VOLUME 00 NO 00

Participation in medical research as a resource-seeking strategy in socio-economically vulnerable communities: call for research and action

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Abstract The freedom to consent to participate in medical research is a complex subject, particularly in socio-economically vulnerable communities, where numerous factors may limit the efficacy of the informed consent process. Informal consultation among members of the Switching the Poles Clinical Research Network coming from various sub-Saharan African countries, that is Burkina Faso, The Gambia, Rwanda, Ethiopia, the Democratic Republic of Congo (DRC) and Benin, seems to support the hypothesis that in socio-economical vulnerable communities with inadequate access to health care, the decision to participate in research is often taken irrespectively of the contents of the informed consent interview, and it is largely driven by the opportunity to access free or better quality care and other indirect benefits. Populations' vulnerability due to poverty and/or social exclusion should obviously not lead to exclusion from medical research, which is most often crucially needed to address their health problems. Nonetheless, to reduce the possibility of exploitation, there is the need to further investigate the complex links between socio-economical vulnerability, access to health care and individual freedom to decide on participation in medical research. This needs bringing together clinical researchers, social scientists and bioethicists in transdisciplinary collaborative research efforts that require the collective input from researchers, research sponsors and funders.

keywords research ethics, clinical trials, informed consent, developing countries, vulnerable populations, equity, health inequalities

Introduction

Ensuring free decision-making when deciding to be part of medical research is a complex subject, particularly in socio-economically vulnerable communities. For instance *comprehension*, one of the cornerstones of the consent procedure may be impaired by illiteracy (Chaisson *et al.* 2011), as well as by a lack of consideration for the local socio-cultural context when informing potential study subjects (Tekola *et al.* 2009; Bull *et al.* 2012; Vreeman *et al.* 2012). But in addition to the information provided during the consent process, other factors may influence people's decision to participate in research, possibly limiting the importance of the informed consent process.

In a recent anthropological study in a semiurban setting in Burkina Faso, Pare Toe *et al.* (2013) reported that

most parents of children enrolled in a malaria paediatric clinical study had taken the decision of participating before starting the informed consent process. Their individual decision was based on information that informally spread through the community and was mainly motivated by the possibility of accessing free and good quality health care during the study period.

The study raises the question whether this also occurs in other African contexts and trials and how these findings relate to potential risk in research participation and to free decision-making. We discussed this question within the Switching the Poles Clinical Research Network (http://www.itg.be/itg/GeneralSite/Default.aspx?L=E&WPID=705&MIID=670, last accessed on 17th August 2014; Tinto *et al.* 2013). This network brings together research institutions from South-East Asia, sub-Saharan Africa and Latin America, with the objective of developing clinical research policies that are compliant with appropriate ethical and methodological standards and that are feasible in resource-constrained settings and programmes. Since the start of the network's activities in 2008, the informed consent process in vulnerable populations was identified as a major challenge by all members, and this resulted in the Institut de Recherche en Science de la Santé (IRSS)/Centre Muraz (Burkina Faso) taking the lead on this topic and carrying out the above-mentioned study (Pare Toe *et al.* 2013).

Besides the IRSS/Centre Muraz, the institutions that participated in the discussion leading to this manuscript were the Medical Research Council Unit (The Gambia), Rinda Ubuzima (Rwanda), the Institute National de Recherche Biomédicale and the University of Kinshasa (DRC), the Centre de Recherches Entomologiques de Cotonou (Benin), the Addis Ababa University School of Public Health (Ethiopia) and the Institute of Tropical Medicine (Belgium).

Clinical research and access to medical benefits

All the participating researchers agreed that in settings with inadequate access to health care, the opportunity of receiving free medical care is often a strong incentive to participation in clinical studies and may result in 'pro-active strategies' for being recruited, independent of the researchers' best efforts to accurately inform potential participants and to underline the experimental nature of the study.

In The Gambia, for instance, exhaustive information about new trials is carefully 'cascaded' through the community hierarchy. The study is first introduced to the village heads (the '*Alkalo*'), who subsequently convey the information to household heads and religious leaders. Additional community sensitisation is organised to provide feedback on findings of previous studies, as well as to introduce the new trial (Afolabi *et al.* 2014). Nevertheless, mothers still actively seek to find out whether their children can be enrolled in any other trials, in order to increase their chances of obtaining the study-related benefits (such as better access to care).

During a study on family planning in Rwanda, women sought out the research site with the specific purpose of being recruited, even without having attended any information sessions in the community or even if knowing that they did not meet the inclusion criteria. The women's willingness to participate seemed to be independent of the detailed information they would later receive during the consent process, as enrolment allowed access to cervical cancer screening and to free testing and treatment for sexually transmitted infections.

