



Published in final edited form as:

*J Acquir Immune Defic Syndr.* 2013 July ; 63(0 2): S155–S160. doi:10.1097/QAI.0b013e31829871fb.

## Preventing HIV among Young People: research priorities for the future

Audrey Pettifor, MPH, PhD<sup>1,2,3</sup>, Linda-Gail Bekker, MD, PhD<sup>4</sup>, Sybil Hosek, PhD<sup>5</sup>, Ralph DiClemente, PhD<sup>6</sup>, Molly Rosenberg, MPH<sup>1</sup>, Sheana Bull, PhD<sup>7</sup>, Susannah Allison, PhD<sup>8</sup>, Sinead Delany-Moretlwe, MD, PhD<sup>2</sup>, Bill G. Kapogiannis, MD<sup>9</sup>, and Frances Cowan, MD<sup>10</sup>  
for the HIV Prevention Trials Network (HPTN) Adolescent Scientific Committee

<sup>1</sup>Department of Epidemiology, Gillings School of Global Public Health, University of North Carolina at Chapel Hill

<sup>2</sup>Wits Reproductive Health and HIV Institute (WRHI), University of the Witwatersrand, Johannesburg, South Africa

<sup>3</sup>MRC/Wits Rural Health and Health Transitions Unit, University of the Witwatersrand, Johannesburg, South Africa

<sup>4</sup>The Desmond Tutu HIV Centre, University of Cape Town, Cape Town, South Africa

<sup>5</sup>Department of Psychiatry, Stroger Hospital of Cook County, Chicago, IL

<sup>6</sup>Rollins School of Public Health, Emory University, Atlanta, GA

<sup>7</sup>Department of Community and Behavioral Health, Colorado School of Public Health

<sup>8</sup>Infant, Child, and Adolescent Research Programs, Division of AIDS Research, National Institute of Mental Health

<sup>9</sup>Maternal and Pediatric Infectious Diseases Branch, Eunice Kennedy Shriver National Institute of Child Health and Human Development

<sup>10</sup>University College London and Centre for Sexual Health and HIV/AIDS Research Zimbabwe

### Abstract

**Objective**—To review the current state of knowledge on the prevention of sexual transmission of HIV in adolescents and to highlight existing gaps and priority areas for future research.

**Background**—A disproportionate burden of HIV infections falls on adolescents, a developmental stage marked by unique neural, biological, and social transition. Successful interventions are critical to prevent the spread of HIV in this vulnerable population.

---

Corresponding author: Audrey Pettifor PhD, Associate Professor, Department of Epidemiology, Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, NC 27599, CB#7435, Fax number: 919 966 2089, Telephone number: 919 966 7439, [apettif@email.unc.edu](mailto:apettif@email.unc.edu).

Meetings at which parts of the data were presented: none

**Conflicts:** Hosek: FHI 360 supported travel to HPTN ASC meeting where paper was conceptualized. Cowan: rec'd support for travel to attend HPTN meeting; has a number of grants/grants pending (UNFPA, DfID, PSI Zimbabwe, UK MRC). Delany-Moretlwe: %FTE on HPTN 068. Rosenberg: NIH-Training program and center grants (T32 HD007168 R24 HD050924)

**Publisher's Disclaimer:** This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

**Methods**—We summarized the current state of research on HIV prevention in adolescents by providing examples of successful interventions and best practices, and highlighting current research gaps.

**Results**—Adolescent interventions fall into three main categories: biomedical, behavioral, and structural. The majority of current research has focused on individual behavior change, while promising biomedical and structural interventions have been largely understudied in adolescents. Combination prevention interventions may be particularly valuable to this group.

**Conclusions**—Adolescents have unique needs with respect to HIV prevention and, thus, interventions should be designed to most effectively reach this population with information and services that will be relevant to them.

## Keywords

Adolescence; HIV; Prevention

---

## Introduction

Young people are disproportionately affected by HIV globally; 25% of infected persons are between 10-24 years (1). Those aged 15-24 comprise 35% of new infections, resulting in 900,000 new infections annually (2). The greatest burden of HIV among young people is in sub-Saharan Africa (SSA). Here, young women have almost eight times the HIV prevalence as same-age men (2) and their annual HIV incidence is an estimated 8% (3, 4). By contrast, in the US and Europe, young men who have sex with men (YMSM) are at greatest risk of infection, particularly YMSM of color (2). While in much of Eastern Europe and Central Asia, young injection drug users and their sexual partners have the highest risk (2). Clearly, adolescents are a heterogeneous population; risk factors for HIV depend both on individual characteristics and social/environmental contexts. This diversity must be addressed in interventions.

In this paper, we highlight the unique needs of adolescents with respect to biomedical, behavioral and structural interventions that present the greatest promise in preventing sexual transmission of HIV. We also highlight existing gaps and priority areas for future research. We use the terms 'adolescent', 'youth' and 'young people' synonymously, defining adolescence as the developmental stage between the ages of 13-24.

