

## PERSPECTIVES PAPER

# Beyond Informed Consent: Ethical Considerations in the Design and Implementation of Sexual and Reproductive Health Research Among Adolescents

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### Abstract

Interest in addressing the ethical issues related to adolescents' engagement in research, especially sexual and reproductive health and rights (SRHR) research is increasing in view of the need to design and implement research that address peculiar SRHR needs of adolescents. These needs include issues of sexually transmitted infections, HIV, AIDS, adverse pregnancy outcomes, community, family and relationship violence and mental health. Unfortunately, adolescents' voluntary participation in research has been limited due to their perceived potential to be coerced into participation, and concerns that they may not fully comprehend the issues related to research risks. As such, many of the regulations for engaging research participants have been defined by age rather than due consideration of psychological development. This paper examines the various potential ethical issues that may impact on decision making when adolescents are engaged in research. These include the need to minimise therapeutic misconception, considerations for recruitment and retention, types and amounts for reimbursement, and engagement of communities of adolescents on advisory boards of studies that involve their population. The potential challenges associated with recruitment of adolescents in early child marriages were also highlighted. (*Afr J Reprod Health 2014; 18[3]: 118-126*)

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**Keywords:** Adolescents, ethics, sexual and reproductive health, research

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### Résumé

L'intérêt dans le traitement des questions éthiques liées à l'engagement des adolescents dans la recherche, la santé et les droits en particulier sexuelle et reproductive (SSR) de recherche est en augmentation en raison de la nécessité de concevoir et mettre en œuvre des recherches qui répondent à des besoins particuliers de la SSR des adolescents. Ces besoins comprennent les questions d'infections sexuellement transmissibles, le VIH, le sida, les résultats défavorables de la grossesse, la communauté, la famille et la violence dans les relations et la santé mentale. Malheureusement, la participation volontaire des adolescents en matière de recherche a été limitée en raison de leur potentiel perçu d'être forcée à la participation, et les préoccupations qu'ils ne peuvent pas comprendre pleinement les questions liées à la recherche des risques. En tant que tel, de nombreux règlements pour engager participants à la recherche ont été définis par l'âge plutôt que tenant compte du développement psychologique. Ce document examine les diverses questions éthiques potentiels qui pourraient avoir une incidence sur la prise de décision lorsque les adolescents sont engagés dans la recherche. Il s'agit notamment de la nécessité de minimiser le malentendu thérapeutique, les considérations en matière de recrutement et de rétention, les types et les montants de remboursement, et l'engagement des communautés des adolescents au sein des conseils consultatifs des études qui impliquent leur population. Les défis potentiels liés au recrutement des adolescents dans les mariages précoces des enfants ont également été soulignés. (*Afr J Reprod Health 2014; 18[3]: 118-126*)

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**Mots-clés:** adolescents, l'éthique, la santé sexuelle et reproductive, de la recherche

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### Introduction

Adolescents are individuals who are between childhood and adulthood, and represent one fifth

of the global population<sup>1</sup>. The World Health Organisation defines the adolescent age range as the second decade of life, 10 to 19 years<sup>2</sup>, while this age limit is often extended to 24 years by

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some other definitions<sup>3</sup>. However, it must be recognized that adolescence is an age of immense physical, psychological and social changes which are often influenced by culture<sup>2</sup>.

The justification for conducting reproductive health research in adolescents is the same as that for any biomedical or behavioral research project. Well designed studies can provide scientific evidence on which to base the design and delivery of appropriate preventive and therapeutic services to this sub-population. The need for research among adolescents has been well articulated. Globally, adolescents bear a disproportionate burden of STIs, HIV and unplanned pregnancy<sup>4</sup> and are therefore a critically important population for targeting reproductive health research and service delivery. Their reproductive health issues differ from those of mature adults in both biological and social aspects. Susceptibility to disease, and social processes that influence sexual relations and access to health information and healthcare services are significantly different in adolescents. Sexual and reproductive health rights of adolescents also differ from that of adults. Without adolescent-specific research, young people will inevitably be offered services that have only been tested in adults. This may present unforeseen side effects or issues with adherence and acceptability of products.

