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Towards an integrated framework for accelerating the end for the global HIV epidemic among young people

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Abstract

For decades the HIV epidemic has exacted an enormous toll worldwide. However, trend analyses have discerned significant declines in the overall prevalence of HIV over the last two decades. More recently, advances in biomedical, behavioural, and structural interventions offer considerable promise in the battle against generalised epidemics. Despite advances in the prevention of transmission and new infections, morbidity and mortality of HIV among young people remains a considerable concern for individuals, couples, families, communities, practitioners, and policy makers around the globe. To accelerate the end of the global HIV epidemic among young people, we must merge existing efficacious interventions with more novel, cost-effective implementation strategies to develop integrated, multilevel combination interventions. The benefits of conceptualising the HIV epidemic more broadly and adopting ecological frameworks for the development of HIV prevention programmes are critical.

Keywords

adolescents; young people; combination prevention; ecological framework

Introduction

The HIV epidemic has taken a toll globally for several decades. Recently, we have witnessed remarkable improvements in the prevention and treatment of HIV. The incidence of HIV worldwide was at its highest in 1997, and since the mid-2000s the rate has declined, with the most significant declines occurring in sub-Saharan Africa and the Caribbean (25% and 42% decline, respectively; between 2001 and 2011) (UNAIDS 2012a). The worldwide prevalence of HIV at the end of 2011 was 34 million, and mortality related to AIDS has decreased (24% decline between 2005 and 2011), mostly attributable to increased availability to antiretroviral therapy (ART) and ongoing decreases in HIV incidence (UNAIDS 2012b). Among women and men, 15-49 years old, HIV prevalence in 2011 was approximately 0.8% globally, and women made up half of the adults living with HIV, a proportion that has withstood nearly two decades (UNAIDS 2012b). In the same year, there

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were nearly 3.4 million children living with HIV, 91% of which were in sub-Saharan Africa (WHO, UNAIDS, and UNICEF 2011).

While reductions in HIV incidence have been encouraging, there are still too many young people becoming infected (O'Brien et al. 2013). We need to accelerate the rate at which we reduce HIV infections and strive for an HIV-free generation. There are several prior resources that synthesise the extant literature on biomedical, behavioural, and structural interventions for HIV prevention (Johnson et al. 2010; Johnson et al. 2011; Kirby, Laris, and Roller 2007; Kim et al. 1997; McCubbin and Patterson 1983; Morrison-Beedy and Nelson 2004; Mullen et al. 2002; Paul-Ebhohimhen, Poobalan, and van Teijlingen 2008; Pedlow and Carey 2003; Pedlow and Carey 2004; Shepherd et al. 2010; Yamada et al. 1999). This article builds on this overarching framework for HIV prevention with adolescents (defined as between the ages of 13-24 years) by highlighting current approaches, challenges and gaps in existing adolescent HIV prevention efforts. Additionally, the existing literature specific to young people and adolescents is limited. Nevertheless, the continued development and examination of HIV prevention interventions coupled with the collective integration of multi-level prevention approaches may accelerate the end of HIV in this population.

Two key barriers to ending the HIV epidemic among young people are the heterogeneity and dearth of empirical evidence on the efficacy of tailored interventions (DiClemente et al. 2008; DiClemente and Wingood 2003; Jackson et al. 2012). Similar to adult populations, many subpopulations of young people (young men who have sex with men, perinatally versus behaviourally infected) have different HIV risks and prevalence rates (Gupta et al. 2008; Morrison-Beedy and Nelson 2004; Macdonell et al. 2013). Despite the absence of a “magic bullet” vaccine to prevent HIV infection, the existing arsenal of evidence-based tools to combat the HIV epidemic has an array of promising behavioural, biomedical and structural interventions. Many of the global efforts to halt the HIV epidemic have primarily focused at the individual-level; modifying individual's HIV-associated risk behaviours as a strategy to prevent HIV transmission (Ford, Calmy, and Mills 2011). From a broader socio-ecological perspective, it is equally important to allocate resources strategically to target the contextual drivers of the HIV epidemic, including the integration of effective sex education for young people (Kirby, Laris, and Roller 2007; Kirby, Laris, and Roller 2006; Kirby 2011). Thus, an integrated implementation approach, which encompasses tailored biomedical, behavioural, and structural interventions as necessary.

