

## PERSPECTIVES PAPER

# Ethics of Ancillary Care in Clinical Trials in Low Income Countries: A Nigerian Case Study

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### Abstract

The ethical conduct of HIV prevention researchers is subject to scrutiny. Many clinical trials take place in low and middle income countries where HIV incidence is high, but the benefits of research are often first enjoyed in high income countries. The provision of ancillary care – medical care provided to clinical trial participants during a trial, which is not related to the research question – is one way in which trial participants can receive direct benefits from their participation in research. We argue that such care is a legitimate benefit of research participation. This care does not constitute ‘undue inducement’ if the research study itself involves minimal risk and is subject to ethical and regulatory oversight. We also argue that research teams working with populations who have sub-optimal healthcare access have a duty to provide ancillary care within agreed limits. These limits should be negotiated to ensure that the research remains feasible and economically viable. (*Afr J Reprod Health* 2014; 18[3]: 135-142)

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**Keywords:** Ancillary care; ethics, HIV prevention, undue inducement

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### Résumé

La conduite éthique des chercheurs dans le domaine de la prévention du VIH est soumise au contrôle. De nombreux essais cliniques ont lieu dans les pays à faible et moyen revenu où l'incidence du VIH est élevée, mais les avantages de la recherche sont souvent d'abord appréciés dans les pays à revenu élevé. La prestation de soins auxiliaires – les soins médicaux fournis aux participants des essais cliniques au cours d'un procès, qui n'est pas liée à la question de la recherche - est une façon pour les participants à l'essai de recevoir des prestations directes pour leur participation à la recherche. Nous soutenons que ces soins constituent un bénéfice légitime de participation à la recherche. Ce soin ne constitue pas «une incitation induite» si l'étude elle-même implique un risque minimal et elle est soumise à la surveillance éthique et réglementaire. Nous soutenons également qu'il incombe aux équipes de recherche qui travaillent avec les populations qui ont accès à des soins de santé sous-optimal de leur fournir des soins auxiliaires dans les limites convenues. Ces limites doivent être négociées pour s'assurer que la recherche demeure réalisable et économiquement viable. (*Afr J Reprod Health* 2014; 18[3]: 135-142)

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**Mots-clés:** Soins auxiliaires, éthique, prévention du VIH, incitations indues

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### Introduction

HIV prevention research is concentrated in populations that have high HIV incidence in order to facilitate timely responses to research questions. In the process of research, co-morbidities may be detected. The high HIV incidence in low income countries means that local healthcare resources may be strained. In such contexts, it is arguably appropriate for the research team to offer ancillary care to participants: i.e. medical care that is not directly related to the research question.

Determining the level of ancillary care that can be offered has been discussed at length in bioethics literature. The concern now is how best to address the health care needs of the research participant without placing an excessive burden on the researchers, while at the same time avoiding providing an ‘undue incentive’ for research participants<sup>1-8</sup>. An ethical tension is perceived between the ethical duty to promote the participants’ wellbeing and the need to ensure that participation is not coerced; alongside this sits the practical problem of how research studies can

afford to offer such care, and how to set defined limits so that this care it remains sustainable throughout the study.

The Nigerian health system is burdened with HIV. Nigeria has the second largest HIV epidemic globally, with 3.1 million people living with HIV and annual new infections increasing by 60% despite a global target to reduce new infections by 50%<sup>9</sup>. Only one in three people who meet the threshold for antiretroviral therapy (ART) access it. Approximately 20% of pregnant HIV positive women access prophylactic ART to prevent vertical transmission to their infants<sup>9</sup>. Reproductive health care is suboptimal and the unmet need for both family planning services and safe birthing options has been documented<sup>9</sup>. Only 39% of births are delivered by skilled birth attendants<sup>9</sup>. Contraceptive prevalence is very low for women who have not been educated, and rises with the educational attainment of women<sup>10</sup>. For example, only 3% of women with no education use a method of contraception compared with 20% with primary education, 29% with secondary education, and 37% with more than secondary education<sup>10</sup>. In general, women do not begin to use contraception until they have had at least one child<sup>10</sup>. The child mortality rate is 128 deaths per 1,000 live births in the 2013 NDHS despite an MDG target to reduce this to 30 deaths per 1,000 live births expected by 2015<sup>10</sup>. In terms of the number of maternal deaths, Nigeria is ranked second in the world behind India and Nigeria is part of a group of six countries in 2008 that collectively accounted for over 50% of all maternal deaths globally<sup>11</sup>. It is apparent through the elevated mortality rates that the lack of access to or use of quality delivery services is an issue of immense importance in Nigeria. Problems such as obtaining money for treatment, distance to health facility and having to take transport are some of the many difficulties stated by women in describing difficulty with accessing healthcare<sup>11</sup>.

