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## Why cervical self-sampling can aid radiotherapy in India in the COVID-19 era

### 1. Elimination of cervical cancer as a public health problem

In order to improve global health, the United Nations sustainable development goals intend to achieve a one-third reduction in premature mortality from non-communicable diseases by 2030 [1]. Cervical cancer is the fourth most common cancer in women, and continues to be a major health problem in low-middle income countries (LMICs). As cervical cancer is both curable and preventable, the World Health Assembly called for its elimination as a public health problem in the first ever initiative for eliminating a cancer worldwide [2]. Although screening plays a vital role in achieving this goal, screening services have been affected considerably during the Coronavirus disease 2019 (COVID-19) pandemic [3]. In particular, screening services have come to a halt in LMICs, which are the major contributors to global mortality from the disease.

### 2. Screening- benefits of self-sampling

Traditionally, screening for cervical cancer has involved visits to healthcare facilities for Pap smears, visual inspection with acetic acid, and clinician-collected human papilloma virus (HPV) testing. HPV testing offers certain advantages: it is more accurate than the Pap test, it can be performed less frequently, and a negative HPV test result is associated with a low risk of cervical cancer. Studies have demonstrated that the accuracy of test results using self-collected and clinician-collected HPV samples are equivalent; reports also suggest that combined self-sampling with Pap smears in HPV positive cases is superior to a Pap smear alone in detecting precancerous lesions.

In a systematic review and meta-analysis including 33 studies (29 randomized controlled trials and 4 observational studies with approximately 369,000 participants in total), that was performed to inform the World Health Organization (WHO) self-care guidelines [4], combined meta-analysis suggested that women who performed self-sampling were twice as likely to accept HPV screening compared to those who received clinician-collected screening. Acceptance was particularly higher in cases where the self-sampling kits were mailed directly to participants' homes or delivered door-to-door by a health worker. The findings therefore indicate that incorporation of HPV self-sampling in cervical cancer screening can increase screening uptake compared with standard of care; this may help achieve 70% global screening coverage by 2030. The WHO therefore recommends self-sampling as part of cervical cancer screening [5]. Although a high proportion of participants in the meta-analysis were from high-income countries, the benefits of HPV

self-screening in the prevention of cervical cancer-related deaths in LMICs are being increasingly recognized [6].

### 3. Cervical cancer problem in India – Impact of the COVID-19 pandemic

Among the LMICs, India alone contributes to nearly a third of cervix cancer related deaths worldwide; the country also recorded the highest number of global deaths from the disease in 2018. Recent National Cancer Registry Programme data from India indicate that cervical cancer continues to be mostly present in locally advanced stages, and chemo-radiation is the most common treatment administered [7]. In view of the vast population, inadequate treatment capacity, difficulties in healthcare accessibility, and considerable levels of financial toxicity among patients, the impact of the pandemic on cancer care is expected to have far-reaching consequences in this nation. A study that assessed lifetime health outcomes in the population at risk for cervical cancer in India during the COVID-19 pandemic, suggested that delays in diagnosis and treatment are likely to increase the risk of death from the disease. The authors estimated that healthcare disruptions during the pandemic would lead to a higher number of deaths from cervical cancer than those averted from COVID-19 [8].

### 4. Radiotherapy availability in India

As in many other low- and middle-income countries, radiotherapy capacity is inadequate in India; accessibility issues also reduce treatment compliance, leading to poor outcomes. Clinicians struggle to deliver timely treatment, as radiotherapy units are characteristically overburdened. In addition, centers delivering conformal radiotherapy are markedly inadequate, and teletherapy units are mostly located in urban areas, particularly reducing accessibility for rural women; this has considerable impact on treatment compliance. Brachytherapy, an essential component of radiation therapy for locally advanced cervical cancer, is only available at select urban facilities, sometimes making accessibility a greater challenge than for teletherapy. Data from a working paper evaluating cancer care under the National Health Protection Scheme funded by the Government of India indicate the urgent need for increasing availability of radiotherapy services nationwide; the paper also suggests the need for significant upgradation of existing radiotherapy facilities by incorporating more advanced technology.