## Why are adolescents a unique population?

Adolescence has been described as 'a period of momentous social, psychological, economic and biological transitions' (5). It is a time when substantial brain development occurs including the capacity for complex, conceptual thinking (6). The combination of a heightened responsiveness to rewards coupled with immaturity in the behavioral control areas of the brain may lead to the risky decisions and emotional reactivity that characterize adolescence (7). The exploration and formation of identity is considered by many to be the primary developmental goal of adolescence (8, 9). Socially, adolescents are searching for a sense of belonging from peers, who influence behavior (10-12). Adolescence is also marked by social transitions such as finishing school, finding employment, independent living, first sexual relationships, pregnancies, and marriage. These milestones occur during a period of decreased adult supervision when young people still have limited knowledge, self-confidence and life skills, which can lead to engagement in behaviors that heighten HIV risk.

## HIV Prevention Among Adolescents

Numerous risk and protective factors operate at multiple levels; including the individual-, dyad- (peer/partner/parent), community- (e.g., school environment) and societal-level. Identifying determinants of risk and protective behaviors is necessary to ensure interventions are appropriate to the population and context where they are delivered. The need for combination HIV prevention strategies, incorporating interventions that address biological, behavioral and structural factors, has been emphasized as central to impacting the epidemic(13). Research is needed on selecting and optimizing these combinations for greatest effect, particularly among adolescents. Significant gaps in HIV prevention knowledge for adolescents remain (Table 1).

### Biomedical Interventions

Recent successes in HIV prevention have been predominately biomedical, and include antiretroviral therapy (ART) for prevention, voluntary medical male circumcision (VMMC), and vaginal microbicides(14-19). Both treatment as prevention (TasP) (ART taken by HIV infected individuals to reduce HIV transmission) and pre-exposure prophylaxis (PrEP) (ART taken by HIV negative individuals to prevent HIV acquisition) demonstrate effectiveness in preventing HIV acquisition or transmission. While PrEP has been found to be effective in one randomized controlled trial (RCT) among MSM(18), results from four trials among heterosexual individuals have been mixed with two trials showing that PrEP was effective(15, 20) and two trials finding no effect(21, 22).

There are numerous reasons why the results of trials among heterosexual individuals may be conflicting, although adherence is likely one of the most important drivers of efficacy (23). In fact, in the VOICE trial, adherence, as measured by drug levels in blood, was particularly low (29%) despite the fact that self-reported adherence and pill count suggested good adherence (90%). Being over the age of 25 was a significant predictor of drug detection in the blood<sup>22</sup> In contrast, data from the Partners PrEP trial found that daily oral Tenofovir (TDF) and emtricitabine/tenofovir (FTC/TDF) was as efficacious in young women under the age of 30 as among all women. Specifically, the efficacy of TDF among women <30 years of age was 77% (95% CI 29,92) and the efficacy of FTC/TDF was 72%, (95% CI 25,90) compared to all women in which efficacy of TDF was 71% (95% CI 37,87) and FTC/TDF was 66% (95% CI (28,84))(24).

While adherence to ART is critical for treatment and prevention, taking medication long-term is challenging. Adolescents with HIV are less likely than adults to be adherent to ART (25-29). A literature review examining medication non-adherence among adolescents suggests that simple solutions remain elusive(30-34). For HIV uninfected youth, low HIV risk perception may result in a lack of interest in or poor adherence to interventions such as PrEP or microbicides (35). Furthermore, adolescents are often not in long-term relationships; it is unclear how partnership characteristics affect adherence to prevention interventions. More research is needed among adolescents to: understand testing, linkage to and retention in care; and understand factors affecting uptake of biomedical prevention interventions.

Vaginal and rectal microbicides, applied topically prior to sex, may be appropriate for young women and men who have sex intermittently. While one trial of coitally dependent vaginal tenofovir was found to show signs of efficacy among women in South Africa(19), use of daily topical tenofovir was found to not be effective in a second trial in Africa(22). The explanation for differences in the studies has been attributed to women not using the product, again stressing that adherence is critical to the efficacy of these interventions(23). Two safety and acceptability trials of a tenofovir gel-based microbicides in adolescent

women are planned in the United States(36) and South Africa (37). A phase II trial of rectally-applied tenofovir gel among men and transgendered women will begin enrollment soon and would benefit from bridging studies to adolescents following sufficient safety signals(38). Research evaluating how best to support uptake, delivery, and adherence will be required to facilitate wide-spread implementation.

Given high levels of unplanned pregnancy and unmet need for contraception among many young women in high-prevalence settings, multi-purpose technologies (MPTs), methods that could prevent HIV, other STIs and pregnancy, are urgently needed.(39) Some products are in development, but their acceptability and safety for adolescent women is unknown. Interventions integrating provision and uptake of sexual and reproductive health services with HIV prevention need to be evaluated.

Voluntary medical male circumcision (VMMC) reduces HIV risk by approximately 65% and reduces risk of STI acquisition and transmission (16, 17, 40). An additional benefit of encouraging early VMMC is that it is almost invariably preceded by HIV testing and counseling (HTC). Given low uptake of HTC in young men in some settings, there is a need to better link adolescent VMMC with interventions to encourage healthy behaviors including regular HIV testing.