The social behavior of younger adolescents also differs from adults in ways that could eventually affect use of sexual and reproductive health products. They are frequently inclined towards risk taking, and are acutely sensitive to peer influence<sup>5</sup>. They also have an impact tendency towards both altruism<sup>6</sup> and rebellion, together with increased sensitivity to body image<sup>7</sup>, privacy, and confidentiality<sup>6</sup>. Adolescents have also been shown to have challenges with adherence to prescribed regimens<sup>8</sup>. These factors can affect their understanding of risks and their capacity to make informed decisions about their long-term best interests<sup>5</sup>. Adolescent behaviours become critically important when considering how to introduce and promote health products to teenagers<sup>5</sup>.

This paper therefore sets out to highlight the various ethical issues that would need to be considered when designing, reviewing and

implementing sexual reproductive health and right (SRHR) research involving adolescents. The authors recognize the importance of the ongoing debate about how to consent adolescents to participate in SRHR research and have discussed this extensively in a prior paper<sup>8</sup>. We therefore focus our discussions on other aspects of SRHR research other than the considerations given to obtaining informed consent from an adolescent. In this paper we discuss the complexities involved in taking balanced decisions that recognise the autonomy of the adolescent and yet balance this with other necessary considerations involved making decision on the ethical integrity of a SRHR research protocol.

## Discussion

### *Developmental Concerns*

Adolescence is divided into 3 developmental periods: early (11years to 14 years), middle (15years to 17 years), and late (18years to 21years)<sup>5</sup>. By mid adolescence (normally around the ages of 14years to 16years), most adolescents' cognitive abilities are roughly the same as biologically mature adults<sup>5</sup>. They are able to understand issues such as long-term risks and the benefits of research. Yet, sensitivity to peer influence and the increased tendency for risk taking are significant factors that must be taken into account when considering their recruitment into health research<sup>5</sup>. There are also physiological and pharmacological developmental considerations that make the enrolment of adolescents into reproductive health research challenging<sup>6</sup>.

These characteristics outlined above have resulted in adolescents being classified as "vulnerable," meaning their capacity to give informed consent freely may be easily compromised. Therefore, from an ethical perspective, adolescents require special protection as a group. We argue that this presents a unique challenge to researchers: to recognize the emerging autonomy of adolescents and the potential benefit of the research, while providing protection from potential research-related harms. This paper focuses attention on early and middle

adolescence for which this decision about level of autonomy is relevant.

### ***Minimising Therapeutic Misconception***

Therapeutic misconception is based on the confusion between the aims of research and those of individualized medical treatment<sup>9</sup>. The primary goal of medical treatment is to help heal the patient, while the primary goal of research is to produce generalizable knowledge. Therapeutic misconception can seriously impair the ability of an otherwise competent person to give true informed consent.

While there is no evidence to suggest that the risk for therapeutic misconception is greater in adolescents when compared to adults, the tendency for therapeutic misconception by adolescents who engage in clinical research may be high due to the potential for low perception of risk, a common reason for therapeutic misconception in research<sup>10</sup>. It would therefore be important that prior to engagement of adolescents in clinical research, prospective participants be helped to fully understand the goals of the research. The recommendation of the National Bioethics Advisory Commission (NBAC) 3.10 states that: *researchers working in developing countries should indicate in their research protocols how they would minimize the likelihood that potential participants will believe mistakenly that the purpose of the research is solely to administer treatment rather than to contribute to scientific knowledge*<sup>11</sup>.

One of the potential consequences of therapeutic misconceptions in sexual and reproductive health clinical research is the risk of disinhibition. Guest et al<sup>12</sup> found no increase in sexual risk behaviour over time during a where HIV negative individuals used antiretrovirals as pre-exposure prophylaxis (PrEP) to prevent sexual acquisition of HIV-1 infection despite concern that PrEP could have resulted in increased sexual risk behaviour and condom migration. A similar result was obtained in the Bangkok trial of PrEP involving drug users,<sup>13</sup> the CAPRISA 004 study<sup>14</sup> and other HIV prevention studies<sup>15-18</sup>. Foss et al however showed that decline in condom used was observed in three of six HIV prevention studies<sup>19</sup> while Sood and

Goldman<sup>20</sup> suggested that population-level sexual risk behaviors increased following breakthroughs in HIV biomedicine. These studies evaluated researches conducted in adults and its finding cannot be extrapolated to predict behavioural outcomes in adolescents.

