

PERSPECTIVES PAPER

Standards and Guidelines for HIV Prevention Research: Considerations for Local Context in the Interpretation of Global Ethical Standards

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Abstract

While international standards are important for conducting clinical research, they may require interpretation in particular contexts. Standard of care in HIV prevention research is now complicated, given that there are now two new biomedical prevention interventions – ‘treatment-as-prevention’, and pre-exposure prophylaxis – in addition to barrier protection, counselling, male circumcision and treatment of sexually transmissible infections. Proper standards of care must be considered with regard to both normative guidance and the circumstances of the particular stakeholders – the community, trial population, researchers and sponsors. In addition, the special circumstances of the lives of participants need to be acknowledged in designing trial protocols and study procedures. When researchers are faced with the dilemma of interpretation of international ethics guidelines and the realities of the daily lives of persons and their practices, the decisions of the local ethics committee become crucial. The challenge then becomes how familiar ethics committee members in these local settings are with these guidelines, and how their interpretation and use in the local context ensures the respect for persons and communities. It also includes justice and the fair selection of study participants without compromising data quality, and ensuring that the risks for study participants and their community do not outweigh the potential benefits. (*Afr J Reprod Health 2014; 18[3]: 55-65*)

Keyword: Standards of prevention, ancillary care, local context, ethical guidelines, research

Résumé

Bien que les normes internationales soient importantes pour mener des recherches cliniques, elles peuvent exiger l'interprétation dans des contextes particuliers. La qualité des soins dans la recherche de la prévention du VIH est maintenant compliquée, étant donné qu'il y a maintenant deux nouvelles interventions de prévention biomédicale - «traitement comme prévention», et la prophylaxie de la pré-exposition - en plus de la protection de la barrière, l'orientation psychologique, la circoncision masculine et le traitement des infections sexuellement transmissibles. Des normes de soins doivent être prises en considération en ce qui concerne à la fois à des orientations normatives et les circonstances des parties prenantes particulières - la communauté, la population de l'étude, les chercheurs et les commanditaires. En outre, les circonstances particulières de la vie des participants doivent être reconnues dans la conception des protocoles d'essais et procédures de l'étude. Lorsque les chercheurs sont confrontés au dilemme de l'interprétation des lignes directrices internationales sur l'éthique et les réalités de la vie quotidienne des personnes et de leurs pratiques, les décisions du comité local d'éthique deviennent cruciales. Le défi devient alors de savoir à quel point les membres du comité éthique sont familiers membres du comité dans ces milieux locaux avec ces lignes directrices, et comment leur interprétation et de l'utilisation dans le contexte local assure le respect des personnes et des communautés. Il comprend également la justice et la bonne sélection des participants à l'étude, sans compromettre la qualité des données, et de s'assurer que les risques pour les participants à l'étude et leur communauté ne l'emportent pas sur les avantages potentiels. (*Afr J Reprod Health 2014; 18[3]: 55-65*)

Mot-clé: Normes de prévention, soins auxiliaires, contexte local, des lignes directrices éthiques, recherche

Introduction

In the last seven years, five new HIV prevention strategies have been introduced. Three of these strategies have been incorporated into country-specific national prevention programs: voluntary

medical male circumcision (VMMC)¹⁻³, pre-exposure prophylaxis⁴⁻⁶ and ‘treatment-as-prevention’ – treating a person with HIV at an early stage in HIV infection to prevent transmission to HIV negative sexual partners^{7,8}. Further research is ongoing on two additional

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strategies – vaginal and rectal microbicides and HIV vaccines⁹⁻¹¹. While new available interventions provide options for HIV prevention, none of them obviates the need for further research, as each has limitations. VMMC has a gender-specific limitation, as clinical demonstrations show it only provides immediate direct protection to men. (Although there is some evolving observational evidence showing a protective effect in women partners of circumcised men¹.) Both PrEP and treatment-as-prevention require ongoing adherence and uninterrupted supply for efficacy, and with treatment-as-prevention, the HIV negative partner has to trust that the HIV positive partner is adhering to medication. New HIV prevention interventions therefore trigger discussions of how these new technologies should be incorporated into ongoing research.