## Special Considerations

Most of the research on biomedical interventions has been conducted in adults, partly due to the ethical complexities of research in minors. Although there is increasing recognition of the importance of engaging children and adolescents in research, there remain ethical, legal and logistical challenges (41, 42). Inclusion of minors in clinical research is governed by ethical principles that vary globally, but generally consider need, risk, benefit, and consent(43, 44). Who consents for adolescent involvement is typically governed by the age of majority by state and/or country with some exceptions. There are also important considerations of appropriate timing of adolescent involvement in research of the clinical development of a product or intervention. Excluding adolescents from these studies may delay access to prevention interventions. It is essential that biomedical prevention interventions be implemented with better understanding of behavioral and contextual factors that impede uptake and adherence. Clearer guidance around safety bridging studies, and when extrapolation to adolescents is acceptable versus when efficacy and/or effectiveness should be demonstrated, is vital for newly developed biomedical interventions (45).

## Behavioral Interventions

Behavioral interventions have been used with the aim of reducing risk for HIV by delaying sexual debut, promoting condom use, and/or reducing concurrency, partner change, or substance use. Numerous behavioral interventions have been evaluated; however, few have HIV endpoints and those that have, have not shown a reduction in HIV incidence(46-48). The US Centers for Disease Control and Prevention (CDC) has identified interventions with good or best evidence for HIV risk-reduction based on their impact on proximate determinants of incidence(49). However, there is the need for critical consideration of the role of these interventions in high prevalence settings. Interventions offered in group settings, such as schools, may be most feasible in resource-constrained environments.

Schools are often used to deliver behavioral interventions because they reach a large number of youth, often prior to sexual debut. Of the three published adolescent HIV prevention RCTs conducted with HIV incidence endpoints, two have been school-based (50-52). None of the studies found an impact on HIV and results were mixed for sexual behavior. Overall, those with greatest success were curriculum-based, adult-led, and followed specific

guidelines ('Kirby characteristics') (53, 54). Combining modalities to deliver biomedical interventions, such as HCT, in schools may lead to greater program uptake.

Understanding the larger context of behavioral interventions is critical to their success(55). Many school-based interventions were implemented in settings where massive gender and power inequities may undermine programs' success (51). Further, issues related to proper intervention implementation and fidelity likely compromised efficacy (56).

There is increasing emphasis on addressing prevention issues with HIV-infected individuals. Positive health dignity and prevention interventions (PHDP) help people living with HIV lead complete and healthy lives and reduce HIV transmission. PHDP involves systematic delivery of a range of combination, behavioral, and sociocultural services within local communities (57). Although the core components of PHDP have been defined, evidence is required to tailor these for use with adolescents in diverse settings and evaluate cost effectiveness.

### Structural/Contextual Interventions

At the structural and contextual level, important drivers of adolescent risk are poverty, discrimination, gender and power inequities, stigma, and environments that are not youth-friendly (48, 58). Few interventions address these structural factors. Given the high prevalence of rape in SSA (59), and that HIV transmission in the context of gender-based violence is common (60), we must examine approaches that tackle HIV prevention within the broader context of gender inequity.

Structural barriers to accessing care need to be addressed for adolescents. Youth-friendly reproductive health services can attract and retain youth in care (61). Health facilities that are successful in making services more adolescent-friendly have consistently included provider training and community activities (54). Given the central role of HTC and biomedical interventions in the prevention landscape, we need to identify the successes of reproductive health services and adapt and/or integrate HIV prevention in these services. Models for youth-friendly services offering testing have been developed (62-64); however, adolescents' uptake of HTC is not well understood. Research to explore how to increase HTC uptake, disclosure of serostatus, and linkages to prevention (e.g. PrEP) and care (e.g. TasP) is required.

It is critical to address limited education and poverty that increase risk for HIV infection (65-68). A recent trial among young women in Malawi showed cash transfers lowered HIV and HSV-2 prevalence and demonstrated positive changes in age of sex partner and frequency of sex acts (69). Providing cash to young women may have allowed them to change partnership characteristics, reducing their risk of HIV infection; however, the mechanism through which such programs work is still unclear. Several large RCTs examining cash transfers with HIV incidence endpoints are currently underway and may help identify the mechanism of action of such interventions (70, 71). There is a need to explore a range of interventions to reduce poverty and improve the financial independence of young people.

Other structural approaches that change social norms through media campaigns or community mobilization can reach large numbers of adolescents. Messages that target larger audiences and work to reinforce HIV prevention and care messages play a key role in normalizing HIV testing and uptake of newer prevention technologies (72). The role of community mobilization to increase uptake of HTC or VMMC is promising, yet understudied. Ultimately, interventions combining multiple strategies with sufficient community coverage are likely to have greatest impact.

