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Review article

Promoting reproductive options for HIV-affected couples in sub-Saharan Africa

O Mmeje,[a] CR Cohen,[b,c] A Murage,[d] J Ong'ech,[e] J Kiarie,[f] S van der Poel[g]

[a] Department of Obstetrics and Gynecology, University of Michigan, Ann Arbor, MI, [b] Department of Obstetrics, Gynecology and Reproductive Sciences, University of California, San Francisco, CA, USA [c] Family AIDS Care and Education Services (FACES), Kisumu, Kenya [d] Department of Obstetrics and Gynaecology, Aga Khan University Hospital, Nairobi, [e] Department of Reproductive Health, [f] Department of Obstetrics and Gynaecology, Kenyatta National Hospital and University of Nairobi, Nairobi, Kenya [g] Department of Reproductive Health and Research, World Health Organization, Geneva, Switzerland

Correspondence: O Mmeje, Department of Obstetrics and Gynecology, University of Michigan, L4100 Women's Hospital, 1500 East Medical Center Drive, Ann Arbor, MI, USA. Email ommeje@umich.edu

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HIV-affected couples face unique challenges that require access to information and reproductive services to prevent HIV transmission to the uninfected partner and offspring while allowing couples to fulfil their reproductive goals. In regions of high HIV prevalence in sub-Saharan Africa, HIV-affected couples require multipurpose prevention technologies (MPTs) to enhance their reproductive healthcare options beyond contraception and prevention of HIV/sexually transmitted infections (STIs) to include assistance in childbearing. The unique characteristics of the condom and its accepted use in conjunction with safer conception interventions allow HIV-serodiscordant couples an opportunity to maintain reproductive health, prevent HIV/STI transmission, and achieve their reproductive goals while timing conception. Re-thinking the traditional view of the condom and incorporating a broader reproductive health perspective of HIV-affected couples into MPT methodologies will impact demand, acceptability and uptake of these future technologies.

Keywords Assisted reproductive services, HIV prevention, HIV-serodiscordant couples, multipurpose prevention technology, safer conception.

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Introduction

HIV-serodiscordant couples, 'a married or cohabiting couple in which one partner is HIV-infected and the other is HIV-uninfected', are an important source of new HIV infections in sub-Saharan Africa,[1,2] where it is estimated that 23.5 million people are HIV-infected.[3] For example, in Kenya, the national prevalence of HIV infection is estimated at 5.6% with an estimated 260 000 HIV-serodiscordant couples.[4] HIV-infected individuals have reproductive desires that cannot be ignored and they knowingly risk HIV transmission in order to conceive.[5–7] In HIV-serodiscordant partnerships in which pregnancy occurs, the risk of HIV acquisition nearly doubles for the uninfected partner compared with partnerships in which pregnancy does not occur.[5] Furthermore, providing fertile HIV-infected women with the possibility of preserving their fertility and a safer option for conception is empowering given the stigma and isolation that they may already encounter as a result of their HIV status, particularly in cultures where reproduction defines one's value in society.[8–10] The reproductive desires and intentions of HIV-infected individuals have not been adequately addressed, particularly in low-resource environments,[11] in relation to decreasing the risk of unintended pregnancy and transmission of HIV, other sexually transmitted infections (STIs), and resultant infertility. Infertility is a global public health problem with great implications, specifically in HIV-affected couples (Figure 1). Therefore, the reproductive intentions and prolonged periods of unprotected intercourse required to achieve pregnancy among HIV-infected individuals may reduce the impact of HIV prevention efforts unless comprehensive reproductive services, including multipurpose technologies (MPTs), equally address contraception, childbearing desires and prevention of HIV/STIs.[12,13] Redefining our view of the condom as a model MPT with integration of comprehensive HIV and reproductive care counselling and education with provision of safer conception strategies will successfully achieve the goal of prevention.