Standard of care for participants in a clinical trial has long been acknowledged as a contentious issue. In 1997, the *New England Journal of Medicine* drew attention to the fact that antiretroviral-based mother-to-child prevention regimens were being tested against placebo^{13,14}, despite the fact that three years earlier, the mother-to-child prevention trial ACTG 076 showed a complex AZT-based regimen was effective in reducing HIV transmission from mothers to infants¹⁵. The ACTG 076 regimen was deemed too expensive and infeasible in low- and middle-income countries where the overwhelming majority of mother-to-child transmissions occur. Accordingly, international authorities, including the World Health Organization (WHO), decided further trials of simpler, cheaper regimens should occur in these countries, and simpler regimens should be tested against placebo¹⁶. Articles in the *New England Journal of Medicine* which denounced placebo-controlled trials caused outrage, and scientific, bioethical and public opinions were divided^{17,18}.

Existing ethical guidance, specifically the Declaration of Helsinki (1996), stated that participants in a research study should be provided the ‘best proven’ therapeutic or diagnostic method. Thus, testing simpler regimens against a placebo in lower income countries was, according to one side of the debate, implementing a double standard

that was unfair and exploitative¹³. Supporters of placebo-controlled trials argued that the placebo was ethically justified, given that none of the countries involved in the trials were financially able to implement the ACTG076 regimen, and there were no other proven options at that time¹⁶.

There are some very important parallels between the mother-to-child prevention controversy of 1997 and the current situation with new prevention technologies. In contemporary times however, the question is how to determine the standard of prevention in new prevention trials, given that partially effective interventions have now been established as HIV prevention strategies, yet these strategies have not been implemented in all settings where HIV prevention trials may or are taking place.

There are significant tensions between the imperative to conduct rigorous research on matters of global public health importance, such as establishing cheaper and more feasible HIV biomedical prevention approaches, and the need to provide optimal protection for the participants involved in these studies. There are also complex issues of capacity, feasibility, local politics and cultures which inform the context in which research into the use of new technologies is conducted. Some questions therefore remain unanswered. What kinds of interventions are health systems able, and willing, to pay for? Are systems in place to ensure that people can reliably access drug-based interventions? Will people adhere?

While many of these issues have already been addressed with regards to antiretroviral therapy, the context in which these issues have to be positioned for HIV prevention is different for a number of reasons. For one, adherence has already proved to be a major barrier to effective drug-based HIV prevention in trials in populations of African women^{19,20}. But then there is the question of which guidelines should be used to structure ethics committees’ decision-making on international HIV prevention research: national or international ethical guidance?

Current international ethical guidance from UNAIDS stipulates that state-of-the-art prevention interventions should be added to the ‘standard of prevention’ in new research studies as the

interventions are validated or approved by relevant authorities²¹. This is contested however by weaker institutional-based guidelines, such as those produced by the HIV Prevention Trial Network in the US and the Medical Research Council guidelines in the UK^{22,23}. A key component of the contestation is whether or not people enrolled in research studies should have access to higher standards of prevention/care than other members of their local communities. We will address this question with regard to HIV prevention research using Nigeria as a case study, paying particular attention to the local cultural context, challenges with access to general and reproductive healthcare, and economic drivers of clinical research impact on the interpretation of global ethical standards.

The Nigerian Context

Nigeria is a populous and diverse nation – English is its official language, but more than 350 different languages spoken across the nation. It is oil-rich, but low on the United Nations Human Development Index²⁴. Nigeria is home to the largest population in Africa, about 61% of whom live on less than \$US1.25 a day. It also has the second largest population of people living with HIV in the world²⁴. One third of babies born with HIV in sub-Saharan Africa are born in Nigeria²⁵. Access to sexual and reproductive health care services is poor. Despite the global goal to reduce mother-to-child HIV transmission by 90%, only 22% of pregnant women living with HIV in Nigeria access PMTC programs, compared with 88% in South Africa. Similarly, only 20% of women with HIV in Nigeria access contraception, compared with 62% in South Africa²⁵.