Youth are the greatest users of Internet and mobile devices globally (73, 74), with high usage reported even in developing countries (75)(76). Use of such methods should easily and cost-effectively reach a large youth population using this medium and develop tailored programs to make messages relevant to each recipient (77). Early computer-based interventions showed potential to improve sexual health outcomes for youth (78-80). Current interventions are harnessing the interactive power of social media sites like Facebook and Twitter with promising results (81)(82, 83). Mobile phones can also be used as a platform to deliver preventive interventions (84, 85), or to improve adherence to ART (86). There is a need for rigorously evaluated interventions that effectively link technology to clinic-based efforts to foster safer sexual health behaviors and treatment adherence (77).

## Conclusions

Despite the high risk of HIV transmission among young people, few rigorously designed prevention interventions with HIV endpoints have been evaluated. Many interventions focus on changing individual-level behaviors rather than addressing the larger contextual and structural landscape within which young people live. Further, few studies have explored the use of biomedical interventions among young people. While biomedical prevention offers considerable promise, further research is needed to determine the applicability, safety and efficacy of these approaches among youth. The factors affecting HIV risk are complex and will require a combination approach incorporating a supportive behavioral, structural and/or biomedical intervention. Developing a prevention menu where adolescents, depending on their phase of transition and sexual activity, may tailor their individual prevention package, would represent a major advance in preventing HIV among youth.

## Acknowledgments

**Sources of support:** UM1 AI068619

## References

1. Nugent, R. Youth in a Global World. Washington, D.C.: Population Reference Bureau; 2006.
2. UNAIDS. UNAIDS Report on the Global AIDS Epidemic. Geneva: 2010.
3. Gouws E, Stanecki KA, Lyerla R, Ghys PD. The epidemiology of HIV infection among young people aged 15-24 years in southern Africa. *AIDS*. 2008 Dec; 22(4):S5-16. [PubMed: 19033755]
4. Pettifor AE, Rees HV, Kleinschmidt I, et al. Young people's sexual health in South Africa: HIV prevalence and sexual behaviors from a nationally representative household survey. *AIDS*. 2005 Sep 23; 19(14):1525-34. [PubMed: 16135907]
5. The Panel on Transitions to Adulthood Growing up global: the changing transitions to adulthood in developing countries: a review of published data. Washington, D.C.: 2005.
6. Schmithorst VJ, Yuan W. White matter development during adolescence as shown by diffusion MRI. *Brain and cognition*. 2010 Feb; 72(1):16-25. [PubMed: 19628324]
7. Casey BJ, Jones RM, Hare TA. The adolescent brain. *Annals of the New York Academy of Sciences*. 2008 Mar.1124:111-26. [PubMed: 18400927]
8. Erikson, EH. *Childhood and Society*. New York: W. W. Norton & Company; 1950.
9. Erikson, EH. *Identity: Youth and crisis*. New York: W. W. Norton & Company; 1968.
10. Brooks-Gunn, J.; Graber, J. What's sex got to do with it? The development of sexual identities during adolescence. In: Contrada, RJ.; Ashmore, RD., editors. *Self, Social Identity and Physical Health*. 1. Oxford; Oxford University Press; 1999.
11. Flisher AJ, Chalton DO. Adolescent contraceptive non-use and covariation among risk behaviors. *The Journal of adolescent health : official publication of the Society for Adolescent Medicine*. 2001 Mar; 28(3):235-41. [PubMed: 11226847]