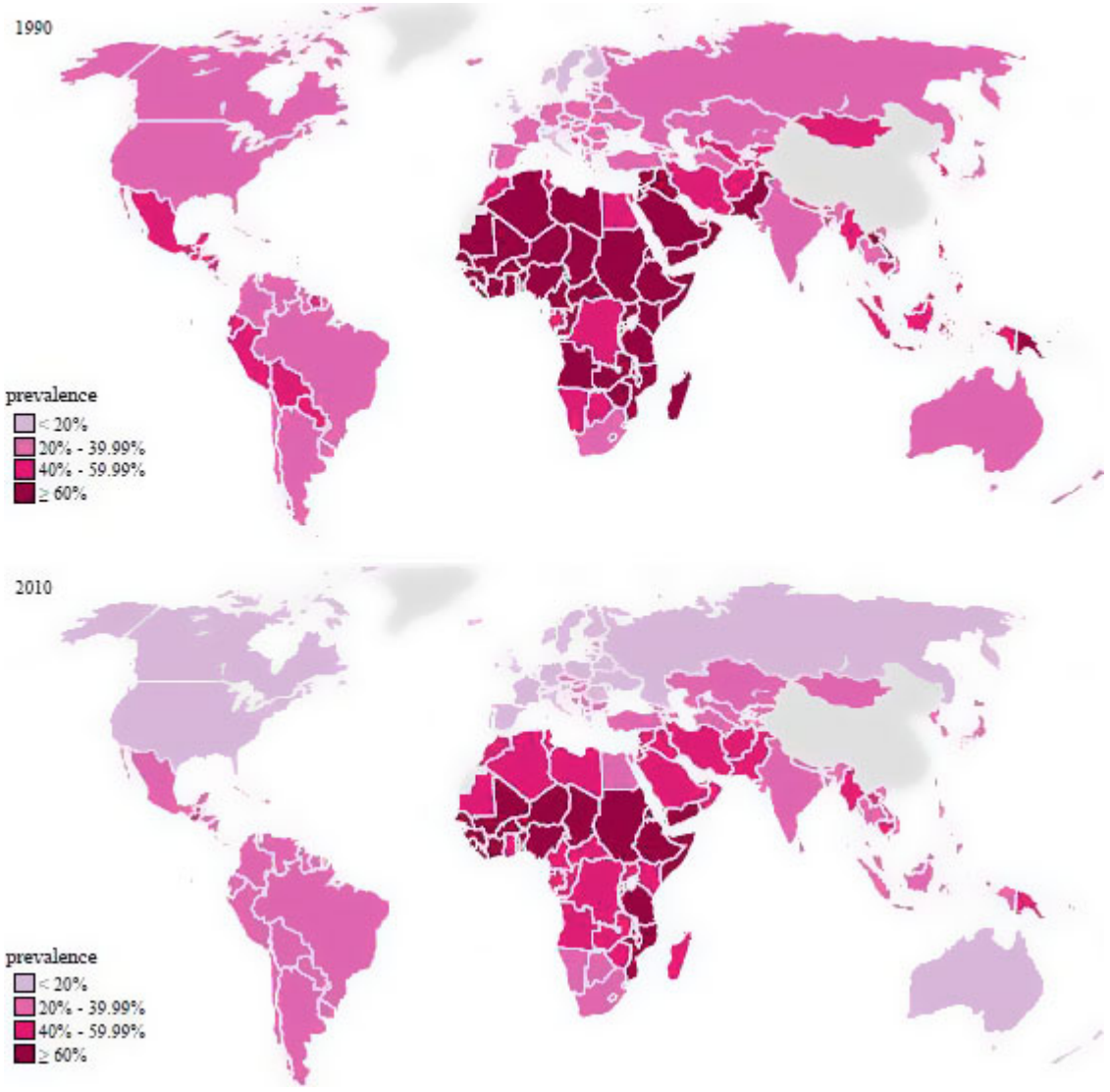

Figure 1. 2010 WHO Analysis: prevalence of primary (upper map) and secondary (lower map) sub/infertility among women aged 20–44 reporting unsuccessful attempts at conception in the prior 5 years. *PLoS Med* 2012;9:e1001356.