Pelvic radiotherapy, and brachytherapy in particular, is resource-intensive and places a considerable burden on existing radiotherapy

facilities. In addition, as locoregional control is poorer in locally advanced stages, many patients require salvage and palliative treatment, further increasing the burden on the low-resource healthcare system. Although screening is key to addressing the cervical cancer problem in this scenario, the COVID-19 pandemic has caused major disruptions in screening services in India, and many patients in the community are waiting for a diagnosis [9]. In the absence of urgent measures, the post-pandemic surge in the need for radiotherapy is likely to overwhelm existing radiation oncology services, with wide-ranging consequences.

### 5. Why self-sampling needs to be promoted urgently

Reports have shown that HPV self-screening is more acceptable for most women as hospital visits are not required, and privacy is respected. These issues are particularly relevant in India, where most at-risk women live in diverse rural communities. Low literacy rates, poor understanding of screening benefits, and social and cultural barriers are some of the major factors that hinder efforts for widespread screening coverage. The disruption to healthcare services caused by the pandemic has further worsened the existing scenario, paving the way for a post-pandemic surge of cervical cancer cases. In view of the existing weaknesses of the healthcare system, this is expected to overwhelm cancer care facilities. Allowing early cases to go undetected will therefore lead to an unprecedented increase in cancer mortality in the coming years.

### 6. Why it may be possible in India

Studies indicate that HPV self-screening entails lower costs compared to clinic-based screening, and allows for a lower screening frequency [10]. These issues are particularly relevant in the Indian context, where access is restricted to many remote and rural areas with a high incidence of cervical cancer. In view of limited community health worker availability at this time, providing self-sampling kits to all eligible women on a door-to-door basis may not be feasible. Nevertheless, it may still be possible to continue opportunistic screening at all levels, and spread awareness regarding HPV self-testing at the time of COVID-19 vaccination; willing eligible women may also be provided with self-sampling kits at that time.

HPV testing offers greater sensitivity in detecting precancerous lesions when combined with Pap smears; this entails a greater workload on existing cytology services. However, this should not be a major limitation as initiatives for incorporating artificial intelligence-based diagnostics are already underway in India; the processing of larger sample numbers arising from additional confirmatory examination is therefore becoming more feasible than in the past.

It is therefore essential that in addition to health promotion, efforts are made to increase the availability of HPV self-sampling kits; it will also be necessary to ensure that women are educated on their appropriate use.

### 7. Implementation of the strategy

Owing to the limited infrastructure and funding available for cancer screening, it is essential for the strategy to be implemented in a phased manner. The National Rural Health Mission has designated trained female community health activists (ASHA workers) to act as healthcare mobilizers; they are also key motivators for cervical cancer screening. It will therefore be possible to spread awareness on the benefits of self-screening and HPV testing, and to demonstrate the procedure of sample collection. As many rural women in India are illiterate, it will be

necessary to provide ASHA workers with appropriate visual aids to improve understanding on the procedure.

### 8. Cost implications

Data from a report on the cost-effectiveness of camp-based screening in India indicate that 5-yearly HPV testing would involve approximately 1.2-fold higher expenditure than 3-yearly visual inspection with acetic acid, owing to higher costs related to laboratory equipment and sample transportation [11]. Notably, the analysis assumed that sample collection and visual inspection would be performed by a trained health worker under the supervision of a medical officer. As human resources and organization contribute to over 40% of the expenditure involved in camp-based screening [11], self-sampling could offset some of the costs.

### 9. Impact on radiotherapy services

Although higher detection may increase the number of diagnosed cervical cancer cases, presentation at an earlier stage may reduce the burden on radiotherapy services. Patients diagnosed in early stages may be treated surgically, if eligible. Among those requiring definitive chemoradiation, presentation before involvement of the pelvic wall or adjoining structures may improve prognosis, thereby reducing the need for salvage or palliative radiotherapy. The need for interstitial brachytherapy, which is mostly required for cases with distal vaginal involvement, bulky tumors with poor response to external beam radiation, and recurrent disease, may also be reduced in cases detected earlier.

Despite difficulties caused by the pandemic, prudent coordination and planning may prevent a tsunami of cervical cancer in India, thereby helping radiotherapy services offer timely care to the vast population. This will in turn help meet the goals of the WHO within the planned timeframe.

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### Competing interests

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