12. Swartz L, Kagee A, Kafaar Z, et al. Social and behavioral aspects of child and adolescent participation in HIV vaccine trials. *Journal of the International Association of Physicians in AIDS Care (Chicago, Ill : 2002)*. 2005 Dec; 4(4):89–92.
13. Coates TJ, Richter L, Caceres C. Behavioural strategies to reduce HIV transmission: how to make them work better. *Lancet*. 2008 Aug 23; 372(9639):669–84. [PubMed: 18687459]
14. Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med*. 2011 Aug 11; 365(6):493–505. [PubMed: 21767103]
15. Baeten JM, Donnell D, Ndase P, et al. Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. *N Engl J Med*. 2012 Aug 2; 367(5):399–410. [PubMed: 22784037]
16. Bailey RC, Moses S, Parker CB, et al. Male circumcision for HIV prevention in young men in Kisumu, Kenya: a randomised controlled trial. *Lancet*. 2007 Feb 24; 369(9562):643–56. [PubMed: 17321310]
17. Gray RH, Kigozi G, Serwadda D, et al. Male circumcision for HIV prevention in men in Rakai, Uganda: a randomised trial. *Lancet*. 2007 Feb 24; 369(9562):657–66. [PubMed: 17321311]
18. Grant RM, Lama JR, Anderson PL, et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *N Engl J Med*. 2010 Dec 30; 363(27):2587–99. [PubMed: 21091279]
19. Abdool Karim Q, Abdool Karim SS, Frohlich JA, et al. Effectiveness and safety of tenofovir gel, an antiretroviral microbicide, for the prevention of HIV infection in women. *Science*. 2010 Sep 3; 329(5996):1168–74. [PubMed: 20643915]
20. Thigpen MC, Kebaabetswe PM, Paxton LA, et al. Antiretroviral preexposure prophylaxis for heterosexual HIV transmission in Botswana. *N Engl J Med*. 2012 Aug 2; 367(5):423–34. [PubMed: 22784038]
21. Van Damme L, Corneli A, Ahmed K, et al. Preexposure prophylaxis for HIV infection among African women. *The New England journal of medicine*. 2012 Aug 2; 367(5):411–22. [PubMed: 22784040]
22. Marrazzo, J.; Ramjee, G.; Nair, G., et al. Pre-exposure Prophylaxis for HIV in Women: Daily Oral Tenofovir, Oral Tenofovir/Emtricitabine, or Vaginal Tenofovir Gel in the VOICE Study (MTN 003); Conference on Retroviruses and Opportunistic Infections; Atlanta, GA. 2013;
23. Amico KR, Mansoor LE, Corneli A, Torjesen K, van der Straten A. Adherence Support Approaches in Biomedical HIV Prevention Trials: Experiences, Insights and Future Directions from Four Multisite Prevention Trials. *AIDS and behavior*. 2013 Feb 23.
24. Murnane, PM.; Celum, C.; Kahle, EM., et al. Daily Oral Pre-exposure Prophylaxis in Highly Effective among Subsets of Highest-risk Participants: Partners PrEP Study; Conference of Retroviruses and Opportunistic Infections (CROI); Atlanta, GA. 2013;
25. Belzer ME, Fuchs DN, Luftman GS, Tucker DJ. Antiretroviral adherence issues among HIV-positive adolescents and young adults. *The Journal of adolescent health : official publication of the Society for Adolescent Medicine*. 1999 Nov; 25(5):316–9. [PubMed: 10551660]
26. Fetzer BC, Mupenda B, Lusiana J, Kitetele F, Golin C, Behets F. Barriers to and facilitators of adherence to pediatric antiretroviral therapy in a sub-Saharan setting: insights from a qualitative study. *AIDS patient care and STDs*. 2011 Oct; 25(10):611–21. [PubMed: 21823909]
27. Murphy DA, Wilson CM, Durako SJ, Muenz LR, Belzer M. Antiretroviral medication adherence among the REACH HIV-infected adolescent cohort in the USA. *AIDS care*. 2001 Feb; 13(1):27–40. [PubMed: 11177463]
28. Barclay TR, Hinkin CH, Castellon SA, et al. Age-associated predictors of medication adherence in HIV-positive adults: health beliefs, self-efficacy, and neurocognitive status. *Health psychology : official journal of the Division of Health Psychology, American Psychological Association*. 2007 Jan; 26(1):40–9.
29. Rudy BJ, Murphy DA, Harris DR, Muenz L, Ellen J. Patient-related risks for nonadherence to antiretroviral therapy among HIV-infected youth in the United States: a study of prevalence and interactions. *AIDS patient care and STDs*. 2009 Mar; 23(3):185–94. [PubMed: 19866536]
30. Bain-Brickley D, Butler LM, Kennedy GE, Rutherford GW. Interventions to improve adherence to antiretroviral therapy in children with HIV infection. *Cochrane database of systematic reviews (Online)*. 2011; 12:CD009513.

