

LETTER TO THE EDITOR

Outcome of the randomized control screening trials on oral, cervix and breast cancer from India and way forward in COVID-19 pandemic situation

Dear Editor,

Indian researchers have conducted the randomized control screening trials on oral, cervix and breast cancers in different locations of India.¹⁻⁵ These screening procedures were both simple and inexpensive. The outcomes of the trials were published in the high impact journals. Implementation and execution of these randomized control screening trials in Indian setup was a challenging task.

According to the oral cancer screening trials, performing three rounds of visual inspection of the oral cavity will prevent at least 37 000 deaths worldwide.¹ Visual examination of the cervix following the application of 3% to 5% acetic (VIA) acid in one-time screening for cervix cancer revealed a 35% reduction in mortality (0.65 95% confidence interval [CI] [0.47-0.89]) when compared to the control arm.² After four rounds of screening in the Mumbai VIA trial, it was reported that using the VIA screening test as a screening tool may avoid 22 000 cervical cancer

deaths and 72 600 deaths in countries with poor resources each year.⁴ When a single round of cervical cancer screening using human papillomavirus (HPV) testing was conducted in the Osmanabad district, the results revealed a substantial reduction in the rate of advanced cervical cancers and related fatalities when compared to the control group.³ Furthermore, according to the Mumbai breast cancer screening trials, clinical breast examination by trained primary health care workers in four rounds resulted in nearly 30% reduction in mortality (0.71 95% CI [0.54-0.94]) among women aged ≥ 50 years.⁵

There were 80 654 women involved in the VIA study from Tamil Nadu,² 151 538 women in the Mumbai study for cervical and breast screening,^{4,5} 131 746 women in the cervical cancer screening by HPV testing, cytologic testing and VIA³ and 191 873 people in the oral cancer screening trial.¹ This sample size includes both intervention and control arms. All together more than half million people were involved

TABLE 1 Randomized control screening trials on oral, cervix and breast cancers conducted in India

Publication	1	2	3	4	5
Location	Trivandrum District, Kerala, India	Dindigul District, Tamil Nadu, India	Osmanabad District, Maharashtra, India	Mumbai, Maharashtra, India	Mumbai, Maharashtra, India
Screening test	Oral visual inspection	VIA screening	HPV testing, Cytology and VIA screening	VIA screening	Clinical Breast Examination
Provider	Trained Health workers	Trained Nurses	Trained Auxiliary nurse midwives	Primary Health workers	Trained female primary health workers
Sample size	191 873	80 654	131 746	151 538	151 538
Screening round	3	1	1	4	4
Surveillance	Trivendrum PBCR, HBCR of RCC, source visits and household visits	Dindigul district PBCR, Medical records, Source visits, Household visits by registry staff	District death-registration offices, hospital records, annual home visits by Barshi registry staff	Primarily through door to door visits and later cross checked the data with Mumbai Cancer Registry	Primarily through home visits and later cross checked the data with Mumbai Cancer Registry
Outcome	34% reduction in the mortality in tobacco or alcohol users (0.66 95% CI [0.45-0.95])	35% Reduction in the cervical cancer mortality (0.65 95% CI [0.47-0.89])	53% significant reduction in rate of advanced cervical cancer (0.47 95% CI [0.32-0.69]) and 48% reduction in associated mortality in HPV testing group (0.52 95% CI [0.33-0.83])	31% reduction in Mortality in the screening group (0.69 95% CI [0.54-0.88])	Nearly 30% reduction in mortality in women ≥ 50 and older (0.71 95% CI [0.54-0.94])

Abbreviations: CI, confidence interval; HBCR, Hospital Based Cancer Registry; HPV, human papillomavirus; PBCR, Population Based Cancer Registry; RCC, Regional Cancer Centre; VIA, visual inspection with acetic acid.

in these trials. Table 1 summarizes the details of these trials. There is strong evidence from these randomized control screening trials that we can prevent the deaths from oral, cervix and breast cancer by implementing simple screening tests.¹⁻⁵ The Population-Based Cancer Registry (PBCR) of the respected locations of the screening trials has played an important role in providing incidence and mortality data to the randomized control screening trials.¹⁻⁵




There are several challenges in implementing screening/early detection programs for these cancers in COVID-19 pandemic. The program managers of the screening programs must adjust their practises to simultaneously safeguard the people from COVID-19 and also prevent these cancers. To combat this, we may need to employ alternative methods such as self-sampling for HPV,^{6,7} self-breast examination and self-oral inspection. The program administrators should use print, social media and television campaigns, to raise awareness of self-sampling of HPV, self-breast examination and oral examination. The collection of self-samples can be done with the assistance of a health workers. In Indian setup, health workers plays an important role in cancer prevention activities.⁸ The community must be trained to send images of suspected breast and oral premalignant lesions to the program manager using the mobile phone, who can further facilitate the diagnosis and treatment for the people who have tested screen positive.