Biomedical interventions

In the past few years alone, there have been extraordinary developments in biomedical approaches to HIV prevention. Biomedical strategies for preventing HIV leverage medical and public health approaches in targeting biological-level systems to prevent infection, reduce infectiousness, and to decrease vulnerability to HIV. It is important to note that biomedical strategies, while effective, do not change an individual's or population's HIV risk behaviours, but rather they affect biological mechanisms and processes that reduce the risk of infection if an individual is exposed to HIV. Additionally, although variation exists in the efficacy of biomedical interventions, measured as their effectiveness in reducing HIV infection, emerging literature suggests that biomedical HIV prevention strategies can play a

promising and significant role in the future of HIV prevention. Below we briefly review biomedical strategies.

Male and female condoms

Globally, sexual intercourse remains the primary route of HIV transmission in generalised epidemics (Ross, Dick, and Ferguson 2006). Fortunately, there is accumulating empirical evidence that male latex condoms, when used consistently and correctly, are effective in preventing transmission of STIs, including HIV (Foss et al. 2007; Pinkerton and Abramson 1997). Prior studies have suggested effectiveness is approximately an 80% reduction in HIV incidence (Weller and Davis-Beaty 2007). However, the population-level effectiveness of male condom use is less well-established (Padian et al. 2008).

Female condoms, an alternative to male condoms, have demonstrated effectiveness in preventing HIV transmission (French et al. 2003; Gallo, Kilbourne-Brook, and Coffey 2012; Padian et al. 2008). One advantage of female condoms is that women can actually apply them without reliance on male partners. However, there are barriers (i.e. female condom self-efficacy) surrounding the usability and acceptability of female condoms that need to be better understood (French et al. 2003; Gallo, Kilbourne-Brook, and Coffey 2012), as well as variability worldwide in accessibility and cost of female condoms (Gallo, Kilbourne-Brook, and Coffey 2012). Despite prior trials demonstrating effectiveness, the lack of consistent and correct use markedly reduces their effectiveness as an HIV prevention strategy that can be widely disseminated in most generalised epidemics (Gallo, Kilbourne-Brook, and Coffey 2012; O'Brien et al. 2013). Variability in usability, acceptability, accessibility, and cost of condoms has been problematic in countries with generalised epidemics.

HIV Testing and Counselling (HTC)

The use of HIV Testing and Counselling (HTC) can serve to detect HIV infection and provide a pathway to treatment services (WHO 2011). Additionally, couples-delivered HTC can help identify partners who are HIV-positive or at-risk of becoming HIV-positive, thus supporting couples' safe sexual behaviours as well as disclosure of HIV status among partners (Burton, Darbes, and Operario 2010; Dunkle et al. 2008). HTC as a stand alone intervention may not be sufficient (Ross 2010); thus, the integration of HTC and other interventions is essential. Implementation of HTC has been limited (Nakanjako et al. 2007; Sanders et al. 2010) and healthcare systems vary greatly insofar as staffing, availability of services, and linkage to services that complement HTC. The HTC approach has also been identified by public health researchers as a promising large-scale strategy to reducing community levels of infectivity (Attia et al. 2009; Dieffenbach and Fauci 2009; Donnell et al. 2010).

Treatment as Prevention (TasP)

Historically, most HIV prevention efforts worldwide have focused on the prevention of HIV transmission versus the implementation of treatment-focused interventions (Ford, Calmy, and Mills 2011). Due to decreasing costs of available HIV treatments, more recent global responses have shifted towards the large-scale implementation of HIV treatment as a prevention strategy (UNAIDS 2012b; Holmes et al. 2012). Studies of HIV-positive partners

have observed that antiretroviral (ARV) therapy may provide a significant reduction in the risk of HIV transmission to HIV-negative partners, suggesting that ARV therapy decreases infectivity (Ray et al. 2010). Findings from the HPTN 052 randomised clinical trial comparing ARV plus HIV primary care versus HIV primary care alone among HIV serodiscordant couples observed that early initiation of ARV treatment markedly reduced (96% reduction) rates of HIV-1 infection (M. S. Cohen et al. 2011).

Pre-exposure Prophylaxis (PrEP)

Pre-exposure prophylaxis (PrEP) is a newer medical and public health method for HIV prevention wherein HIV-negative individuals consume a pill on a daily basis to reduce their risk of HIV (Baeten et al. 2013). Prior studies have demonstrated a substantial reduction in the risk of acquiring HIV in a variety of populations, including heterosexual men, women, MSM, and injection drug users (Choopanya et al. 2013; Grant et al. 2010; Paltiel et al. 2009; Thigpen et al. 2012). As a subpopulation of men who have sex with men, young men who have sex with men account for much of the increase in incident HIV worldwide, yet there have been a disproportionately lower number of PrEP effectiveness trials that included young men who have sex with men (Pace et al. 2013). The evidence suggests that PrEP may be most effective when used in combination with other HIV prevention strategies, including one study where men who have sex with men and transgendered women received Truvada (tenofovir plus emtricitabine) in conjunction with other HIV prevention strategies (Grant et al. 2010). Another study demonstrated a 62% reduction in HIV acquisition among heterosexual men and women in Botswana (Thigpen et al. 2012).