As clinical research is rapidly expanding in low and middle income countries (LMIC) where it is easier to recruit a large number of participants with drastically reduced costs, questions arise over what the researchers owe to the host population and what obligations they have to the individual

research subjects. Due to Nigeria's large and young population, with more than half of the population below 29 years<sup>2</sup>, Nigeria is an attractive clinical trial destination for international researchers. This brings with it the risk of exploitation, where economic interest in conducting clinical research could potentially conflict with the best interests of trial participants<sup>13</sup>.

The expansion of research activity brings with it risks as well as benefits. While Nigeria has recently reviewed and strengthened its ethical and regulatory review structures, research in developing countries with relatively weak health system infrastructure has the potential to exploit participants, particularly if monitoring systems are suboptimal<sup>14</sup>. Nigerians have had recent experience of such studies, such as the Pfizer Trovan trial during the meningitis epidemic of 1996, in which sick children were treated experimentally with an untested drug without adequate consent and five died<sup>15,16</sup>. Negative experiences of clinical research reverberate through communities, making people distrustful of the medical research establishment and less inclined to participate in future studies, even when studies address questions that are salient to community health needs. Against this background, it is not surprising that research teams must work in collaboration with communities to understand their health priorities and to address some of those needs within the research context. This way, research teams might experience better recruitment. However, this raises two important questions. First, can health services that are provided within a clinical trial setting constitute an 'undue inducement' to participate? Second, how can researchers determine the scope of ancillary care fairly and reasonably, without placing too great a burden on the research budget?

International guidance identifies the main obligations of researchers to be consideration of trial subjects' rights, safety and well-being over the interest of science and society<sup>17,18</sup>. This provides a sound reason for researchers to attend to the clinical needs of the trial subjects who have willingly volunteered themselves to the increase of medical knowledge. There is however a lingering

concern that provision of a higher standard of healthcare to research participants could be a form of 'soft coercion' or 'undue inducement'.

### ***Undue inducement***

The concept of 'undue inducement' is that the excessive rewards offered to trial participants could lure people into participating in a research project against their best interests, and risk serious harm<sup>19</sup>. As Emanuel points out, this definition comprises several distinct components: (1) An excessive offer – an offer of a good that is irresistible in the context; (2) Poor judgment – the participant will exercise poor judgment with respect to his or her best interests in order to take up the excessive offer; (3) Risk of serious harm – this poor judgment leads to the likelihood that the person will risk serious harm to his or her best interests<sup>9</sup>. When applying this definition, one can see how the 'undue inducement' concept is relevant to a practice such as payment for organ donation. If a person were to agree to 'donate' an organ (such as a kidney), and receive disproportionate compensation for pain, suffering and loss of income, this would be a prime example of 'undue inducement'. 'Undue' because live organ donation is inherently risky. A large sum of money intended for compensation could persuade an impoverished person to undergo that risky surgery, which may result in lifelong health complications. If the level of risk was acceptable only because of the money offered, that is a perfect example of 'undue inducement'.