Nigeria's large population, more than half of whom are under 29yrs²⁶, its considerable disease burden, and the large number of treatment naïve patients makes the country a potential destination for the conduct of clinical trials²⁷. The high number of new HIV infections - more than 300,000 people acquired HIV in 2012²⁵.

Nigeria has systems and structures in place for the regulation of research to reduce the potential for study participants' exploitation and abuse. These include structures for the national

coordination and regulation of institutional health research committees²⁸, a National Code of Health Research Ethics²⁹, the Clinical Trial Unit of the National Agency for Food and Drug Administration and Control that oversees the conduct of clinical trials³⁰, the national HIV research policy³¹, the national HIV research agenda³², and the HIV vaccine research plan³³. A vibrant community engagement platform also serves as the national HIV prevention research watchdog³⁴.

The guidelines governing health research in Nigeria²⁹ clearly articulate the need for robust collaborative relationships involving communities in research, in addition to requirements of social or scientific value, scientific validity, fairness, culturally appropriate informed consent, independent review, and an overall maximisation of benefits and minimisation of risks. The national HIV research policy clearly articulates this also, while the national HIV research agenda describes the coordination and implementation framework for the conduct of HIV related research in Nigeria. These national documents consistently reiterate the need for the design of culturally appropriate research. Unfortunately, these guidelines are not specific on what elements of the protocol need to be 'culturally appropriate', and there is no guideline on how a 'culturally appropriate' study design should look. However, the National Code of Health Research Ethics places emphasis on the inclusion of laypersons and representatives of the two main religions in the country (Muslim and Christians) on the ethics committee as these individuals represent the people and determine the 'cultural appropriateness' of the study protocol²⁹. In an effort to build the competency of laypersons to perform these roles, the country has organised specific trainings for laypersons since 2008. This was initially instituted by the New HIV Vaccine and Microbicide Advocacy Society³⁵ and has since been continued by the West Africa Bioethics Society. The subsequent section of this manuscript discusses elements of research protocols that would require local considerations for due interpretation of the context of practice, and how this might apply to the conduct of HIV prevention research in Nigeria.

Informed Consent and Rights of Study Participants

The Nigerian National Code of Health Research Ethics is explicit in requiring that risk is minimised and health related benefits maximised in research²⁹. Minimising risks needs to be understood as including the risk of exploitation and social harm as well as medical risk. For Nigeria, the larger majority of the population does not have formal education, and basic literacy above age 15 years is 61%²⁴. Accordingly attention needs to be paid to ensuring effective communication about research, especially the consenting process.

First, for valid consent, people need to understand what they are agreeing to, including the key concepts involved in any given research project. Information about research projects must be communicated in local languages. Where literacy is absent, forms of communication that that are not dependent upon the written word need to be developed, and education about prospective trials should be community wide rather than limited to potential participants only, so that community members can discuss and debate the merits and demerits of the trial.

One of the challenges to conducting research in Nigeria is the wide diversity in language. Developing consent forms in varied languages may be daunting and an uphill task. However, the country seems to have devised a means of addressing this challenge. One which has been done over the years in the various national surveys conducted – including the national demographic health survey – is to translate only key words /phrases (including sensitive ones) for each selected community during the training of interviewers. Interviewers then use the semi-translated documents as master copies. This approach was used for the 2007 and 2012 National HIV/AIDS Reproductive Health Surveys^{36,37}, as well as the 2005, 2007 and 2010 Integrated Biological and Behavioural Surveillance Surveys conducted in Nigeria³⁸⁻⁴⁰. This local contextualisation of international ethics guidelines on informed consent currently falls short in two areas – the requirement for backward and forward translation of document into appropriate local

languages, and the submission of the translations to ethics committee for approval. However, the local practice for informed consent seems to be acceptable to the research regulatory bodies and now serves as a norm of practice for national research projects conducted in the country.