In the absence of supportive data, researchers who recruit adolescents into SRHR research may need to demonstrate how the research would address the potential for such misconception. Further, they might need to take steps to minimize or eliminate it. This will require some investment in developing educational processes within the informed consent procedure that not only provide critical information but also allow for questions, discussion, and assessment of potential participants' understanding of key concepts.

### ***Participant Recruitment***

Adolescents attending prenatal and family planning clinics are often selected for enrolment into SRHR studies because their attendance at these clinics presupposes that the adolescent is sexually active, may have or have had multiple partners, and is already familiar with clinical procedures. There are good grounds to consider such adolescents as "mature minors", as this recognises the social reality of the study population. Acknowledgment of this reality may make supplemental parental consent less necessary, as parents may not be aware of their children's sexual lifestyle.

This prospect may however be fraught with challenges especially when 'emancipated minors' are defined by their marital status. Marriage implies that the child's parent is free from parental custody and control, and that the child is legally entitled to make almost all of his or her own decisions. In countries in Africa, Asia and the Middle East with high prevalence of child marriage, the enrolment of married adolescents 10years to 13years into studies would be associated with considerable ethical and legal challenges. While marriage may offer the individual autonomy to consent to study participation, concerns about obtaining consent based on understanding the ramifications of the study – including risks and benefits – remains.

Considerations for parental or spousal consent for study participation would be out of place in this situation. Neither would it be ethical to exclude potential study participants from studies that would be potentially beneficial based on the ethical and legal quagmire posed by child marriage. Where researchers need to consider the enrolment of minors emancipated by marriage, due consideration should be given to assessment of the capacity of the minor to understand, discern and appreciate the benefits and risks of the proposed research. This should involve due consideration for age, ability, experience, education, exhibited judgment, conduct, and appreciation of relevant risks and consequences. The dilemma now arises when there is a need to decide on how to obtain consent from an emancipated minor who is still adjudged to be a child based on assessment of the competency of the child to make informed decision and yet, where participation in a study could be of significant benefit for the child. Providing in-country guidelines on how to handle such ethical dilemmas would indeed be of great help in resolving some of these thorny issues.

Recognition also needs to be given to those adolescents who are homeless or those who live on their own. These children make considerable decisions for themselves. When adjudged to be matured enough to understand, discern and appreciate the benefits and risks of a proposed research, such individuals should have the right to consent to study participation especially when such research entail no more risk than what such individuals might reasonably assume on their own.

However, not all SRHR research conducted amongst adolescents would focus on those who are sexually active. Adolescents could be recruited from schools, workplaces and other formal and informal arenas. The place of recruitment of adolescents for study participation may also influence the consenting process. This association has not been clearly recognized and discussed in many guidance documents. Some guidelines propose that consideration should be given to allowing adolescents to consent unassisted to SRHR research, as long as the parents or legal guardians are unlikely to "object" to the adolescent's participation, the study is 'low risk' and the protocol justifies why adolescents should

be included as participants'<sup>21</sup>. The onus would now rest on the researcher to provide evidence to show the unlikelihood of the community objecting to the conduct of such a study without parental consent. One approach would be to hold extensive community consultation about the proposed study prior to finalization of the study protocol to seek the views, opinions and permission of the community for adolescent consent for study participation. The UNAIDS/WHO guidance document on ethical considerations in biomedical HIV prevention trials<sup>22</sup> and the UNAIDS/AVAC document on good participatory practice<sup>23</sup> both provide guidance on how to conduct such community consultations. Documentation of the dialogue and agreements are expected and this document should be submitted along with the study protocol for ethics committee review.