It is much harder to apply Emmanuel's definition of undue inducement to clinical research projects that have undergone regulatory and ethical review. One of the aims of such reviews is to minimise risk. Furthermore, if the 'good' on offer is improved access to healthcare – with healthcare being acknowledged as a fundamental human right – it is hard to see how this is against a potential participant's best interests, particularly if the potential participants' access to healthcare is otherwise suboptimal. While the offer of improved healthcare might be an inducement, in that it will influence the decision to participate, it is not an 'undue' inducement if it does not persuade the

person to practice poor judgment and undertake excessive risk. Therefore, we can safely conclude that while the offer of healthcare might potentially exert persuasive influence over a potential participant's decision to take part in a clinical trial, it in itself is not an ethical problem if the clinical trial is well regulated and risks to the participants are minimised.

### ***Is ancillary care a duty?***

Following Emanuel's argument, we allow that ancillary care provision is an inducement, in that access to better healthcare may be the factor that persuades a person to participate in a trial. Such inducement is not undue or inappropriate, however, if the risks of the research have been minimised and there is adequate ethical oversight of the study. We should therefore consider whether ancillary care constitutes a just recompense for research participation.

Generally, the benefits of health research are such that it adds information about health to the store of human knowledge, and may provide specific information that could improve health outcomes for particular populations. However, there are instances in research where participants do not benefit directly. For instance, in a randomised control trial, participants may or may not receive the investigational intervention depending on their randomisation, and that intervention may or may not actually prove beneficial. Investigational interventions could also be shown to be harmful, as was demonstrated in the microbicide trial COL1492, where participants receiving the intervention were more likely to acquire HIV than those receiving placebo<sup>20</sup>. While post-trial access is an ethical requirement for interventions that prove successful<sup>21</sup>, not all trials have positive results. Also, some interventions may be irrelevant post-trial for former participants (such as access to HIV prevention interventions, if a participant has acquired HIV whilst on the trial). Thus, ancillary care provision complies with the principle of beneficence, defined as the obligation to act in the interests of others, as it supplies a health good to participants which is in their interests<sup>22</sup>.

HIV prevention research is concentrated in high-incidence populations and frequently in developing countries where access to health care may be suboptimal. Yet the benefits of research in terms of population-wide roll out are more likely to occur first in high income countries. An example is the experience of pre-exposure prophylaxis (PrEP) research. Clinical trials for PrEP were predominantly conducted in LMIC, but so far the intervention has only been approved in the United States (though there are demonstration sites elsewhere). Thus, experience to date in HIV prevention research shows that trial populations may not receive any timely direct benefit from research outcomes (such as access to a newly established product). Therefore the ancillary care provided by the research study may be the *sole* direct benefit of participation for some participants. Accordingly, in instances where trial participants' access to healthcare outside the research study is suboptimal, we suggest that provision of ancillary care is a duty. Using the principle of justice, trial participants may be deemed *entitled* to ancillary care firstly because the lack of adequate care under existing health provisions is wrong, and secondly that their contribution to human health through their research participation warrants the provision of some reciprocal benefit<sup>22</sup>.

The concept that the provision of ancillary care to research participants is a duty of the researcher has been proposed by numerous scholars, who have grounded the obligation in different principles. This has resulted in models of ancillary care that address the scope and limitations of the obligation in different ways. Miller and Weijer<sup>23</sup> proposed that a researcher has a fiduciary duty to research participants, which maximises ancillary care obligations. Merritt and colleagues<sup>2</sup> defined the obligation as being based on the duty of rescue which could be applied both to urgent and non-urgent health needs. Both Hooper<sup>24</sup> and Pratt and colleagues<sup>8</sup> defined the obligation of using different formulations of justice. Bright and Nelson<sup>6</sup> developed a model based on research site capacity, which limits the obligation to providing healthcare to situations where the need is urgent,

and takes into account the capacity of the research site to provide particular healthcare services<sup>6,4</sup>.

Belsky and Richardson<sup>1,5</sup> provide a particularly persuasive rationale for considering ancillary care as a duty and responsibility that researchers accept when they obtain participants' consent for medical research. When participants consent to researchers examining their bodies, samples and medical records, Belsky and Richardson argue that researchers have been entrusted with particular aspects of participants' health, and therefore cannot disclaim all responsibility for those people. This duty also defined as 'partial entrustment' is limited and subject to particular conditions that will be discussed below.