Secondly, international standards require that consent be obtained from study participants who have developed the competency to understand the full ramifications of the study process and thus, can make an informed decision about study participation. For this reason, consent is sought from individuals who are considered adults by the law. The legal definition of adulthood in Nigeria, however, is complex and there are also a number of laws that refer directly to the legal capacity of minors to consent on their own behalves.

The Nigeria constitution recognises the age of adulthood to be 18yrs⁴¹. However, it also recognises married women as matured minors⁴², and entitles them to the privileges of an adult. The Child Rights Act⁴³ however recognises 16 years old adolescents as old enough to give consent for research participation. The section 7 of the Nigeria Labour Law Act 1990⁴⁴ on the other hand, defines children as those below 14 years. For Nigeria, ethics committee have often operated on the definition of adulthood using the Nigeria Labour Law Act 1990 thereby enabling adolescents 15 years and above to give informed consent especially during the conduct of national surveys. The interpretation of the laws and the operations of the ethics committee would however face challenges with regard to children and young adolescents less than 14 years of age who are married.

Nigeria has one of the highest rates of early marriage in the world⁴². As the constitution recognises married women as matured minors⁴², married women of any age can give independent consent for study participation where the laws of the country recognises the autonomy of the woman. The Nigerian judiciary also recognises Sharia law⁴⁴ under which adolescents as young as 10-14 years can be married. While there are public debates, discussions and outcry against child marriage, the practice still continues⁴⁵. Thus, where internationally funded research is to be conducted in Northern Nigeria where the Sharia

Law is in effect, it is imperative that the ethical dilemmas raised regarding the recruitment of young married adolescents are articulated and resolved. This is particularly important as young female adolescents have multiple sexual and reproductive health challenges including increased risk for HIV infection. The need to involve adolescents in sexual and reproductive health research has been articulated by several authors^{46,47}. However, the challenge researchers and ethics committee would have to deal with is the need to balance accepted customs, practice and religion and the application of international ethics regulation. Should married underage adolescents be excluded from participation in multi-national studies of benefit to these individuals due to the contention there is about child marriage, or do you accept the local laws and practice and recruit under-aged adolescents and accept the consent obtained from them as valid? Respect for the principle of justice would imply that adolescents in child marriage cannot be excluded from research they otherwise could benefit from simply because of circumstances they find themselves. Yet, young adolescents are assumed not to be competent enough to give informed consent due to their inability to comprehend the entire ramification of the risks and benefits associated with a research. Unfortunately there is no documentation accessed by the study team on any research that had tried to address this challenge.

Thirdly, the majority of research conducted locally is unfunded, meaning that researchers personally bear research-related costs⁴⁸. This has significant implications for the conduct of clinical research. International research ethics guidelines stipulate that study participants are not burdened by study related costs⁴⁹. Local researchers have argued that standard of care costs should not be their responsibility, and should be covered by the patient. This argument is contrary to the interpretation given to many of the guidelines on the conduct of research: research teams are expected to bear the cost of providing study-related care for the recruited study participants. The Nigerian National Code of Health Research Ethics provides no clear regulation on this²⁹ and so ethics committees becomes burdened by efforts to balance the requirements of international

regulations with the realities of the lives in which local research is conducted.

Social Issues

Social issues in Nigeria result in researchers facing real quandaries regarding fair participant selection. Nigeria recently passed the Same Sex Marriage (Prohibition) Act⁵⁰. Under this Act, same-sex marriage results in a 14 year prison sentence, and it also criminalises displays of same-sex affection and prohibits gay clubs, societies and organisations from serving those who engage in same sex activities⁵⁰. The Act defies international human rights principles, but has received significant public support within Nigeria, with many considering same sex relationships against the culture and religion of the country⁵¹.