At the International Conference on Population Development in 1994, the accepted definition of reproductive health, implied that women and men have the right to be 'informed [about] and have access to safe, effective, affordable and acceptable methods of family planning... and appropriate healthcare services that will enable women to go through pregnancy and childbirth and provide couples with the best chance of having a healthy infant.'[14] This definition of reproductive health has shaped and defined the health strategies of various governmental and nongovernmental organisations including that of the World Health Organization's (WHO) Department of Reproductive Health and Research. The vision of WHO's Reproductive Health and Research division, which was adopted by United Nations member states in 2004, is 'the attainment by all people of the highest possible level of sexual and reproductive health.' Their intent is to conduct and support research initiatives and develop public health policies that strive for a world in which women and men 'have access to sexual and reproductive health information services.' This is premised on the concept of reproductive rights and assurance of choice when meeting the needs of diverse populations, particularly those that have been neglected and at risk. The current reproductive health paradigm addresses universal access in the following five areas: maternal and newborn health, 'family planning' – contraception and infertility services, preventing unsafe termination of pregnancy, management of reproductive tract infections and STIs, including HIV, and promo-

tion of sexual health. Linking WHO's sexual and reproductive health and HIV prevention objectives and programmes will enhance development of MPTs for the empowerment of women through the prevention of HIV/STIs and the provision of reproductive options.

Despite the intention of public health policies that provide universal access to reproductive healthcare services, the reproductive desire to have children by HIV-affected individuals and couples has not been adequately addressed. Furthermore, access to safe assisted fertility interventions has been neglected within the global reproductive health agenda and 'family planning' discussions for HIV-serodiscordant couples.[15] Comprehensive reproductive services for HIV-affected couples should not only provide contraceptive services but also fertility services for those desiring children. According to WHO sexual and reproductive health guidelines for women living with HIV/AIDS men and/or women with HIV/AIDS 'may be more likely to have difficulty getting pregnant and to request assistance. These women should be given full support for counselling and advised of their options, including adoption and assisted reproduction, if available'.[16] Both simple and complex assisted reproductive techniques, for HIV-affected couples with underlying infertility or subfertility, can provide a means for conception that prevents partner transmission. Before the use of fertility services, healthcare providers should consider educating and counselling HIV-affected couples on fertility awareness methods and performing a fertility evaluation in the couple to assess for underlying infertility, which may help to direct them to the appropriate reproductive services. Simple fertility methods include timed vaginal insemination and sperm washing (SW) with intrauterine insemination (IUI); and where indicated and economically feasible more complex interventions such as in vitro fertilisation (IVF) with or without intracytoplasmic sperm injection (ICSI) as HIV prevention interventions. In HIV-serodiscordant couples, a water-based lubricated male condom is a critical fertility care technology for safe collection of semen that avoids sexual HIV transmission in conjunction with any of the above methods. These reproductive interventions avoid extended exposure with unprotected intercourse in couples desiring children.

All of these methods require the consistent use of male condoms or, if found acceptable, female condoms, which would decrease the incidence of pregnancy and HIV/STI transmission. Most importantly, the range of reproductive methods offered with the consistent use of condoms will allow HIV-infected men and women the option of choosing the method best suited to their current situation and reproductive health priority, either for contraception or safer conception. As a result of rebranding the condom this presents new motivation to increase consistent condom use. Overall, options that address the full complement of reproductive health needs will enhance uptake and acceptance of MPT methodologies. Pharmaceutical methods, such as the use of anti-retroviral therapy in the HIV-infected partner, have been demonstrated to decrease the risk of sexual HIV transmission.[17,18] In addition, anti-retroviral therapy may be administered to the uninfected partner in an HIV-serodiscordant relationship during the periconception period as pre-exposure prophylaxis.[19] A recent report from the UK has shown that timed unprotected intercourse along with the use of pre-exposure prophylaxis by the HIV-uninfected female in the periovulatory period demonstrated feasibility and decreased the risk of sexual and perinatal HIV transmission.[20] Hence, safer conception practices that use either a reproductive or pharmaceutical intervention should be part of the arsenal of options offered to HIV-serodiscordant couples. MPTs are being developed to address a complementary component to provide contraception; however, they can be innovatively modified to address the needs of safer conception.

Worldwide, the gap in access and provision of reproductive healthcare services for HIV-infected individuals affects their quality of life and social status.[11] An expanded reproductive health paradigm, which includes MPTs, is needed to enhance awareness, options, and access to reproductive services for HIV-affected women and men.