The 'partial entrustment' model differentiates itself from the notion that a researcher must meet all of a participant's unmet health needs<sup>23</sup>. It also differs from the opposite position, that research is intended to provide generalised knowledge so the researcher does not have physician-like duties to provide 'extraneous' health services unrelated to the aims of the trial<sup>25</sup>. Instead, it articulates the researcher's obligation with precision, focusing on conditions that are discovered while carrying out study procedures, and having regard to the depth of the relationship and the vulnerability of the research participants.

### ***Limitations on the duty***

The ethical justification of ancillary care does not require delivery of unlimited health care to participants during trials, but rather to provide solutions to a limited subset of health conditions causing severe morbidity and mortality in host communities, as well as those uncovered during the research process<sup>26</sup>.

The partial entrustment model defines researcher obligations as falling short of the duty that a physician has to a patient, in that it is limited to treatment of conditions that become apparent through the research processes. Further, the partial entrustment model includes consideration of other morally relevant facts, such as the depth of the relationship between the participant and the research project, and the risks and or burden borne

by the participants all affect the scope of the obligation. For instance, a three-year study that requires monthly attendance at a clinic would produce greater research obligation than a study that involves a one-off sample collection and no ongoing monitoring. Material conditions such as the vulnerability of the participants (whether or not they have meaningful access to care by other means) and the ability of the research study to bear the costs without jeopardising the aims of the research are all taken into account. This model recognises that an excessive burden shouldn't be placed on researchers to provide ancillary care for every conceivable health condition, as to do so would discourage them from conducting studies in developing countries which would prevent the benefits that can arise from participation in research<sup>3</sup>.

While we broadly accept the limits defined in the 'partial entrustment' model, and agree that research teams cannot be made accountable for every condition that trial participants might experience, we would extend the model to include provision of care or prophylaxis for conditions that may be commonly neglected but that are endemic, and simple, and cheap to manage: for example, the treatment for worms. In addition, we consider that there is justification for considering on a case-by-case basis unusual but urgent healthcare needs that arise in the participant population, even if these fall outside the scope of partial entrustment.

Finally, we consider that research teams need to develop effective working relationships with local health service providers in order to complement local service provision, to avoid overloading services, and to maximise care opportunities. Where possible care plans for ancillary care provision should be negotiated with local health care providers, and at the completion of the trial, plans put in place to ensure that continuity of care post-trial can be managed between the different providers<sup>8</sup>.

### ***Ratcheting up standards***

The issue of whether improved healthcare introduced in the context of a research study should be sustainable when that study ends is a

complex one. On the one hand, it is certainly desirable for improved standards to remain in place at the conclusion of a trial. On the other hand, we argue that if an intervention is urgently required by a trial participant, it should be provided by the study team if it does not cause undue burden to the team, and if it is achievable within resources of the researchers at the time of need. The possibility that intervention might not be feasible outside the controlled study setting ought not to preclude providing the intervention when the need arises.

Benatar and Singer argued in an influential paper that the ethical aim regarding standards of care should not necessarily be to replicate the care offered elsewhere, but to aim to shift the standard of care from the baseline upwards in a given context<sup>27</sup>. We agree that this is important, and should be supported by study teams working to improve health infrastructure and most importantly to develop the capacity of local health workers to improve services in an ongoing, sustainable way. Many ancillary care needs can be anticipated at the outset of a study, and their costs budgeted<sup>2</sup>. Building local partnerships, and negotiating the delivery and services between the local providers and the study facilities should therefore be possible, and is certainly desirable. Planning to shift service delivery to the local providers at the trial's conclusion should be planned well in advance and supported by trial resources<sup>8</sup>.