Gay and other men who have sex with men (MSM) face specific sexual and reproductive health issues, including lack of access to HIV prevention interventions, HIV testing stigma, and increased risk of HIV acquisition in the absence of condom use. The need to conduct HIV prevention studies with this community can therefore, not be ruled out. This would require targeted recruitment which may expose volunteers to extreme social harms, including loss of liberty and violence. The Nigerian National HIV/AIDS Strategic Plan (2010-2015) acknowledges consolidation of human right protections for most at risk populations, including MSM, in order to maximise HIV prevention, treatment and care objectives⁵², but the recent legislation obviously makes this impossible, particularly as it targets organisations that support and provide services to MSM as well as the men themselves. As it is hard to see how the benefits of research could outweigh major risks to participant safety, it is likely that only coincidental recruitment of MSM will be possible unless there is major social, political and legislative change. Even collecting data within research studies on criminalised sex practices, such as male to male sex, is ethically problematic in a rights-constrained environment, given that any breach of confidentiality of data could have extreme consequences. A likely consequence of the criminalisation in Nigeria is that individuals may ascribe HIV acquisition to heterosexual exposure

and not mention any same-sex risk activity, affecting the reliability of data. Ethics committees would therefore have to give due consideration to the design of research studies that would collect data on male to male sexual practices and behaviours in view of the implications for participant recruitment and data integrity.

Beyond the ethical consideration for the design of studies, it would not be deemed proper to conduct research with this vulnerable community in Nigeria. The international (CIOMS) guideline notes that research in very vulnerable subjects is only justified where: (i) the research could not be carried out equally well with less vulnerable subjects; (ii) the research is intended to obtain knowledge that will lead to improved diagnosis, prevention or treatment of diseases or other health problems characteristic of, or unique to, the vulnerable class— either the actual subjects or other similarly situated members of the vulnerable class; and (iii) research subjects and other members of the vulnerable class from which subjects are recruited will ordinarily be assured reasonable access to any diagnostic, preventive or therapeutic products that will become available as a consequence of the research⁴⁹.

However, despite the recent Act, the nation is planning to conduct the 2014 Integrated Behavioural and Biological Sentinel Survey (IBBSS); a survey similar to what was conducted in 2007 and 2010. (Morenike Folayan, personal communication). While these data is relevant for planning, the country is yet to develop any national HIV intervention programme for MSM. The 2014 IBBSS may therefore not be justifiable in the light of interpretations of the international guidelines. The local interest in generating further data for monitoring HIV prevalence in the community seems to be the key rationale for the study approval, but this is arguably not justified, given the extreme vulnerability caused by the Act.

Standard of HIV Prevention

The Nigeria antiretroviral (ARV) treatment guidelines are reasonably close to WHO standards, but not identical. The National Guidelines for HIV and AIDS Treatment and Care in Adolescent and Adults (2010) recommend initiation of ARV for

people with CD4 counts of 350 or below, which does not meet the current WHO recommendation of offering initiation of ARV at CD4 counts of 500 or below (with priority given to those with severe or advanced HIV disease)⁵³. The Nigerian treatment guidelines are aligned with WHO however in that immediate initiation of ARV is recommended for those with concurrent TB, HBV, pregnant women and those in serodiscordant relationships, regardless of CD4 count. This last inclusion, immediate treatment for those in serodiscordant relationships, is for the public health benefit of reducing onward transmission to HIV negative sexual partners. Treating people with HIV for the prevention benefit to partners is best practice prevention, yet it has implications for future research: sero-discordant couples are unlikely to be targeted for future HIV research, given that the protection offered by this strategy is high.

The Nigerian National Code of Health Research Ethics states that equipoise – a genuine state of uncertainty as to whether or not an intervention will be superior to the standard against which it is tested (current best practice or placebo) – is a stipulated requirement for clinical trials²⁹. This supports the proposition that proven interventions should be considered for participants in HIV biomedical prevention trials, including PrEP and treatment-as-prevention, regardless of whether these interventions are currently available in the country.