MPTs and safer conception

The MPTs (i.e. anti-retroviral therapy, monoclonal antibodies and contraceptive impregnated gels, rings and barrier devices) in development are not readily available on the market for high-risk individuals or HIV-serodiscordant couples to use for prevention of HIV/STIs or in conjunction with safer conception interventions. None of the proposed products can be used to prevent transmission/acquisition of STIs while allowing HIV-serodiscordant couples the option of safely conceiving with safer conception interventions. The only product that may provide HIV-serodiscordant couples with the opportunity to fulfil their reproductive right of childbearing when they desire and also prevent HIV transmission/acquisition is the condom (male or female). Furthermore, the proposed and ongoing preclinical and clinical studies of these MPT products have yet to evaluate the impact of anti-retroviral therapy, monoclonal antibodies and contraceptive agents on the reproductive tract (i.e. impact on sperm, endometrial environment for implantation and embryo development). Despite some of the promising evidence supporting the use of MPTs, their availability, accessibility and acceptability are still in question. If high-risk individuals and HIV-affected couples are presented with options that meet their full reproductive and HIV/STI prevention needs, demand and acceptability will be likely to increase. To ensure a suc-

cessful platform, the MPT development strategies need to address prevention, contraceptive and fertility needs of high-risk individuals and HIV-affected couples.

The state of affairs: reproductive guidelines for HIV-affected couples

At the beginning of the HIV epidemic in 1985 in the USA, the Centers for Disease Control and Prevention (CDC) discouraged HIV-infected women from having children because of the poor prognosis associated with HIV infection and the risk of perinatal transmission. Advances in HIV prevention and treatment have allowed HIV-infected individuals to live longer and pursue their reproductive goals; as a result there are now recommendations guiding individuals in this process.[21] The American College of Obstetrics and Gynecology (ACOG) recommends that in HIV-serodiscordant partnerships with an HIV-infected man, 'assisted conception with sperm washing for intrauterine insemination or intracytoplasmic sperm injection may be safer than timed unprotected intercourse with regard to HIV transmission.'[22] Similarly, the American Society for Reproductive Medicine (ASRM) recommends that 'when an affected couple requests assistance to have their own genetically related child, they are best advised to seek care at institutions with the facilities that can provide the most effective evaluation treatment and follow-up.'[23] Furthermore, ASRM asserts that in couples with an HIV-infected man, the use of sperm preparation techniques coupled with IUI or ICSI have been demonstrated to be highly effective in preventing seroconversion of HIV-uninfected women and offspring.[23] In HIV-serodiscordant couples with an HIV-infected female, timed vaginal insemination in the periovulatory period is a low-cost fertility intervention that couples can use to prevent sexual HIV transmission while attempting conception. A collected semen sample obtained after either natural coitus with a water-based lubricated condom or ejaculation into a clean cup is inseminated with a syringe into the vagina during the periovulatory period. However, advanced assisted reproductive techniques may still be indicated in the presence of underlying infertility.[19,24–26] The position statements of these organisations are also in agreement with that of the European Society of Human Reproduction and Embryology.[27] In Spain, some clinicians endorse timed unprotected intercourse in HIV-serodiscordant couples desiring children when the following conditions are met: an undetectable serum HIV-RNA, anti-retroviral therapy in the infected partner, absence of genital tract infections, and a normal fertility evaluation in the couple.[28,29] However, some argue that timed unprotected intercourse should not be endorsed in high-risk HIV-serodiscordant couples who wish to conceive. Unprotected sexual intercourse in high-risk situations when the above conditions cannot be assured is discouraged; therefore, preconception counselling, SW-IUI or ICSI are ideal options when the male partner is HIV-infected.[30,31] Most recently, there have been clinical and laboratory innovations resulting in lower cost IVF interventions, which may be adapted for low-resource environments.[32]

Reproductive services in high-resource countries

The use of assisted reproductive services such as SW-IUI or IVF should not only be considered as a method of enhancing fertility or addressing underlying infertility but as a critical component of the HIV prevention armamentarium coupled with consistent condom use.[33] In the USA, there have been no reported cases of HIV transmission to the HIV-uninfected female partner with the use of SW and ICSI.[33,34] Similarly, there have been no reported cases of HIV transmission with the use of standardised SW-IUI techniques worldwide.[34–36] In high-resource countries (World Bank classifications), assisted reproductive services for HIV-affected couples are available and have been determined to be effective and safe in retrospective studies.[37] However, these services are not accessible and/or affordable to the majority of couples in need, specifically in the public healthcare arena in low-resource settings.[38] HIV-serodiscordant couples receiving assisted reproductive services in Italy, believed that it was 'not right to withhold something as important to procreation [from] people because they have a disease'[8] because it provided a safer alternative to natural conception, although not risk-free. Overall, couples living with HIV believe that society has a moral obligation to help them find solutions that will assist in overcoming their barriers to access and providing options through information on safer conception alternatives to natural conception.[8]