While we consider that contribution to sustainable service improvement to be very important, we do not however think that the lack of sustainability should preclude providing a particular service should an urgent need arise which the trial team has the capacity to address it. To do so would be a failed opportunity to demonstrate care for the individuals who comprise the trial population – and providing this type of exceptional care may also be critical in establishing trust between the researcher and the research participants.

### ***Ancillary care in practice***

An example of an extraordinary ancillary care need arising in a trial is demonstrated in a case

study from a Tanzanian microbicide trial site by Valley and colleagues<sup>28</sup>. In this study the scope of ancillary care had been carefully negotiated with the community and local healthcare service providers so that it matched locally available best practices. The research team however did not rigidly adhere to their plan. They responded on the basis of the 'rule of rescue'. When a participant presented with an emergency life threatening condition that was unrelated to the trial and outside the scope of agreed ancillary care, the researchers provided exceptional life-saving care and the site bore the cost for this. This example could be seen as an illustration of Bright and Nelson's capability approach<sup>8</sup>, which emphasises the requirement to respond to urgent needs. It also fits the precept articulated by Merritt and colleagues<sup>2</sup> that being in the right place at the right time with the right access to the needed resources can define the obligation to provide ancillary care.

The issue of ancillary care in HIV prevention trials has been discussed by Haire<sup>29</sup> in a qualitative study of principal investigators of such trials. One key issue that arose regarding ancillary care in this study was whether or not the provision of ancillary services should be uniform across all study sites. An example was whether or not to offer Pap smear testing in multicentre microbicide studies where different sites had very different healthcare infrastructure. The problem was that while the research teams could conduct the Pap smear tests, some sites could not link the women who had abnormalities to treatment and care services. Thus the research teams arrived at a compromise: that they would provide Pap testing only at sites where women could then be referred for treatment, but not at sites where treatment for cervical dysplasia was not available through the local infrastructure. The rationale for this was that it maximised health benefits at sites where Pap testing could be linked to treatment, but did not cause harm at sites where there were no treatment linkages, where an abnormal diagnosis would lead to increased stress rather than curative treatment.

The provision of good ancillary care, in particular reproductive health care, was cited by the principal investigators as a critical to gaining and maintaining the communities' trust for this

study. The researchers also spoke of strong personal motivation to ensure that participants had access to appropriate care through the study, pride in what they achieved, and of the need to negotiate how care was provided through robust community consultation.

### ***Lack of ancillary care provision in the failed Nigerian PrEP study***

In 2004, a study of oral tenofovir as pre-exposure prophylaxis for HIV began in Nigeria, with a community information event occurring at the first national advocates meeting of the New HIV Vaccine Microbicides Advocacy Society (NHVMAS)<sup>30,31</sup>. The advocates raised many issues with the research, including the need to understand it better before the trial commenced. On subsequent occasions NHVMAS members raised issues including potential problems with adherence, the lack of formal community input into the trial protocol and management, poor access to ART for seroconverters, and inadequate ancillary care. With regard to ancillary care, the advocates argued specifically that the researchers should aim to meet all of the health care requirements of the participants who enrolled on the study.

Neither the ancillary care requirement nor the other issues raised by advocates were addressed in this trial. This trial was halted in 2005. While the stated reasons for trial closure were good clinical practice concerns, it is doubtful as to whether the trial could have succeeded given the lack of negotiation of issues deemed critical to the community advocates. A similar study in Cambodia was shut down in 2004 due to issues with miscommunication, negotiation and community acceptability<sup>30,33</sup>. The importance placed on ancillary care access by the advocates demonstrates the primacy of this issue for populations with inadequate healthcare access. By providing for the healthcare needs of such populations while undertaking research, researchers can demonstrate that participants are more than just a means to an end. Thus, ancillary care can be seen as a critical obligation for ethical, non-exploitative research in LMIC, especially

those conducted in communities where local healthcare is inadequate.

