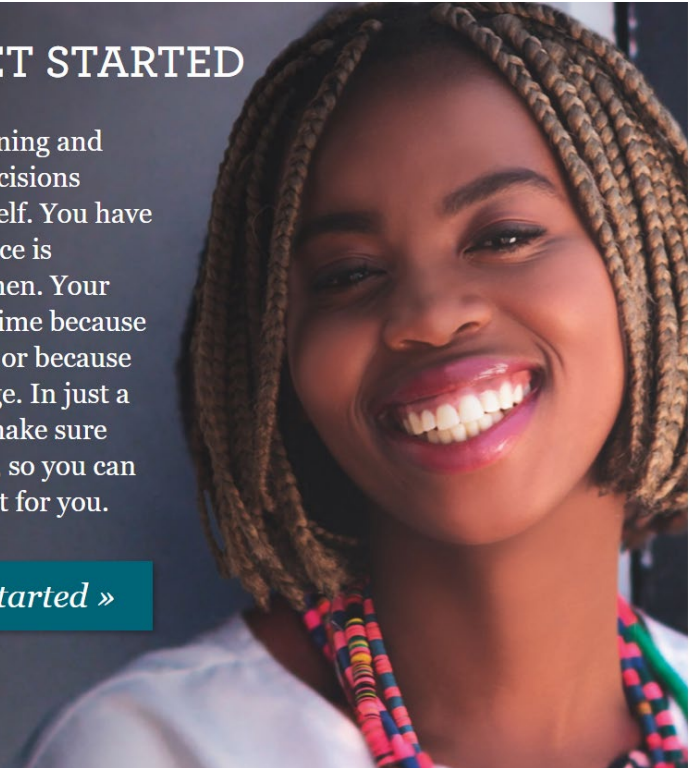
3. Use of technology

- Stimulates demand for products
- Enhance engagement
- Link to SRH services and products
- Provides support for product adherence

BEFORE WE GET STARTED

Choices about family planning and HIV prevention are big decisions about taking care of yourself. You have choices, and the right choice is different for different women. Your choices may change over time because things in your life change, or because what matters to you change. In just a few minutes, we want to make sure you know all your options, so you can find methods that are right for you.

get started »



- **4. STI prevention products and HIV vaccines**
 - DoxyPEP trials in adolescents
 - No vaccine trials have been conducted in adolescents



5. Engage adolescent boys and young men (ABYM) in HIV research

- Focus has been on AGYW
- ABYM have poor HIV testing, linkage to care, ART suppression, and retention in care
- Gender responsive interventions and programs

Makusha & Gittings, 2024



Ethical Considerations

1. Early engagement with stakeholders, from study design

- IRBs
- Regulators
- Parents and community members
- Youth CABs



2. Clear informed consent and assent process

- aim of the study,
- requirements for participation,
- risks and benefits
- voluntary nature of the study
- Information should be provided in a "comprehensive, concise, clear, relevant, and understandable manner."
 - use of visual aids and multimedia

Ethical considerations for clinical trials on medicinal products conducted with minors, 2017



3. Review of policy and regulatory requirements

a. Parental waiver for adolescents who are

- estranged from their parents/guardians,
- emancipated, or
- it would be contrary to the best interests of the adolescent to seek consent from the parent

b. Mandatory inclusion of adolescents in adult trials

N. Faruqi et al, 2023

Conclusion

- Adolescents are still at substantial risk of HIV acquisition
- Clinical trials still play a pivotal role in the development of HIV prevention products and services
- There various lessons learnt from previous HIV prevention trials that have been conducted before
- Gaps still exist
- The safety and protection of adolescents should always be a priority and at the forefront when developing clinical trials recruiting adolescents



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