In the USA, less than 3% of assisted reproductive practices registered with the ASRM provide services to couples in whom one or both partners are HIV-infected.[23] The limited access and barriers to services have been attributed to concerns about transmission to clinical personnel and contamination of gametes and embryos stored on clinical premises; however, there have been no reported cases of occupational HIV transmission to personnel, gametes or embryos in clinical settings that would support limiting services to HIV-affected couples.[23] The current costs of assisted reproductive services have made it an unattainable service for a significant proportion of HIV-affected couples—in high-, low- and middle-income countries. Current estimates in high-income countries can range from US $10,000 to 17,000 per cycle of advanced assisted reproductive services and can be as high as US $25,000.[39] In

low- and middle-income countries, the International Federation for Fertility Services (IFFS) has found that the average cost is from US $3,000 to 8,000 per cycle, which is proportionately more expensive based upon GDP values in these countries.[40]

Despite evidence supporting a decreased risk of HIV transmission in serodiscordant partnerships with the use of safer conception techniques, there are few prospective studies evaluating the acceptability and feasibility of these methods among HIV-serodiscordant couples who desire children, especially in sub-Saharan Africa. Although SW-IUI represents one of the lower cost options, the CDC has not changed its recommendation since 1990 against SW-IUI. The CDC's position is based on a single reported case of HIV seroconversion in a woman using improper techniques.[41,42] As a result, the use of approved assisted reproductive technology for male HIV-infected serodiscordant couples has been limited to SW-ICSI in the USA, which has also limited the availability of these services because of the high costs and restricted access, particularly in public health settings. The National Perinatal HIV Hotline and Clinicians Network ('The Perinatal HIV Hotline') as of March 2013 reported only 17 clinics offering IVF and seven offering SW-IUI to HIV-serodiscordant couples.[43] The number of service providers may be limited as a result of the existing CDC recommendations. As of 2003, the CDC outlined three components that must be fulfilled before it would change its policy statement and consider the endorsement of insemination for HIV-affected couples: expansion of the follow-up of European women inseminated with processed semen, evaluation of the effectiveness of laboratory techniques for removing HIV from semen, and evaluation of the transfer of technology of semen processing to non-research settings.[42] We believe that the evidence required to support new policy guidelines endorsing the use of SW-IUI by the CDC as a safer method of conception for HIV-affected couples already exists; however, the decision has not been overturned. Global leaders who shape public policy agendas should reconsider the scientific evidence that could enhance the provision of safer conception options as MPTs to HIV-affected couples desiring children.

Reproductive services in sub-Saharan Africa

The pronatalist nature of many low-resource countries defines individuals through parenthood and children are highly valued by cultural norms.[44,45] In sub-Saharan Africa, many HIV-infected women and men express a desire for children either immediately or in the near future and being without a child attracts significant stigma.[11] HIV-infected women report that pregnancy and childbirth are ways for them to regain their sense of womanhood and sexuality, often making childbearing a high personal priority.[46] To these women, 'family planning' is not just prevention and management of unwanted pregnancy but also planning for their family with the assistance of their healthcare provider and the provision of clinical services.[45] Therefore, in cultures where self-worth and identity are inextricably linked to childbearing, encouraging HIV-affected couples to abstain from reproduction or to consistently use condoms while not providing any support and information on options to safely conceive is unrealistic. Therefore, the incorporation of safer conception strategies with condoms as an MPT is critical to addressing reproductive desires, HIV/STI prevention and contraception depending on the circumstances and reproductive desires of the HIV-infected individual.