There are cases where parental consent had not been received for adolescent participation in clinical studies and parents or other adult community members have subsequently objected to the study. Where the interpretation of what is 'low risk' is dependent on persons whose capacity to make such judgment may be compromised, then the potential for more cases of litigation arising from research procedures considered unethical is feasible. The human papilloma virus vaccine demonstration project initiated by PATH, USA in collaboration with the Indian Council of Medical Research (ICMR) and the state governments of Andhra Pradesh and Gujarat, India illustrates how problems can occur with proxy consent<sup>24</sup>. In this case, female adolescents aged 10 years to 14 years in boarding schools were recruited into a 'demonstration project' following the directive from the State (Andhra Pradesh) that hostel wardens sign the consent forms on behalf of the parents or guardians. The study was suspended after seven of the 23,000 vaccinated girls died. Enquiries into the study by an independent State committee showed that there were gross violations of the concept of consent and the legal requirement for it. Also, the body which gave ethical approval for the study and ethical guidance to the State was a collaborator on the project implying conflict of interest.

'Opt out' consenting approaches are popular in schools where there may be challenges with

obtaining consent from parents (perhaps because the student does not give the consent form to the parent or parents are not literate enough to read the consent document). With an opt-out approach, a letter must be sent to parents or legal guardians at least two weeks before research activities begin and may not be sent home with the young person<sup>25</sup>. This is intended to ensure delivery of the letter so that if the parent has an objection to the research, he or she can decline to participate. The 'opt-out' approach implies that the adolescent is eligible to give assent for study participation in the absence of a consent form from the parent or legal guardian that states that the child should not participate in the research. It is a passive parental consent procedure commonly used in school settings where the research involves no more than minimal risk to the subjects; the waiver will not adversely affect the rights and welfare of the adolescent, participant selection is based on classroom membership. The opt-out approach has often times resulted in increased students' participation in school based studies<sup>26,27</sup> and is attractive for researchers seeking to facilitate adolescent recruitments into studies.

Matthews et al<sup>28</sup> debunked the speculations that have given credence for value placed on the opt-out consenting approach. They were able to demonstrate high levels of written parental consent for adolescents' participation in a school based HIV prevention research in South Africa. Despite their finding, the authors highlighted the need for researchers to actively engage in dialogue with the community in which the research is conducted to decide on appropriate strategies for obtaining informed consent that is appropriate for the study. This recommendation once again underscores the importance of effective community dialogue in the planning and implementation of large studies involving adolescents.

### ***Retention of Participants***

The number of visits and visit time required for each participant in some SRHR research such as a biomedical HIV prevention study (microbicide, vaccine) is considerable and may be challenging for an adolescent. The recognition of such burden midway along the trial could result in participants withdrawing from further study participation. This

has implication for trials. To ensure the power of a clinical trial to establish authenticity of its result, retention rates need to be as high as 80%<sup>29</sup>. Research teams may then become more strategic in 'inducing,' 'luring' or providing 'soft coercion' to study participants in an effort to ensure study retention<sup>30</sup>.

Ethical review of protocols needs to be sensitive to this potential. The protocol development teams for SRHR research conducted with adolescents must recognize the need not to put undue pressure on participants. The number of study visits needs to be clearly explained upfront, with reminder systems put in place. Offering of peer support to adolescents through the involvement of adolescent organizations and community advisory boards could greatly improve the commitment of participants who are adolescents.

### ***Transport Reimbursement***

Ethics committees may have challenges in identifying what the appropriate transport reimbursement (otherwise called reimbursement payment)<sup>31</sup> should be for adolescents engaged in research, given that many research projects pay transport reimbursement sums that far exceed actual transport fees. The justification for this practice is that the difference serves as compensation for time, inconvenience and efforts expended during the research. Thus, this reimbursement has become a de facto form of payment for service. For example, past microbicide studies conducted amongst sex workers in Nigeria approved sums between \$5.00 and \$10.00 as transport reimbursement (personal communication with six PIs engaged with microcode trials in Nigeria). If such a trial were to be conducted amongst adolescents providing independent consent, consideration would have to be given to the appropriateness of such a sum, given the potential for a disproportionate reimbursement to act as a form of undue inducement. How will the ethical principle of justice be applied in such situation?