Despite promising findings from early trials, outcomes from clinical trials involving PrEP have varied greatly (van der Straten et al. 2012). Variance has been attributed to differences in adherence rates, acute stage of HIV infection of partner(s), integrity of vaginal epithelium and biological determinants of HIV (van der Straten et al. 2012). Additionally, PrEP as a preventive tool may be the most appealing option when used with high-risk populations (Baeten et al. 2013). Nevertheless, more research is needed to validate the existing findings associated with the use of PrEP to prevent HIV acquisition and whether this biological prevention strategy is appropriate for younger adolescents (Pace et al. 2013).

Voluntary Medical Male Circumcision (VMMC)

Voluntary medical male circumcision (VMMC) is a preventive strategy involving the removal of the foreskin, performed by medical professionals who are trained to implement this surgical procedure. Prior studies suggest that VMMC can reduce male risk of acquiring HIV from sexual intercourse with women by up to 60% (Bailey et al. 2007; Gray et al. 2007; Weiss et al. 2008), and existing evidence also suggests an association between VMMC and a reduction in STI incidence in women (Gray et al. 2009; Hankins et al. 2009; Wawer et al. 2009). Furthermore, a systematic review of the literature cites upwards of a 20% decrease of HIV incidence in women who reported sexual involvement with circumcised men (Weiss, Hankins, and Dickson 2009).

Statistical models suggest that if scaled-up and implemented rapidly, VMMC could potentially thwart the incidence of new HIV infections in high HIV prevalent countries that

currently have low rates of VMMC (Hankins et al. 2009; Njeuhmeli et al. 2011). If universal access to VMMC was implemented widely in sub-Saharan Africa, for instance, nearly 5.7 million new HIV infections and 3 million deaths could be prevented over the next two decades (Williams et al. 2006).

Despite these advances in biomedical interventions, many challenges remain for use with young people, along with numerous gaps in knowledge. For example, the formulation and pharmacokinetics of pharmacological interventions have not been appropriately investigated for safe use in adolescents (Sohn and Hazra 2013; Pace et al. 2013). Additionally, the use of male and female condoms has shown great promise in accelerating the end of HIV, but consistent and increased use is still needed (O'Brien et al. 2013). Moreover, the existing HIV prevention literature on strategies for integrating and coordinating pharmacological interventions into combination prevention frameworks with young people is still in its infancy (Yehia et al. 2013).

Behavioural interventions

Behavioural interventions are strategies geared towards influencing HIV-related risk behaviours to reduce HIV infection and transmission (i.e. widespread condom use, delayed onset of sexual debut) as well as supporting the diffusion, adoption, and adherence to biomedical interventions (Coates, Richter, and Caceres 2008; Johnson et al. 2011; Potts et al. 2008). Biomedical interventions are valuable but are often not sufficient as stand alone interventions. The Achilles' heel of these interventions is adherence to medication, whether TasP or PrEP (Coates 2013; Brown et al. 2013). However, complementing biomedical interventions with behavioural interventions may markedly enhance their efficacy. Thus, behavioural interventions that foster enhanced medication adherence and reduce sexual risk-taking could be an important component of the scale-up of biomedical prevention.

Meta-analytic results suggest that behavioural interventions can effectively reduce young people's risk for incident STIs, increase condom use, delay sexual debut and/or reduce rates of sex and increase sexual negotiation skills (Johnson et al. 2011). In delivering behavioural HIV interventions, community mobilisation strategies may provide the most promising opportunity to increase large-scale uptake of HIV prevention strategies (Sweat et al. 2011; Tan et al. 2012; Townsend, Mathews, and Zembe 2013). Prior studies demonstrated that the uptake of HTC can be enhanced in communities with diverse cultures and infrastructures (Sweat et al. 2011). Community-based organisations within at-risk communities may be best positioned to understand the unique cultural drivers behind the HIV epidemic within their communities (Chillag et al. 2002; Chowdhury et al. 2013). In this way, community-level strategies can target community norms, stigma, and other community-level barriers that may directly or indirectly sustain risk behaviours, which can have marked effects on rates of HIV incidence and transmission (Khumalo-Sakutukwa et al. 2008).