31. Fernandez MI, Hosek S, Warren JC, Jacobs RJ, Hernandez N, Martinez J. Development of an easy to use tool to assess HIV treatment readiness in adolescent clinical care settings. *AIDS care*. 2011 Nov; 23(11):1492–9. [PubMed: 22022853]
32. Garvie PA, Flynn PM, Belzer M, et al. Psychological factors, beliefs about medication, and adherence of youth with human immunodeficiency virus in a multisite directly observed therapy pilot study. *The Journal of adolescent health : official publication of the Society for Adolescent Medicine*. 2011 Jun; 48(6):637–40. [PubMed: 21575827]
33. Gray WN, Janicke DM, Fennell EB, Driscoll DC, Lawrence RM. Piloting behavioral family systems therapy to improve adherence among adolescents with HIV: a case series intervention study. *Journal of health psychology*. 2011 Jul; 16(5):828–42. [PubMed: 21441357]
34. Wohl AR, Garland WH, Wu J, et al. A youth-focused case management intervention to engage and retain young gay men of color in HIV care. *AIDS care*. 2011 Aug; 23(8):988–97. [PubMed: 21390879]
35. Pugatch D, Bennett L, Patterson D. HIV Medication Adherence in Adolescents. *Journal of HIV/ AIDS Prevention & Education for Adolescents & Children* 2002. 2002 Aug 19; 5(1-2):9–29.
36. Kapogianis, B. National Institute of Health and Microbicides Trial Network plan safety and acceptability trial of tenofavir gel-based microbicide in adolescent women. 2012.
37. FACTS. Follow-on African Consortium for Tenofavir Studies (FACTS). 2011. cited; Available from: [http://www.iprexnews.com/pdfswhatisNew/FACTS\\_Overview\\_June2011.pdf](http://www.iprexnews.com/pdfswhatisNew/FACTS_Overview_June2011.pdf)
38. Microbicide Trials Network 017: A Phase 2 Randomized Sequence Open Label Expanded Safety and Acceptability Study of Oral Emtricitabine/Tenofovir Disoproxil Fumarate Tablet and Rectally-Applied Tenofovir Reduced-Glycerin 1% Gel. [cited 2013 March 7]; Available from: <http://www.mtnstopshiv.org/news/studies/mtn017>
39. Thurman A, Clark M, Doncel G. Multipurpose prevention technologies: biomedical tools to prevent HIV-1, HSV-2, and unintended pregnancies. *Infectious Diseases in Obstetrics and Gynecology*. 2011; 2011:1–10. [PubMed: 21836811]
40. Auvert B, Taljaard D, Lagarde E, Sobngwi-Tambekou J, Sitta R, Puren A. Randomized, controlled intervention trial of male circumcision for reduction of HIV infection risk: the ANRS 1265 Trial. *PLoS Med*. 2005 Nov.2(11):e298. [PubMed: 16231970]
41. Jaspan H, Tucker T, Wright P, Self S, Sheets R, al. e. Inclusion of Adolescents in preventative HIV Vaccine Trials: public health policy and research design at a crossroads. *Journal of acquired immune deficiency syndromes (1999)*. 2008; 47(1):86–92. [PubMed: 17984759]
42. DiClemente RJ, Ruiz MS, Sales JM. Barriers to adolescents' participation in HIV biomedical prevention research. *Journal of acquired immune deficiency syndromes (1999)*. 2010 Jul; 54(1):S12–7. [PubMed: 20571418]
43. Nelson RM, Lewis LL, Struble K, Wood SF. Ethical and regulatory considerations for the inclusion of adolescents in HIV biomedical prevention research. *Journal of acquired immune deficiency syndromes (1999)*. 2010 Jul; 54(1):S18–24. [PubMed: 20571419]
44. Jaspan HB, Soka NF, Strode AE, et al. Community perspectives on the ethical issues surrounding adolescent HIV vaccine trials in South Africa. *Vaccine*. 2008 Oct 23; 26(45):5679–83. [PubMed: 18782594]
45. Pettifor A, Bekker LG. Adolescent enrolment in HIV prevention trials. *Lancet*. 2012 Aug 18.380(9842):646. [PubMed: 22901878]
46. Kamali A, Quigley M, Nakiyingi J, et al. Syndromic management of sexually-transmitted infections and behaviour change interventions on transmission of HIV-1 in rural Uganda: a community randomised trial. *Lancet*. 2003; 361:645–52. [PubMed: 12606175]
47. Koblin B, Chesney M, Coates T. Effects of a behavioural intervention to reduce acquisition of HIV infection among men who have sex with men: the EXPLORE randomised controlled study. *Lancet*. 2004 Jul 3-9; 364(9428):41–50. [PubMed: 15234855]
48. Padian NS, McCoy SI, Karim SS, et al. HIV prevention transformed: the new prevention research agenda. *Lancet*. 2011 Jul 16; 378(9787):269–78. [PubMed: 21763938]
49. Centers for Disease Control and Prevention. Compendium of Evidence-Based HIV Behavioral Interventions. 2011. [cited 2012 October 22]; Available from: <http://www.cdc.gov/hiv/topics/research/prs/compendium-evidence-based-interventions.htm>