The government of India has started the screening program for cervix, breast and oral cancers in different parts of India.⁹ The current system should ensure that screen positive cases are diagnosed and treated. Not only is the screening test a crucial part of the randomized trial, but it also provides easy access to diagnosis and treatment for screen positive cases. All randomized control trials have demonstrated a decline in mortality as a result of a good referral system for diagnosis and effective treatment. The expertise gained by the Indian researchers must be used for capacity building and developing infrastructure in low-resource settings for early detection of breast, cervix and oral cancer.

Countries with a high burden of oral, breast and cervix cancers, along with a population-based cancer registry, a good referral system of diagnosis and treatment, trained human resources and financial sustainability, can implement the screening programs. According to the reports, low- and middle-income countries have lot of limitations in implementing screening programs, so they should focus and prioritize early detection programs. The early detection program mainly focuses on raising awareness about cancer symptoms and making diagnosis and treatment more accessible for symptomatic cases.¹⁰ Policymakers must be made aware of the importance of utilizing these evidence of the randomized controlled trials to control oral, breast and cervical cancers, as well as the need to organise preventative activities in light of the COVID-19 pandemic.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

Atul M. Budukh 
 Rajesh Dikshit 
 Pankaj Chaturvedi 

Centre for Cancer Epidemiology, Tata Memorial Centre, Homi Bhabha National Institute, Mumbai, India

Correspondence

Atul M. Budukh, Centre for Cancer Epidemiology, Tata Memorial Centre, Homi Bhabha National Institute, Mumbai, India.
 Email: budukham@tmc.gov.in

ORCID

Atul M. Budukh  <https://orcid.org/0000-0001-6723-802X>
 Rajesh Dikshit  <https://orcid.org/0000-0003-4830-0486>
 Pankaj Chaturvedi  <https://orcid.org/0000-0002-3520-1342>

REFERENCES

1. Sankaranarayanan R, Ramadas K, Thomas G, et al. Effect of screening on oral cancer mortality in Kerala, India: a cluster-randomised controlled trial. *Lancet*. 2005;365(9475):1927-1933. [https://doi.org/10.1016/S0140-6736\(05\)66658-5](https://doi.org/10.1016/S0140-6736(05)66658-5) PMID: 15936419.
2. Sankaranarayanan R, Esmey PO, Rajkumar R, et al. Effect of visual screening on cervical cancer incidence and mortality in Tamil Nadu, India: a cluster-randomised trial. *Lancet*. 2007;370(9585):398-406. [https://doi.org/10.1016/S0140-6736\(07\)61195-7](https://doi.org/10.1016/S0140-6736(07)61195-7) PMID: 17679017.
3. Sankaranarayanan R, Nene BM, Shastri SS, et al. HPV screening for cervical cancer in rural India. *N Engl J Med*. 2009;360(14):1385-1394. <https://doi.org/10.1056/NEJMoa0808516> PMID: 19339719.
4. Shastri SS, Mitra I, Mishra GA, et al. Effect of VIA screening by primary health workers: randomized controlled study in Mumbai, India. *J Natl Cancer Inst*. 2014;106(3):dju009. <https://doi.org/10.1093/jnci/dju009> Epub 2014 Feb 22. PMID: 24563518; PMCID: PMC3982783.
5. Mitra I, Mishra GA, Dikshit RP, et al. Effect of screening by clinical breast examination on breast cancer incidence and mortality after 20 years: prospective, cluster randomised controlled trial in Mumbai. *BMJ*. 2021;372:n256. <https://doi.org/10.1136/bmj.n256>.
6. WHO Recommendations on Self Care Interventions: Human Papillomavirus (HPV) Self-Sampling as Part of Cervical Cancer Screening. Geneva: World Health Organization; 2020 Licence: CC BY-NC-SA 3.0 IGO. <https://www.who.int/publications/i/item/WHO-SRH-2012>.
7. Polman NJ, Ebisch RMF, Heideman DAM, et al. Performance of human papillomavirus testing on self-collected versus clinician-collected samples for the detection of cervical intraepithelial neoplasia of grade 2 or worse: a randomised, paired screen-positive, non-inferiority trial. *Lancet Oncol*. 2019;20(2):229-238. [https://doi.org/10.1016/S1470-2045\(18\)30763-0](https://doi.org/10.1016/S1470-2045(18)30763-0) Epub 2019 Jan 15. PMID: 30658933.
8. Budukh A, Maheshwari A, Bagal S, et al. Factors influencing women to participate in cervical cancer screening by providing menstrual pads: A population-based study from rural areas of Maharashtra state, India. *Indian Journal of Cancer*. 2021. https://doi.org/10.4103/ijc.ijc_910_19.
9. Ministry of Health and Family welfare Government of India. Operational framework: Management of common cancers. 2016. <http://nhsrcindia.org/sites/default/files/Operational%20Framework%20Management%20of%20Common%20Cancers.pdf>. Accessed June 5, 2021.
10. WHO Report on Cancer: Setting Priorities, Investing Wisely and Providing Care for All. Geneva: World Health Organization; 2020 Licence: CC BY-NC-SA 3.0 IGO. <https://www.who.int/publications/i/item/who-report-on-cancer-setting-priorities-investing-wisely-and-providing-care-for-all>. Accessed June 7, 2021.