## Conclusion

We argue that the provision of ancillary healthcare is not an 'undue inducement'. Ancillary care meets a legitimate need and is clearly in the interest to participants who have otherwise compromised access to healthcare. While this care might provide an incentive for trial participation, it is not an ethical concern if the studies in question have been designed to minimise risk and have adequate review and oversight to protect study participants. The provision of healthcare and clinical research both have moral value and are intended to relieve suffering and illness and produce generalizable knowledge that will be useful to human health.

Morally, it is wrong for people not to have access to optimal healthcare. So, providing improved care in the context of a research study is, we argue, obligatory, but it also needs to be a limited obligation, so that the provision of care does not impede the goals of the research. Therefore we consider models such as 'partial entrustment', the provision of simple, basic preventative treatment or care for endemic illnesses or infections and the application of the 'rule of rescue' as appropriate for defining and limiting the obligation of researchers in context, so that more people can benefit from improved healthcare, and that trial participants receive only a recompense for their contribution to the store of knowledge.

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## Contribution of Authors

Bridget Haire and Olesgun Ogundokun conducted literature searches and desk reviews of documents for this article. Both authors contributed to the conception of the article. Bridget Haire prepared the manuscript that was

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## References

1. Belsky L, Richardson HS. Medical researchers' ancillary clinical care responsibilities. *BMJ*. 2004; 328(7454):1494-6.
2. Merritt MW, Taylor HA, and Mullany, LC. Ancillary care in community-based public health intervention research. *Am J Public Health*. 2010;100 (2):211-6.
3. Richardson HS. Gradations of researchers' obligation to provide ancillary care for HIV/AIDS in developing countries. *Am J Public Health*. 2007; 97(11):1956-61.
4. Richardson HS. Comment on 'a capacity-based approach for addressing ancillary-care needs: implications for research in resource limited settings'. *Journal of Medical Ethics*. 2012;38(11):677-8.
5. Richardson HS. Incidental findings and ancillary-care obligations. *The Journal of Law, Medicine & Ethics*. 2008; 36(2):256-70.
6. Bright PL, Nelson RM. A capacity-based approach for addressing ancillary care needs: implications for research in resource limited settings. *Journal of Medical Ethics*. 2012.
7. Hyder AA, Merritt MW. Ancillary care for public health research in developing countries. *JAMA*. 2009;302(4):429-31.
8. Pratt B, Zion D, Lwin KM, Cheah PY, Nosten F, Loff B. Ancillary care: From theory to practice in international clinical research. *Public Health Ethics*. 2013; 6(2):154-69.
9. Sagay AS. Current State of AIDS Epidemic in Nigeria: Role of ARVs on PMTCT. *Biomedical HIV Prevention Forum*. 2013. Available at: [www.nhvmas-ng.org/forum/confslides.php](http://www.nhvmas-ng.org/forum/confslides.php). Accessed 27 March 2014.
10. National Population Commission [Nigeria] and ICF Macro. Nigeria Demographic and Health Survey 2013 Preliminary Report. Abuja, Nigeria and Calverton, Maryland: National Population Commission and ICF Macro. October 2013.
11. Bankole A, Sedgh G, Okonofua F, Imarhiagbe C, Hussain R and Wulf D. 2009. Barriers to Safe Motherhood in Nigeria. New York: Guttmacher Institute. Available at: [www.guttmacher.org](http://www.guttmacher.org) Accessed 6 June 2014.
12. National Population Commission [Nigeria] and ICF Macro. Nigeria Demographic and Health Survey 2008 Preliminary Report. Abuja, Nigeria and Calverton, Maryland: National Population Commission and ICF Macro, 2009.
13. New HIV Vaccine and Microbicide and Advocacy Society (NHVMAS). Nigeria- A Haven for Clinical trials. Sept 15, 2012. Available at: [http://www.nhvmas-ng.org/news.php?news\\_id=66](http://www.nhvmas-ng.org/news.php?news_id=66)