Prior research on standards of prevention has shown that in instances where new prevention interventions are delayed until they have been incorporated into national policy, inequities emerge between trial sites in different countries – for example, with regard to access to VMMC, where Ugandan PrEP trial participants had to wait longer than those in Kenya, and thus had a higher risk of HIV acquisition⁵⁴. While provision of higher standards of prevention within trials creates inequity with the community from which the trial participants are drawn, on the positive side it also promotes the development of infrastructure that could eventually support community-wide provision⁵⁵.

The argument for providing state-of-the-art HIV prevention interventions within trials,

however, needs nuance. For example, the efficacy of daily oral PrEP in clinical trials is population specific. PrEP efficacy has been demonstrated in HIV serodiscordant relationships⁵, for people who inject drugs⁵⁶, in heterosexual relationships⁶ and in MSM⁴, but the intervention was futile in two trials of African women who were not in ongoing serodiscordant relationships^{19,20}.

Thus while PrEP is biologically efficacious, it is not necessarily effective in all contexts, particularly where adherence is a problem. The problem of adherence was one of the issues articulated by NHVMAS regarding the initial PrEP trial of 2005 in Nigeria⁵⁷. Community advocates voiced concerns that adhering to daily medication in the absence of illness might present a potential major challenge for trial success in the country as uptake and use of pills is typically poor. Supportive evidence is the preference for use of injectable contraceptive rather than the daily pills, and the preference for injections over pills for the management of ill health⁵⁸. This was borne out in the FEM-PrEP and VOICE trials^{19,20}. For this reason, in some instances it could be justifiable to consider whether or not to add daily oral PrEP to prevention packages for trials targeting people not in ongoing serodiscordant relationship in a country like Nigeria. Such a decision however would need to be made collaboratively with full stakeholder engagement to ensure that the pros and cons of particular trial designs are understood by potentially participating communities, and that there is agreement on the rationale for inclusion or non-inclusion of some standard of prevention in the trial design.

However, getting a community to the level of research literacy where it could participate in such complex decision-making would necessarily be a demanding task. This requires investment over time especially for targeted continuous research literacy interventions in potential study communities, translation of trial related materials into local languages and commitment to working collaboratively including having community participants present and adequately resourced to operate at decision-making level within proposed research projects.

Ancillary Care

Ancillary care – care delivered to trial participants that is not directly related to the research question – is important for maximising the health benefits of research participants⁵⁹. One consideration in HIV prevention care in recruiting women is the use of contraception to prevent pregnancy. In a country with low contraceptive prevalence⁶⁰ and poor levels of access to healthcare to ensure safe motherhood⁶⁰, delivery of premium reproductive health services is crucial. This includes access to the safest modern methods of contraception, and a well-managed continuum of care for women who do become pregnant during research.

In HIV prevention trials, the use of long acting contraceptives is often preferred. Injectable contraception has the advantage of providing long lasting protection (2-3 months) that is not coitally dependant. It is important however that research sites provide access to reliable, safe, effective contraception for women at high risk for HIV infection who are often recruited into studies. What is optimal contraception for women at high risk of HIV has been a vexed question since several trials showed some increase in HIV risk, particularly in association with the hormonal injectable DMPA in women infected with HSV-2⁶¹.

Recent analysis from the VOICE trial suggests that NET-EN, an alternative injectable contraceptive, did not increase HIV risk in women with HSV-2⁶¹. Accordingly NET-EN would be the optimal choice of contraception for women participating in HIV prevention studies. In Nigeria however, NET-EN is not readily available in the public family planning service. Where available, the uptake is low because it requires monthly injections. DMPA, a three monthly injectable is far more acceptable and more widely available. Even if monthly injectable contraception could be established as a new norm within trials, there remains the issue of sustainability.