In low-resource environments, the cost, availability and knowledge of assisted reproductive services may limit their accessibility to HIV-affected couples.[38] To date, three assisted reproductive clinics in Nairobi, Kenya provide safer conception interventions for HIV-affected couples desiring children (Dr A. Murage personal communication). Although timed unprotected intercourse is theoretically an acceptable intervention because it can be easily adapted and accepted by healthcare providers and HIV-affected couples in low-resource environments, there are inherent challenges to its use and reliability as the only safer conception option for HIV-affected couples. It may be unethical to recommend timed unprotected intercourse as a means of safer conception for high-risk HIV-serodiscordant couples despite the lack of costs associated with this method in low-resource environments where adherence to anti-retroviral therapy and HIV RNA viral load assessments is not readily available. Furthermore, in HIV-serodiscordant couples in sub-Saharan Africa with underlying infertility (Figure 1), conception may not occur so unprotected sexual encounters aimed at achieving conception may be futile with continued risk of HIV transmission. Other safer conception interventions require evaluation to expand the repertoire of services and options available to HIV-affected couples desiring children. Redefining reproductive health strategies to include access to fertility services and innovative uses for MPT beyond contraception has the potential to improve the nature and quality of reproductive services for women and men worldwide.

Expansion of the reproductive health paradigm for HIV-affected couples

Closing the reproductive services gap will require an acknowledgement and support of the reproductive intentions and fertility desires of HIV-affected couples.[47] Therefore, public health agencies, ministries of health, policy makers, healthcare providers, researchers and donors must first acknowledge the reproductive intentions as well

as the associated challenges of preventing HIV transmission in HIV-serodiscordant couples who desire a biological family.[13] Closing the gap in clinical services will require integration of reproductive healthcare services into HIV prevention interventions along with the development of evidence-based clinical guidelines for healthcare providers. These guidelines will expose the research and product gaps creating a need for MPTs that address multiple reproductive health needs.

Implementation studies need to be conducted to ensure that the successful outcomes reported in high-resource settings can be replicated in low-resource environments with a high HIV prevalence. These studies should evaluate whether interventions such as consistent condom use with timed vaginal insemination during the periovulatory period and SW-IUI are feasible and acceptable to healthcare providers and HIV-affected couples as components of HIV prevention interventions. The findings of these studies will help to define the cadre of best practices for reproductive fertility services and product demands that will meet the satisfaction of healthcare providers and HIV-affected couples. Enhancing the understanding of healthcare providers around HIV-related stigma may require adoption of new skills that will create an engaging environment for reproductive discussions and preconception counselling with HIV-affected couples. These discussions will help facilitate the continuum of care from preconception to the postpartum period once pregnancy is achieved. Furthermore, reproductive healthcare training programmes are needed to effectively enhance the availability and quality of information provided to HIV-affected individuals.[48] Preservice training for nurses, clinical officers, medical officers and community health workers has been critical to the successful scaling up of HIV prevention, care and treatment services in low-resource environments.[49] Expanding the perspective of healthcare providers in training on the full spectrum of 'family planning' will have a great impact on changing the mindset of future generations to improve the lives of those they serve. In low-resource environments, public–private partnerships may help to bring technical expertise, research and equipment, which may improve the provision of affordable assisted reproductive services[50] and interventions that include innovative MPTs.

Conclusion

An expanded reproductive health paradigm requires redefining the 'family planning' vision while embracing the fertility intentions of all women and men, including those with HIV, who maintain a desire to have children. In an expanded reproductive health paradigm, fertility evaluations and assisted reproductive services should not only be considered for the infertile but also for those seeking safer conception and for HIV prevention. MPT product development should focus on the multipurpose nature and characteristics inherent to the condom. Like the condom, new MPTs should offer: short-term or single use, prevention of HIV/STIs and subsequent infertility, and unintended pregnancy. Providing fertile HIV-infected women with the possibility of preserving their fertility and a safer option for conception is empowering given the stigma and isolation they may already encounter as a result of their HIV status, particularly in cultures where reproduction defines one's value in society. Despite some of the promising evidence supporting the use of MPTs, their availability, accessibility and acceptability are still in question. The prospect of an HIV-uninfected partner and child may be a strong motivator for uptake of old and new MPTs in the future.

Disclosure of interests

The authors have no competing interests.

Contribution to authorship

The manuscript was conceptualised by OM and SVP while OM was an intern at the WHO. CRC, AM, JO and JK all contributed to the development, writing and review of the manuscript with contributions drawn from their research and clinical experiences with HIV-affected couples. OM and SVP led the writing process.

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