In Ethiopia, researchers observed high levels of implicit expectation from research at personal and community level among residents in rural and socio-economically poor communities. In a recent qualitative assessment conducted in the rural area of Butajira, members of the community expressed their disappointment about a prospective cohort study, as part of the community felt excluded from the benefits allocated to the households included in the cohort, that is medical and school support for children. The project data collectors also iterated that poor rural households tended to consent to participate in the research more rapidly than those with higher socio-economic status.

During a prospective cohort clinical study conducted in lagoon area in Benin, (Nahum *et al.* 2007) many parents who had initially refused to consent for their children, at a later stage reported to the study team, volunteering for recruitment. The researchers observed that this change of attitude was linked to the wish to access the free care benefits provided to recruited children.

In such poor communities, besides the personal benefits, trial participation may be seen as an opportunity for other family members to access better health care. In a malaria study conducted in Kinshasa (Muhindo *et al.* 2013), for instance, some mothers reportedly attempted to obtain additional concomitant medications for recruited children, which in reality they intended to use for some of their sick but not recruited children. The view of the clinical study as a means to access to health benefits is echoed by the observations of researchers in the DRC, who reported a 'selective recall' of the informed consent information: many potential participants focused on the fact that the study team would take care of adverse events and medical problems occurring during the study, while they tended to ignore the

experimental nature and the potential risks attached. In addition, participants from socio-economically vulnerable communities, for example Kasaï province of DRC, are reported to decide on trial participation primarily or solely on the trust they place in their medical caregivers, that is nurses and doctors, believing they will always make the best individually tailored decision for them.

Beside the direct medical benefits, monetary reimbursements for the travel to the study clinic for scheduled and unscheduled study visits also are an incentive for trial participation, as observed by researchers in Burkina Faso, Rwanda, Benin, Ethiopia and DRC. In DRC, this also applied to the reimbursement of food expenses incurred during a study visit or the period of hospitalisation as part of the study. Researchers even noticed that some parents seemed unsatisfied when the trial team announced that their child had successfully completed the follow-up, potentially because of the end of the benefits. Noteworthy, these monetary reimbursements had been approved – and in some cases explicitly required – by the concerned Ethics Committees(s) that considered them fair, that is not representing an undue inducement. The researchers' observations, however, show that for individuals and families living in a disadvantaged socio-economic situation, they were still an incentive to participate. From this perspective, trial participation can be seen as a strategic choice based on a 'risk-benefit assessment' that goes beyond the purely medical and technical aspects of the research.

Informed consent in vulnerable communities: a way forward?

Overall, these anecdotal observations in different settings in sub-Saharan Africa seem to confirm that in socio-economically vulnerable communities, the decision to participate in research is often taken prior to and irrespectively of the contents of the informed consent interview, and it is largely driven by the opportunity to access free and/or better quality care and other indirect benefits.

Populations' vulnerability due to poverty and/or social exclusion should not lead to exclusion from medical research and, as such, research is most often crucially needed to address their specific health problems. The goal therefore is to strive for a balance between the risk of exploitation and the relevance of the research implemented in these populations (Ravinetto *et al.* 2013). To reduce the possibility of exploitation, explorative research is ongoing in our network, addressing certain challenges related to illiteracy and poor comprehension in the informed consent process, for example the development of multimedia tools for delivering the informed consent information (Afolabi *et al.* 2014), or of context-adapted assessments of understanding before confirming enrolment (Saidu *et al.* 2013; Afolabi *et al.* 2014). However, achieving full comprehension is essential but not sufficient to secure the freedom to decide, as in many contexts, the risks related to the research intervention –even if well explained and well understood – are overshadowed by the risk of not being included in the research and losing the related benefits. In other words, for these vulnerable communities, the study-related benefits (including, but not limited to, free access to quality health care during the study period) remain a strong incentive to study participation, irrespective of the accuracy of the informed consent procedure and despite other local cultural concerns (Peeters Grietens *et al.* 2014). As suggested, the participation in the trial becomes a pro-active strategic choice to secure otherwise unavailable health and non-health resources, and it is not necessarily based on poor comprehension of the study risks, but on a 'risk-benefit assessment' that takes into consideration factors other than those usually considered in the protocol design.

There is therefore the need to further investigate the complex links between socio-economical vulnerability, access to health care and individual freedom to decide on participation in medical research. This goes beyond the simple improvement of the informed consent procedure and requires an interdisciplinary approach that includes clinical researchers, social scientists and bioethicists, as well as the collective input from researchers, Ethics Committees, sponsors and funders.

Acknowledgements

This Switching the Poles Clinical Research Network is funded by the Belgian Directorate-General for Development Cooperation (DGD) under the Framework Agreement 3 (FA3) with the Institute of Tropical Medicine, Antwerp (Belgium).

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