50. Cowan FM, Pascoe SJ, Langhaug LF, et al. The Regai Dzive Shiri project: results of a randomized trial of an HIV prevention intervention for youth. *AIDS*. 2010 Oct 23; 24(16):2541–52. [PubMed: 20881473]
51. Ross DA, Changalucha J, Obasi AI, et al. Biological and behavioural impact of an adolescent sexual health intervention in Tanzania: a community-randomized trial. *AIDS*. 2007 Sep 12; 21(14):1943–55. [PubMed: 17721102]
52. Doyle AM, Ross DA, Maganja K, et al. Long-term biological and behavioural impact of an adolescent sexual health intervention in Tanzania: follow-up survey of the community-based MEMA kwa Vijana Trial. *PLoS Med*. 2010 Jun.7(6):e1000287. [PubMed: 20543994]
53. Ross, D. Preventing HIV/AIDS in young people : a systematic review of the evidence from developing countries: UNAIDS interagency task team on HIV and young people. Geneva: 2006.
54. Napierala-Mavedzenge, S.; Doyle, A.; Ross, D. HIV Prevention Among Young People in Sub-Saharan Africa: A Systematic Review. Ross, D., editor. London: Dept Epidemiology and Pop Health, LSTMH; 2010.
55. Mathews C, Aarø LE, Grimsrud A, et al. Effects of the SATZ teacher-led school HIV prevention programmes on adolescent sexual behaviour: cluster randomised controlled trials in three sub-Saharan African sites. *International Health*. 2012; 4(2):111–22.
56. Michielsen K, Chersich MF, Luchters S, De Koker P, Van Rossem R, Temmerman M. Effectiveness of HIV prevention for youth in sub-Saharan Africa: systematic review and meta-analysis of randomized and nonrandomized trials. *AIDS*. 2010 May 15; 24(8):1193–202. [PubMed: 20375876]
57. Sharer, MF. A Transitioning of Care and Other Services for Adolescents Living with HIV in Sub-Saharan Africa. Arlington, VA: AIDSTAR-One; 2012.
58. McCoy SI, Watts CH, Padian NS. Preventing HIV infection: turning the tide for young women. *Lancet*. 2010 Oct 16; 376(9749):1281–2. [PubMed: 20851461]
59. Dartnall E, Jewkes R. Sexual violence against women: The scope of the problem. *Best Pract Res Clin Obstet Gynaecol*. 2013 Feb; 27(1):3–13. [PubMed: 22940107]
60. Jewkes R, Sikweyiya Y, Morrell R, Dunkle K. The relationship between intimate partner violence, rape and HIV amongst South African men: a cross-sectional study. *PLoS One*. 2011; 6(9):e24256. [PubMed: 21935392]
61. Ross, D.; Dick, B.; Ferguson, J. Preventing HIV/AIDS in young people: a systematic review of the evidence from developing countries: UNAIDS interagency task team on HIV and young people. Geneva: World Health Organization; 2006.
62. MietAfrica. Literature Review: Youth-Friendly Health Services. 2011
63. WHO FCH CAH. Adolescent Friendly Health Services - An Agenda for Change. 2002
64. Centers for Disease Control and Prevention. HIV Testing Among Adolescents: What Schools and Education Agencies Can Do. 2012.
65. Barnighausen T, Hosegood V, Timaeus IM, Newell ML. The socioeconomic determinants of HIV incidence: evidence from a longitudinal, population-based study in rural South Africa. *AIDS* (London, England). 2007 Nov; 21(7):S29–38.
66. Hargreaves JR, Bonell CP, Morison LA, et al. Explaining continued high HIV prevalence in South Africa: socioeconomic factors, HIV incidence and sexual behaviour change among a rural cohort, 2001-2004. *AIDS* (London, England). 2007 Nov; 21(7):S39–48.
67. Madise N, Zulu E, Ciera J. Is poverty a driver for risky sexual behaviour? Evidence from national surveys of adolescents in four African countries. *African journal of reproductive health*. 2007 Dec; 11(3):83–98. [PubMed: 20698061]
68. Msisha WM, Kapiga SH, Earls F, Subramanian SV. Socioeconomic status and HIV seroprevalence in Tanzania: a counterintuitive relationship. *International journal of epidemiology*. 2008 Dec; 37(6):1297–303. [PubMed: 18820319]
69. Baird SJ, Garfein RS, McIntosh CT, Ozler B. Effect of a cash transfer programme for schooling on prevalence of HIV and herpes simplex type 2 in Malawi: a cluster randomised trial. *Lancet*. 2012 Apr 7; 379(9823):1320–9. [PubMed: 22341825]

70. HIV Prevention Trials Network. HPTN 068: Effects of Cash Transfer for the Prevention of HIV in Young South African Women. 2011. [cited 2012 November 1, 2012] Available from: [http://www.hptn.org/research\\_studies/hptn068.asp](http://www.hptn.org/research_studies/hptn068.asp)
71. National Institute of Health. Reducing HIV in Adolescents (RHIVA). 2012. [cited 2012 November 1, 2012] Available from: <http://clinicaltrials.gov/ct2/show/NCT01187979>
72. Bharath-Kumar U, Becker-Benton A, Lettenmaier C, Fehringer J, Bertrand JT. Communication and the antiretroviral treatment rollout: beyond the medical model. *AIDS education and prevention : official publication of the International Society for AIDS Education*. 2009 Oct; 21(5): 447–59. [PubMed: 19842828]
73. Horrigan, J. Mobile Access to Data and Information. 2008. [cited 2012 1/24/2012]; Available from: <http://www.pewinternet.org/Reports/2008/Mobile-Access-to-Data-and-Information.aspx>
74. Rainie, L. The rise of cell phone text messaging. 2005. [cited 2012 1/24/2012]; Available from: <http://www.pewinternet.org/Commentary/2005/March/The-Rise-of-Cell-Phone-Text-Messaging.aspx>
75. NielsenWire. Cellphones and Global Youth: Mobile Internet and Messaging Trends 2011. Jan 11. 2011 [cited 2012 January 22]; Available from: [http://blog.nielsen.com/nielsenwire/online\\_mobile/cellphones-and-global-youth-mobile-internet-and-messaging-trends/](http://blog.nielsen.com/nielsenwire/online_mobile/cellphones-and-global-youth-mobile-internet-and-messaging-trends/)
76. Kreutzer, T. *Emerge 2008*. Cape Town: 2008. Assessing Cell Phone Usage in a South African Township School.
77. Bull, SS. *Technology Based Health Promotion*. 1. Thousand Oaks, CA: Sage; 2010.
78. Albarracin D, Gillette JC, Earl AN, Glasman LR, Durantini MR, Ho MH. A test of major assumptions about behavior change: a comprehensive look at the effects of passive and active HIV-prevention interventions since the beginning of the epidemic. *Psychological bulletin*. 2005 Nov; 131(6):856–97. [PubMed: 16351327]
79. Albarracin D, Kumkale GT, Johnson BT. Influences of social power and normative support on condom use decisions: a research synthesis. *AIDS care*. 2004 Aug; 16(6):700–23. [PubMed: 15370059]
80. Jemmott JB 3rd, Jemmott LS. HIV risk reduction behavioral interventions with heterosexual adolescents. *AIDS (London, England)*. 2000 Sep; 14(2):S40–52.
81. Moreno MA, Vanderstoep A, Parks MR, Zimmerman FJ, Kurth A, Christakis DA. Reducing at-risk adolescents' display of risk behavior on a social networking web site: a randomized controlled pilot intervention trial. *Archives of pediatrics & adolescent medicine*. 2009 Jan; 163(1):35–41. [PubMed: 19124701]
82. Bull SS, Breslin LT, Wright EE, Black SR, Levine D, Santelli JS. Case study: An ethics case study of HIV prevention research on Facebook: the Just/Us study. *Journal of pediatric psychology*. 2011 Nov-Dec;36(10):1082–92. [PubMed: 21292724]
83. Levine D, Madsen A, Wright E, Barar RE, Santelli J, Bull S. Formative research on MySpace: online methods to engage hard-to-reach populations. *Journal of health communication*. 2011 Apr; 16(4):448–54. [PubMed: 21391040]
84. Juzang I, Fortune T, Black S, Wright E, Bull S. A pilot programme using mobile phones for HIV prevention. *Journal of telemedicine and telecare*. 2011; 17(3):150–3. [PubMed: 21270049]
85. Levine D, McCright J, Dobkin L, Woodruff AJ, Klausner JD. SEXINFO: a sexual health text messaging service for San Francisco youth. *Am J Public Health*. 2008 Mar; 98(3):393–5. [PubMed: 18235068]
86. Lester RT, Ritvo P, Mills EJ, et al. Effects of a mobile phone short message service on antiretroviral treatment adherence in Kenya (WelTel Kenya1): a randomised trial. *Lancet*. 2010 Nov 27; 376(9755):1838–45. [PubMed: 21071074]