The debate about appropriate 'transport reimbursement' for study participants' is a recurrent issue at many trial sites in developing countries. For many study participants, these

transport reimbursements serve as a source of income to support home care and in some cases, businesses<sup>32</sup>. Study participants also see transport reimbursement as a form of payment for service as this is often the only time in the research when there is monetary exchange between the researcher and the study participant.

Ethical discussions have focused on avoiding undue inducement in the design and implementation of research studies. For adolescent participation, the monetary 'gift' that comes in the form of transport reimbursement may provide a disproportionate incentive. It is important to duly balance the application of ethical principles when considering what should be the appropriate transport reimbursement to be paid to young adolescents engaged research. In this case, consideration should be given to equity and justice while avoiding the potential for coercion.

One possible solution to this problem is to directly compensate participants for the time expended on the research, and to link the level of compensation to age and family responsibility. For example Bagley et al<sup>33</sup> advocates a wage-payment model for compensating adolescents for the time and effort of research participation similar to the position adopted by Folayan and Alman<sup>34</sup>. This allows for standardization of compensation, gives due recognition of the time and investment in the research process, and ensures age appropriate proration of the money given in exchange for the service rendered.

### **Community Engagement**

Community engagement is increasingly acknowledged as necessary to conducting acceptable research<sup>35</sup>. Community engagement and buy-in is an essential part of the preparatory work especially in longitudinal studies. Communities expect to be and should be integrally involved in the development and implementation of research which affects them.

Active engagement of community members promotes recruitment and retention of adolescents in the research<sup>7</sup>. Engagement involved the conduct of outreaches, discussions and education about the need to enroll adolescents in the research, it's

importance, and information on why the study objectives cannot be achieved through the enrollment of adult participants alone<sup>36</sup>. The expected challenges to be faced during the implementation of the research must be highlighted in ways that make them understandable, and can facilitate community investment in actions to address them. In addition, adolescent perspectives from advocates or adolescent advisory board should be sought at every stage of the research development process.

Very little is known about how to effectively engaged adolescents in research, especially SRHR research. Models need to be evaluated for its appropriateness for engagement of adolescents in research. Ideally, community representatives – often organized into a community advisory board - are expected to give deep thought to issues discussed and raised during the design, implementation and monitoring of long term research. They also need to think about the potential impact and implications of decisions taken and made for community members as a collective and as individuals. The capacity of adolescents to take such deep and long term views of issues may be limited thereby compromising the essence of their engagement as critical community advisory board (CAB) members.

This limitation may be addressed by engaging parents as members of CAB. However, conflicts might emerge in having parents and adolescents sitting together as peers on a CAB in a patriarchal society where there are generational differences in views and perspectives in some instances. Research teams need to think creatively about appropriate models to actively engage adolescents in research design, implementation and monitoring. Such models should empower adolescents to speak up for themselves having understood the concept of risks and benefits of participating in the research<sup>7</sup>.

There is a growing body of knowledge on how to conduct SRHR research among adolescents especially in the field of HIV/AIDS<sup>37-41</sup>. The US-based Adolescent Trial Network which explore HIV related issues in infected and HIV at-risk adolescents, age 12 through to 24years have examples of models for effectively engaging adolescents in the design and implementation of

research<sup>42-44</sup>. The South African based HIV in Adolescents (SASHA) project which recruited 12 to 17 year old adolescents over a 42 months period provide additional evidence<sup>45</sup>. As more studies on adolescents are conducted, we would learn more about how some of these ethical challenges were addressed, and what peculiar ethical concerns we need to deal with as we move into the future.

## Conclusion

Cultural sensitivity exists about open discussion about sex. The ethical dilemma of engaging adolescents in research in general, and SRHR research specifically, is also intertwined with ethics and regulatory issues. All these will make debates about the ethics of engagement of adolescents in SRHR research a major topical issue for a long time to come. The growing body of new research on SRHR which recruit adolescents would continue to provide the field with new insights on how to plan and implement adolescent focused SRH research in the most ethical and yet scientifically rigorous ways.

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## Contribution of Authors

MOF conceived the idea of the paper. BH, AH, of BB and MOF collected the papers needed for the writing of the manuscript, were both engaged in the preparation of the manuscript and gave final consent to its publication.

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