Challenges in behavioural HIV prevention and implementation

Scale-up and multilevel coordination of both behavioural and biomedical interventions may be best implemented by community-based organisations (Yehia et al. 2013), but the implementation of behavioural interventions is in dire need of integrated HIV prevention

models that are tailored to the needs of specific communities (Coates 2013). Future research should explore novel ways to combine behavioural and biomedical interventions as one strategy for maximising their effectiveness.

Technology-driven interventions

Among some of the more novel integrated prevention approaches are those that leverage behavioural intervention technology (BIT) for increased uptake, scale-up, and implementation with minority and adolescent communities (Brown et al. 2013). In particular, technology that builds upon existing evidence-based interventions (EBIs) using agent-based modeling, social network analysis, intelligent/adaptive technology, and computational linguistics to translate efficacious interventions that could potentially lead to widespread, cost-effective implementation of technology already used by many adolescents and young adults worldwide (Brown et al. 2013). However, the use of technology does have potential drawbacks, and approaches moving forward should utilise community-based participatory approaches to minimise distrust and maximise efficacy (Brown et al. 2013; Veinot et al. 2013; Wallerstein and Duran 2006).

Structural interventions

Structural approaches target macro-level social, cultural, economic, environmental, and political factors, such as discrimination, poverty, gender inequality, health and socioeconomic disparities, stigma, and social norms (Gupta et al. 2008; Pettifor et al. 2013). Structural interventions (or contextual interventions) are also critical in sustaining individual and community-level interventions, as many of the barriers to the successful adoption and implementation of biomedical and behavioural interventions can be averted on the macro-level through macro-level implementation of structures and processes that support these evidence-based interventions (DiClemente 2013; Wingood, Rubtsova, et al. 2013).

Thus, structural approaches seek to affect the “structures” or contextual factors that enhance HIV vulnerability, often in the form of government policies or transformational processes. For instance, policies that impose narrow budgetary restraints on HIV detection and treatment efforts may have deleterious effects on HIV prevention efforts (DiClemente 2013; Sales, Milhausen, and DiClemente 2006). Prior research suggests that structural interventions may be effective strategies for reducing HIV incidence in areas with both low prevalence of HIV (D. A. Cohen, Wu, and Farley 2006) as well as areas of high HIV prevalence (Pettifor et al. 2013). Additionally, structural interventions in conjunction with individual-level biomedical and behavioural interventions may create greater demand generation for HIV prevention and treatment services along the cascade of care (J. Cohen 2004).

Mass media strategies for HIV prevention have also shown promise as structural interventions, particularly with adolescents at heightened risk for HIV-related sexual behaviour (DiClemente, Salazar, and Crosby 2007). A culturally sensitive mass media HIV prevention tailored for African American adolescents was tested in a multi-city trial yielded a reduction in HIV-associated sexual risk behaviours (Romer et al. 2009). Other global studies have also observed reductions in sexual risk behaviours (Hausser and Michaud

1994). The use of mass media as a structural HIV intervention may be more useful as a component of a larger integrated, multilevel approach than as a standalone intervention strategy.

Challenges in structural HIV prevention and implementation with young people

Structural approaches are effective at promoting sustainability; however, structural approaches in conjunction with other interventions may yield the highest levels of HIV intervention efficacy. There are few existing integrated models that include effective biomedical, behavioural, and structural interventions into a 'package' of preventive interventions, although the need for inclusion of structural approaches within combination prevention strategies is evident, particularly combination prevention approaches tailored for young people (Vermund et al. 2013; Wingood, Rubtsova, et al. 2013). Future research should seek to better understand the structural barriers (i.e. low levels of education, social norms, health literacy, community health beliefs) that exist mitigating adolescents' and young people's uptake of efficacious interventions such as HTC (Pettifor et al. 2013; Navarra et al. 2013).

Scale-up and cost-effectiveness

Despite reductions in cost associated with HIV treatments coupled with promising behavioural approaches for HIV prevention, the large-scale implementation of integrated, multilevel interventions will be challenging. Given the existing constrained economic environment, HIV prevention efforts should focus on the adaptation, translation, and scale-up of evidence-based interventions. Additionally, fiscal constraints make it essential to redefine programme efficacy in terms of cost, in addition to programmatic measures such as impact and outcomes. Moving forward it will be imperative that policy makers, program administrators, researchers and practitioners utilise economic evaluation techniques coupled with more traditional program implementation strategies when deciding to scale-up integrated HIV prevention efforts.

For instance, PrEP and VMMC are useful biomedical interventions, but the cost of universal PrEP scale-up (such as an option B+ for every young person in sub-Saharan Africa) may serve as a barrier, as the costs of implementing such an intervention may outweigh the benefit (Wingood, Dunkle, et al. 2013). Many geographic areas experience a lack of medical and public health staffing, so task-shifting and task-sharing responsibilities between public health professions and allied health professionals may aid in cost-effective implementation of integrated sexual health interventions (Coates 2013; Callaghan, Ford, and Schneider 2010; Sanders et al. 2010).