The evidence about the association between HIV and the use of progesterone containing contraception is evolving with research planned explore this possible association⁶¹. However, while

research is ongoing, it would be expected that HIV prevention trials take the evolving evidence about the possible association of contraception and HIV into consideration when planning access to services and education on family planning options for study participants. The available evidence suggests researchers and programmers all err on the side of caution, which could mean either switching from DMPA to NET-EN or always providing condoms (male or female) for dual protection from HIV, other STIs and unplanned pregnancy. Of note however, all clinical trials of HIV prevention interventions, including the VOICE study, advocate consistent condom use alongside hormonal contraception and provide free condoms to participants. Thus the data showing increase risk with DMPA comes from a context where dual protection was being advocated and supported with free condom access, though the results suggest condom use was not consistent⁶¹.

Other data on condom uptake show usage is currently quite low in Nigeria, and that there are barriers in particular to use of the female condoms including availability, partner acceptability, cost, and problems with insertion^{62,63}.

International guidelines addressing hormonal contraception and HIV risk would require that clients' access to NET-EN be enhanced as much as possible. However, for a community where there is a strong preference for DMPA due to the convenience of the product, a marginal increase in risk needs to be weighed against the major health benefits of reliable and convenient contraception. The evidence linking DMPA to increased HIV risk is not conclusive, and the population at risk may prefer the riskier product due to convenience of use. Unfortunately, the use of contraception is very low in Nigeria (the current use of any method of contraceptive by and a modern method of contraceptive by married women in Nigeria is 13.5% and 10% respectively)³⁸ and efforts must be made to continue to promote access to contraception by all women who need it. Ethics committees are likely to conclude that the participants themselves should make the choice of contraceptives, with the proviso that the increased inconvenience of NET-EN would require additional adherence support. However this means that participants with low perceptions³⁸ of HIV

risk will have to make a choice between two contraceptives, one of which (DMPA) is very much more convenient.

Conclusion

HIV prevention research is being conducted in developing countries in an era of changing socio-cultural, political, legal and economic circumstances. Yet, more HIV prevention research is needed despite the unique series of challenges countries may face, as the case study of Nigeria demonstrates. The large population and high number of HIV infections means that research is likely to be feasible, but there are serious problems for research in working in a rights-constrained environment. While the research ethics infrastructure and policy framework have been strengthened in recent years, the criminalisation of same-sex couples and services that provide support for same-sex attracted people are barriers to well-conducted ethical research. The marriage of very young girls and women poses another problem regarding inclusion or exclusion from research.

The issue of contraceptive choice and HIV risk is a complex one, as three-monthly injectable contraception is the norm for the small percentage of Nigerian women who use contraception, and the introduction of a safer but less convenient product may be less acceptable. Ethics committees and community advisory boards as well as potential participants need to work together to help ensure participants are receiving a broad spectrum of know HIV prevention options in clinical trials.

With regard to the issue of trial participants accessing higher standards of care than others in their communities, the risk that participants undertake justifies this privilege, as discussed with regards to different forms of injectable contraceptives. Every effort should be made, however, to eventually make such improvements in care available and sustainable at population level. This issue should be one discussed with local ethics committees, investigators, and sponsors prior to initiating HIV prevention studies.

The lessons from this case study show that in Nigeria there are local peculiarities that need to be taken into consideration in the design of

multinational studies, such as biomedical HIV prevention research studies. We can also infer that other communities will have local specific customs and practices that need to be accommodated. When researchers are faced with the dilemma of interpretation of international ethics guidelines and the realities of the daily lives of persons and their practices, the decision of the local ethics committee becomes crucial. The challenge then becomes how familiar ethics committee members in these local settings are with these guidelines, and how their interpretation and use in the local context continues to ensure the respect for persons and communities, ensure justice including the fair selection of study participants in ways that data quality is not compromised, and that risks for each study participants and their community do not outweigh the potential benefits associated with the conduct of the research. This would require that vulnerable population groups are not further marginalised through their research participation, and that the research is designed in collaboration with relevant communities, with services negotiated to ensure that existing health service infrastructure is strengthened and that the protection of participants' wellbeing – social as well as biomedical - is recognised as paramount.

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