DISCUSSION

# "Informing" and "consenting": ethical concerns regarding illiterate and vulnerable participants in clinical trials

**RAJAN DEWAR[1], VINITA PARKASH[2], LACHLAN FORROW[3]**

**[1]Assistant Professor, Department of Pathology, Member, Ethics Advisory Committee, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston MA, USA; Affiliate Faculty, Harvard Divinity School – Program in Science, Religion and Culture, Faculty, South Asia Institute, Harvard University, Cambridge, MA USA [2]Associate Professor, Department of Pathology, Yale University School of Medicine, New Haven, CT USA [3]Associate Professor of Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, past President, Hôpital Albert Schweitzer, Lambarene, Gabon; Member, Institutional Review Board, Dana Farber Harvard Cancer Center, Harvard Medical School, Boston, MA USA Author for correspondence: Rajan Dewar e-mail: rdewar@bidmc.harvard.edu**

We appreciate the article by Eric Suba (1), highlighting some inadequacies in trials comparing various methods of screening for cervical cancer. Our response pertains to his reference to the Office for Human Research Protections (OHRP) raising concerns about issues relating to informed consent. We wish to present our perspective on the process of "informing" and "consenting" vulnerable patients in low- and middle-income countries (LMICs).

We have seen in the course of our own work (RD and VP) in South India that many of the women receiving care attend the clinics with their children in their arms or poised on their hips. This, together with the fact that many have low literacy levels, means that in most cases, when consent is obtained, the woman merely listens while a social worker reads out the document and explains how the particular clinical test (for example, the Pap smear to screen for cervical cancer) will benefit her. The social worker then records that consent has been obtained for the test. In another resource-limited setting, the Lambarene region of Gabon, staff members of the Medical Research Unit of the Albert Schweitzer Hospital report that decisions to participate in research trials often appear to be based on expectations of a beneficial clinical caregiving relationship, rather than an appreciation of the risks and benefits described in the consent documents (2). A recent study has confirmed that the level of understanding of research subjects in sub-Saharan Africa has frequently been "poor", even when western methods and documents have apparently been applied carefully to obtain informed consent (3).

We find it extremely difficult to understand how the workers involved in the studies conducted by Shastri et al, or Sankaranarayanan et al, explained the risks and benefits of the different arms, as well as the process of randomisation to the women in these settings. We are also uncertain about what the women actually understood. We especially wonder how the women consented to participating in a no-treatment arm. Did the informed consent document explicitly state that "you will not have any tests done, just as you have never had any done till now and would not have any conducted in the future"? Women all over the world, including those who agree to participate in clinical trials and those who are illiterate or otherwise, are a generally intelligent, concerned and thinking lot when it comes to decisions on healthcare and family welfare. However, the pressures of the daily toil of rearing their families can lead them to become indifferent and disinterested in long-drawn explanations and discussions regarding risks and benefits. Under these circumstances, they tend to take a benefit-based view of the matter, harbouring the expectation that their well-being is paramount in a "care-taker–care-receiver" relationship.

We sincerely believe that the sacrosanct relationship between care-taker and caregiver is based on humanism and a deep respect, or even reverence – as Albert Schweitzer suggested – for each fellow human being. The existence of a signed document does not demonstrate that this respect was actually present. Serious problems have occurred in western countries too (the Tuskegee and Willowbrook studies are examples), and there have been shortcomings even after improved safeguards were put in place to address them (4). Given the trials highlighted by Dr Suba and the recent HPV vaccination trials, which were terminated abruptly in India (5,6), there is clearly an urgent need for LMICs to find ways to ensure that all persons invited to participate in a research trial are treated with full respect. Efforts must be made to ensure that their expectations of what participation means are accurate, and that their participation is truly informed and voluntary. We need further studies of the informed consent process in LMICs where trials are conducted and on the perspective of prospective research participants so as to be able to understand how to ensure this. The existence of signed documents is, by itself, inadequate to prove the existence of objective informed consent by the participants in a study or trial.

### *Statement of authorship*

*All the authors have contributed equally to this paper.*

*This article was published online on August 8, 2014, at ijme.in.*

**References**

1. Suba EJ, on behalf of the Viet/American Cervical Cancer Prevention Project. US-funded measurements of cervical cancer death rates in India: scientific and ethical concerns [Internet]. *Indian J Med Ethics.* 2014 Jul-Sep [cited 2014 Aug 5];11(3):167-75. Epub 2014 Apr 17. Available from: http://ijme.in/index.php/ijme/article/view/2072/4511
2. Agnandji ST, Tsassa V, Conzelmann C, Kohler C, Ehni HJ. Patterns of biomedical science production in a sub-Saharan research center [Internet]. *BMC Med Ethics*. 2012 [cited 2014 Jul 1];13:3. doi:

10.1186/1472-6939-13-3 Available from: http://www.biomedcentral.com/1472-6939/13/3
3. Afolabi MO, Okebe JU, McGrath N, Larson HJ, Bojang K, Chandramohan D. Informed consent comprehension in African research settings. *Trop Med Int Health*. 2014 June;19(6):625–42. doi: 10.1111/tmi.12288
4. Weinfurt KP, Seils DM, Lin L, Sulmasy DP, Astrow AP, Hurwitz HI, Cohen RB, Meropol NJ. Research participants' high expectations of benefit in early–phase oncology trials: are we asking the right question? *J Clin Oncol*. 2012 Dec 10;30(35): 4396–400. doi: 10.1200/JCO.2011.40.6587
5. Sengupta A, Shenoi A, Sarojini NB, Madhavi Y. Human papillomavirus vaccine trials in India. *Lancet*. 2011Feb 26; 377(9767):719. doi: 10.1016/S0140-6736(11)60270-5
6. Feinberg M. HPV vaccine suspension in India. *Lancet*. 2010 Nov 13;376(9753):1644–5. doi: 10.1016/S0140-6736(10)62094-6

# Assessing capabilities in India today and the role of "outside" opinions

**GITA JAYARAM[1], RAJAN DEWAR[2], RATNA RAMAN[3], SWAMINATHAN RAJENDIRAN[4], VINITA PARKASH[5]**

**[1]Consultant, Cancer Screening Program, Hindu Mission Hospital, Tiruchirapalli; Pathologist, Ramakrishna Diagnostic Center, Ooty 643 001, The Nilgiris, Tamil Nadu INDIA [2]Assistant Professor of Pathology, Harvard Medical School, Boston, MA, USA, Member, Ethics Advisory Committee, BIDMC, Affiliate Faculty, Harvard Divinity School, Cambridge, MA, USA [3]Department of Social Sciences, Delhi University, New Delhi INDIA [4] Professor of Pathology, Sri Ramachandra Medical College, Chennai, Tamil Nadu INDIA [5]Department of Pathology, Yale University School of Medicine, New Haven, CT, USA Author for correspondence: Rajan Dewar e-mail: rajan.dewar@gmail.com**

We have followed the exchange of comments between Dr Sankaranarayanan and Dr Suba (1–3) closely and with interest, but also with rising concern that this angry dialogue will eventually harm rather than benefit the goal to which both aspire (and have devoted considerable effort and time). We hope that the editors of this journal and both parties will agree to a period of cooling down, after which the discussions could be continued in an appropriate technical forum.

However, we wish to make two points. First, medical technologies and diagnostic capabilities are moving targets. While it is entirely reasonable to assess the applicability of techniques on the basis of pilot assessments and historical studies, it is becoming increasingly difficult to do so today. The speed of change in all aspects of the world, including technological advancements, communications and medical developments, is so fast now that technology which was current 10, or even five, years ago is obsolete today. A really long time ago, medical men diagnosed diabetes by tasting a sample of urine. Benedict's test, conducted mostly in specialised laboratories, was the technology in use when most of the authors were training as physicians. Now, a clinical test strip, which is used even in the remotest corners of Indian districts, can diagnose diabetes in a matter of minutes.

Judging the feasibility of cytology-based screening on the basis of assessments carried out 29 years ago (2) may not be entirely valid in the India of today. It is to be noted that the rejection of cytology as a screening measure is not based on the inherent characteristics of the test (demonstrated to unequivocally decrease the incidence of cervical cancer in western countries), but rather on perceived problems in implementation and possible challenges for "follow-up". The failure of patients to follow up, while more pronounced in LMIC countries, is a challenge that plagues all screening protocols, including those in the western world. It may be necessary to engage social scientists, engineers and communications experts to assess the reasons for the failure of patients to return for follow-up, and innovative solutions will have to be sought to address this issue.

The India of today is a technologically advanced society, which is moving progressively towards joining the leading powers of the world in a multitude of ways. India has shown the world that despite all adversities and a very large population, it has the brain-power and will power to provide cutting-edge technology and medical expertise. A case in point is Dr Sangeeta Desai, a renowned pathologist and leader in the field of molecular pathology, who has introduced high-quality molecular diagnostics in India (especially the HER-2/Neu FISH studies, which have changed the paradigm for the management of breast cancer in the country). India has produced leading cytopathologists, including the current President of the American Society of Cytopathology (4) (Ritu Nayar – proudly trained by one of us – GJ). In the light of the strides taken by the country, we hope that assessments of the utility of cytology screening programmes for cervical cancer will be based on the India of today, rather than the India of yesteryear. Our own pilot programmes, conducted for the local NGOs in Thirunelveli, Thanjavur and Tiruchirapalli, Tamil Nadu, indicate that high-quality cervical cytology laboratories can be established in India, at a manageable cost (less than a dollar/patient). We are also piloting an SMS-based messaging system to facilitate follow-up of patients who have tested positive.

Second, the 'foreign-ness' of a person (Dr Suba, in this case) making an argument does not, a priori, indicate that the argument is poor (2). Dr Suba has given shape to the Vietnamese cervical cancer screening project (5) and the experience on the basis of which he speaks is legitimate. In addition, looking in from the outside often helps to make opinions bias-free. External examiners in graduate and post-graduate examinations and doctoral defences serve a similar purpose. They are independent, form an unbiased opinion and are blinded to the candidate's inherent nature. Global health workers such as Paul Farmer(6), are external from a cultural standpoint, but their repeated visits and programmes have helped to generate workable, creative solutions to global health problems[1], as demonstrated in Haiti and Rwanda. At the same time, local physicians, investigators and workers on the ground are essential for finding solutions as they have an