

## EDITORIAL

**Cervical cancer screening trials in India and ethical issues**

Satyanarayana Labani, Smita Asthana

Division of Epidemiology &amp; Biostatistics, Institute of Cytology &amp; Preventive Oncology (ICMR), Noida

**Corresponding Author**

Address for Correspondence: Dr. L. Satyanarayana, 321, City view Apartments, Sector-35, Noida - 201301  
E Mail ID: satyanarayanalabani@yahoo.com

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Cervical cancer is a preventable disease with an annual global load of 528000 new cases and 266000 deaths, majority occurring in low resource countries (LRCs). The magnitude of the disease in India is with 123000 new cases and 67000 deaths every year [1]. Developing countries successfully implemented Pap smear based cervical cancer screening into public health services and achieved reduction in incidence and mortality. With lack of the infrastructural resource requirements and trained technical manpower, LRCs including India do not have current capacity to implement cytology based Pap screening. Several alternatives to Pap testing were extensively studied in observational study settings. Visual inspection with acetic acid (VIA) is considered to be effective alternative method to reduce the disease burden in LRCs. Studies are conducted in randomized trial settings to confirm whether a significant reduction in incidence and mortality can be achieved in a real programme settings.

Recently, some ethical issues raised on the conduct of three Indian cervical cancer screening trials [2]. In clinical research, the ethics is a practice of implementation of acceptable conditions for exposure of some individuals to risks and burdens for the benefit of society at large. The three randomized clinical trials of cervical screening that generated controversial discussions on ethics were from Mumbai [3,4], Osmanabad [5,6] and Tamil Nadu. [7,8] Essential points of debate in the trials under discussion were i) 254 cervical cancer deaths from unscreened control groups, ii) the study participants not given adequate information to provide informed consent, iii) unjustified use of unscreened control group by considering it as standard care and iv) why let people die in screening trials to something that had a known status.

The authors of the three Indian cervical screening trials refuted [9] the above said allegations and claimed these studies are of highest order of scientific and ethical merit with supporting justifications. On the issue of 254 deaths from cervical cancer from unscreened control group, authors describe it as a misuse of statistics in omitting the presentation of 208 deaths from cervical cancer in intervention group and stated that distortion incorrectly implied as the deaths of women was due to lack of treatment. Authors state that the persons who detected with advanced disease on screening are not possible to cure with treatment. The issue raised on informed consent was not agreed upon by authors as the study procedures followed standard methods and reviewed by national and international ethical boards. Regarding the issue of using unscreened group as control, authors state that even as per current standards, the use of placebo or no intervention is acceptable. On the need for conducting the trial, authors stated that when these trials were initiated in the year 2000, there was no evidence whether there would be an effective reduction in incidence and deaths on proposed screening approach and said the conduct of such screening trials was crucial before evolving a public health prevention programme.

The randomized trials are studies of highest strength as compared to observational studies in the confirmation of public health epidemiological evidence. There are a number of observational studies in the evaluation of performance of various cervical screening methods such VIA, Pap smear, Human papillomavirus (HPV). It is simply not possible till date in India to have a country wide Pap smear screening for the known reasons including resources, manpower and quality control. After many years of

non-existence of organized cervical cancer screening programme, the decision to implement and adopt a district level VIA cervical screening in the state of Tamil Nadu and later Sikkim state in India was taken up only after the knowledge from the present trials. It is still not sure whether these VIA pilot demonstrations provide a recommendation that can lead to a country wide public health integrated screening programme. The final findings of implementation programme of Tamil Nadu, and Sikkim should be awaited.

Of course, the definition of ‘no screening’ as a standard care is little un-digestible on its face and it’s most likely to come across the confusions of the type equipoise in a randomized trial setting. It appears there was a thorough scrutiny by national and International review boards and at the time of initiating the trial or even today in India, the practice for cervical cancer is the treatment of symptomatic women when they sought medical attention. Cervical cancer incidence and deaths reported in the annual statistics are due to absence of screening for women at risk of getting cervical cancer. In the strict sense of randomized trial comparisons of study interventions with “no screening” control group may not equalize benefit between groups. The clearances from the high standard ethical boards and publications of trial findings in reputed high level scientific journals indicate presence of allowable considerations at the designing stage to initiate such trials. However, when the benefit of randomized trial interpretations and implications are to be consumed from such future trials, then the choice of sound ethically acceptable option for selecting control group is essential. Interim and post study corrections in randomized trials must be incorporated when necessary.

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