- Accessed 27 March 2014.
14. Ogundokun O. Monitoring – A gradual process. 4 December 2013. Available at: <http://globalhealthtrials.tghn.org/articles>. Accessed 27 March 2014.
  15. Goldstein S. Bioethics takes root in Nigeria. *Global Health Matters Newsletter*/ November / December 2011. 10 (6) 2011. Available at: <http://www.fic.nih.gov/News/GlobalHealthMatters/nov-dec-2011/Pages/bioethics-nigeria.aspx> Accessed 27 March 2014.
  16. Ogundele S, Falade, C.O. Good clinical practice in Nigeria - the way forward. *Annals of Ibadan Post Graduate Medicine*. 2006;4(1):28-32
  17. WMA Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects Available at [www.wma.net](http://www.wma.net). Accessed 27 March 2014
  18. International Conference on Harmonization Guideline for Good Clinical Practice. (ICH-GCP). Available at: [www.ema.europa.eu/docs/en\\_GB/document\\_library/scientific\\_guideline/2009/09/WC00002874.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/scientific_guideline/2009/09/WC00002874.pdf) Accessed 27 March 2014.
  19. Emanuel EJ. Undue inducement: Nonsense on stilts? *The American Journal of Bioethics*. 2005; 5(5):9 - 13.
  20. Van Damme L, Ramjee G, Alary M, Vuylsteke B, Chandeying V, Rees H, et al. Effectiveness of COL-1492, a nonoxynol-9 vaginal gel, on HIV-1 transmission in female sex workers: a randomised controlled trial. *The Lancet*. 2002; 360(9338):971-7.
  21. UNAIDS. Ethical considerations in biomedical HIV prevention trials [Additional guidance point added in 2012]. *Joint United Nations Programme on HIV/AIDS (UNAIDS)*. 2012.
  22. Beauchamp T, Childress J. *Principles of Biomedical Ethics*. 4<sup>th</sup> ed. New York, Oxford: Oxford University Press; 1994.
  23. Miller PB, Weijer C. Fiduciary obligation in clinical research. *The Journal of Law, Medicine & Ethics*. 2006; 34(2):424-40.
  24. Hooper CR. Ancillary care duties: the demands of justice. *Journal of Medical Ethics*. 2010; 36(11):708-11.
  25. Emanuel EJ, Wendler D, Grady C. What makes clinical research ethical? *Jama*. 2000; 283(20):2701-11.
  26. Hyder AA, Merritt MW. Ancillary care for public health research in developing countries. *JAMA*. 2009;302(4):429-31.
  27. Benatar S, Singer P. A new look at international research ethics. *BMJ*. 2000; 321: 824 - 6.
  28. Valley A, Shagi C, Kasindi S, Desmond N, Lees S, Chiduo B, et al. The benefits of participatory methodologies to develop effective community dialogue in the context of a microbicide trial feasibility study in Mwanza, Tanzania. *BMC Public Health*. 2007;7:133
  29. Haire BG. Ethics of medical care and clinical research: a qualitative study of principal investigators in biomedical HIV prevention research. *Journal of Medical Ethics*. 2013;39(4):231-5.
  30. Ukpong M, Falobi, O. The oral Tenofovir controversy: Report of a dialogue between community advocates and researchers on the Phase II Oral Tenofovir (TDF) trial in Nigeria. *Nigeria HIV Vaccine and Microbicide Advocacy Group*. Lagos, Nigeria. 2005.
  31. Ukpong M, Peterson K. Oral Tenofovir Controversy II: Voices from the field. A series of reports of the oral Tenofovir trials with perspectives of community voices from Cambodia, Cameroon, Nigeria, Thailand and Malawi. *New HIV Vaccine and Microbicides Advocacy Society (NHVMAS)*. Lagos, Nigeria. 2009.
  32. Page-Shafer K, Saphonn V, Sun LP, Vun MC, Cooper DA, Kaldor JM. HIV prevention research in a resource-limited setting: the experience of planning a trial in Cambodia. *The Lancet*. 2005;366(9495):1499-503.
  33. Haire BG. Because we can: Clashes of perspective over researcher obligation in the failed PrEP Trials. *Developing World Bioethics*. 2011; 11(2):63-74.