Most recently, the use of technology as an efficient and cost-effective way of implementing large-scale, integrated HIV prevention models has gained substantial traction in the field (Brown et al. 2013). Computer and mobile-based technologies are now incorporating large amounts of contextual data to influence HIV risk behaviours (Brown et al. 2013) and the use of rapid evaluation techniques such as Continuous Evaluation of Evolving Behavioural Interventions (CEEBIT) may help facilitate rapid evaluation, adaptation and scale-up of computationally-based interventions (Mohr et al. 2013). The use of technology with at-risk

adolescents, however, remains understudied (Pettifor et al. 2013), but the potential for rapid, cost-effective scale up is boundless, as youth worldwide are avid users of the World Wide Web. Mobile phone adoption among young people increases annually, as 78% of all young people aged 12 to 17 years in the U.S.A. possess a cell phone, and one in every four young people possesses a smartphone (Madden et al. 2013; Lenhart 2012).

Adopting broader ecological frameworks for HIV prevention with adolescents

The research literature often reduces HIV prevention efforts to biomedical, behavioural, and structural strategies, but there is a need to re-conceptualise the HIV epidemic in terms of multiple, co-occurring psychological, behavioural, sociological, cultural, and economic influences, particularly for adolescents in low-resourced regions of the world (Lowenthal et al. 2014). In doing so, the HIV prevention field may consider adopting broader theoretical perspectives, such as “combination” or ecological models (Ewart 2009; Flay, Snyder, and Petraitis 2009; Hovell, Wahlgren, and Adams 2009; McLeroy et al. 1988; Pettifor et al. 2013; Johnson et al. 2010; Mccubbin and Patterson 1983), to better understand the diversity of influences and dynamics that affect HIV risk, transmission, and incidence (DiClemente, Salazar, and Crosby 2007; Salazar et al. 2010). Broader theoretical frameworks allow for increasingly comprehensive and integrated combination prevention strategies.

In adopting an ecological paradigm, it is assumed that the risk of HIV acquisition and/or transmission occurs as a complex interaction of multiple determinants, each with different “levels of influence”. Therefore, accelerating the end of the HIV epidemic may require an integrated and coordinated approach that sequences the implementation of HIV prevention strategies to amplify intervention effects; in short, yielding higher levels of efficacy than if the interventions were delivered individually (Wingood, Rubtsova, et al. 2013). This may result in optimising HIV prevention efficacy through “prevention synergy” (DiClemente 2013, 259; Wingood, Rubtsova, et al. 2013, S112). Rooted in organisational theory, prevention synergy occurs when pooled interdependence exists between various interventions that are operating at various levels of influence. For instance, biomedical, behavioural, and structural interventions all operate on different levels of influence, and each has a unique impact on individuals, couples, families, communities, organisations, and geographical regions (Wingood, Rubtsova, et al. 2013).

When developing future HIV prevention programmes, it is also critical to consider integrated approaches that incorporate sequential interdependence, which involves a purposeful and planned implementation sequence of interventions (biological, behavioural, and structural) at various levels of influence. For example, a structural (i.e. community-level) intervention aimed at reducing social norms towards HIV among at-risk youth may prompt changes in the way providers engage with young people (i.e. changes in providers’ behaviours) which may, in turn, influence providers’ motivation to engage young people in HIV prevention counselling or promote ARV adherence (Wingood, Rubtsova, et al. 2013).

Conclusion

There have been rapid advances in biomedical technology for HIV prevention. How these technologies will be applied to young people and how likely are young people to adopt, adhere and sustain their use over protracted periods of time is unclear. Further, in the absence of a comprehensive and sequential framework, attempts to implement integrated interventions and use of biomedical, behavioural and structural interventions within an ecological HIV prevention paradigm may result in attenuated, fragmentary or indeterminate effects. The implementation and integration of sex education programming has also demonstrated significant effects in delaying or decreasing sexual risk behaviors in young people worldwide, as well as increases in contraceptive use (Kirby, Laris, and Roller 2007; Kirby 2011). Finally, approaching the scale-up of combination interventions in a strategic, purposeful and planned manner may facilitate intervention reach, adoption, effectiveness, and sustainability. While promising, many of the strategies emphasised above will need to be rigorously evaluated with myriad adolescent populations, in the U.S.A. and globally, to gauge their programmatic efficacy and cost-effectiveness in averting HIV.

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