**Table 1**  
**HIV Prevention Research Gaps for Adolescents**

Area	Knowledge Gap
Biomedical	<ul style="list-style-type: none"> <li>• Methods to enhance monitoring and measurement of adherence to biomedical interventions</li> <li>• Interventions to enhance adherence to biomedical interventions</li> <li>• Acceptability and safety of biomedical interventions</li> <li>• How to enhance uptake of biomedical interventions among adolescents who will benefit from them</li> <li>• How adolescents choose biomedical prevention interventions</li> <li>• How fertility desires and intentions affect uptake and acceptability of biomedical interventions</li> <li>• How sero-status of a couple affects uptake and acceptability of biomedical interventions</li> <li>• Social marketing of biomedical interventions.</li> </ul>
Behavioral	<ul style="list-style-type: none"> <li>• Undertaking formative work to develop culturally appropriate behavioral interventions rather than adapting those based on western psychological models</li> <li>• Understanding how to maintain intervention effects overtime (durability of effect)</li> <li>• Understanding sexual relationship patterns (ie, longitudinal partnership formation, types of partners, frequency of sex)</li> <li>• Methods to obtain valid self-reported risk behaviors and risk perception</li> <li>• How to best use new technologies and media for prevention and care</li> <li>• Partner level interventions- Ability to identify main sexual partners and engage in interventions or refer for care</li> <li>• Adaptation and extension of best-evidence interventions in the US to high-prevalence settings</li> </ul>
Structural	<ul style="list-style-type: none"> <li>• How to effectively and acceptably integrate HIV prevention with other youth friendly services</li> <li>• Role of school health in HIV prevention</li> <li>• Structural barriers to HTC and linkage to care</li> <li>• HTC models and methodologies</li> <li>• Integrated sexual and reproductive health packages</li> <li>• Socio-economic interventions</li> <li>• Interventions that address gender inequity/GBV</li> <li>• Community mobilization to increase uptake of HIV prevention</li> <li>• Utilization of technology (e.g., cell phones or computer) in interventions</li> </ul>
Positive Prevention	<ul style="list-style-type: none"> <li>• Enhancing linkage and retention to care</li> <li>• Greater understanding of the treatment cascade in adolescents</li> <li>• Interventions to assist with disclosure</li> <li>• Integrated reproductive health services, in particular contraception and PMTCT</li> <li>• How best to support the transition from pediatric to adult services</li> <li>• How to tailor clinical services and monitoring for adolescents</li> </ul>
Ethico-legal	<ul style="list-style-type: none"> <li>• Licensure for biomedical- efficacy or extrapolation and safety</li> <li>• Age to roll down to and when in the licensure pathway</li> </ul>

Area	Knowledge Gap
Cross-cutting Practice/Research	<ul style="list-style-type: none"><li>• Issues of consent and consent waiver</li></ul> <hr/> <ul style="list-style-type: none"><li>• Translating interventions from theory/formative research to practice-implementation science</li><li>• Cost-effectiveness</li><li>• Modeling of effect sizes and potential impact of various interventions</li><li>• Combination prevention interventions</li></ul>