



Cervical Cancer

Challenges in Cervical Cancer Prevention: Real-World Scenario in India

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Abstract



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Keywords

- ▶ HPV
- ▶ vaccination
- ▶ public health
- ▶ VILI
- ▶ VIA

In spite of global falling trends, cervical cancer remains a major healthcare challenge for India, South Asia Association for Regional Cooperation region, and other low- and middle-income countries. Our survey was to document the real-world challenges that still exist in India. A total of 316 eligible and complete responses to the 21 questions were analyzed. Screening of mothers and vaccinating their daughters was considered as the most important strategy to prevent cervical cancer by 65.8% (208/316). Screening was offered to all asymptomatic eligible females by 79% (250/316). Improvement in screening rates requires promoting the national program (67.7%; 214/316), strengthening existing infrastructure (62%; 196/316), regular training of primary healthcare workers (57.6%; 182/316), and increasing awareness among schools and colleges (57.9%; 183/316). Almost all responders (93%; 294/316) wanted to have human papillomavirus (HPV) vaccination included in the national immunization schedule. Cost of vaccine was considered a major roadblock. If it became available at INR 250 per dose, 96.8% (306/316) respondents would recommend it for all eligible patients. With the impending availability of this indigenous tetravalent HPV vaccine jointly produced by Department of Biotechnology, Govt of India and Serum Institute of India, the war against cervical cancer just got easier.

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Introduction

Cervical cancer, a preventable and treatable disease, is still a leading cause of mortality among women in developing countries. Global disparities for this disease are unmatched. Almost 84% of all new cases and 88% of mortality occur in resource-limited countries; a figure that is two to four times higher as compared with high-resource countries.¹ As per GLOBOCAN 2020 statistics, 1,23,907 new cases were diagnosed and 77,348 lost their lives in India alone.² So far, the various attempts in tackling this public health problem through screening and vaccination have been discouraging in developing countries. To make an impact, it is important to understand the barriers faced at each level and implement a focused strategy. This study was conducted with the aim of understanding the challenges faced by doctors in India in this fight against cervical cancer. We hoped it would allow us to strengthen our cervical cancer screening and make the human papillomavirus (HPV) vaccination program more robust.

Materials and Methods

We conducted a nationwide online survey among healthcare professional that are involved in care of cervical cancer patients or whose practice included women who might be at risk of cervical cancer. The multiple-choice questionnaire included 21 questions (→Table 1) to understand the real-world problems faced by these professionals and was designed using google docs (<https://docs.google.com>) as previously reported by us.³ The survey links were shared through WhatsApp groups and email links of various national professional bodies. Responses were collected between January 12 and January 15, 2023. All duplicate, incomplete, and redundant replies were deleted before analysis. The eligible responses were then tabulated and analyzed; the results of which are presented below.

Results

A total of 367 healthcare professionals responded of which 316 were eligible for analysis (clinicians from India whose practice included cervical cancer patients).

Question 1: On November 17, 2020, the World Health Assembly (WHA) announced its target by 2030 of screening 70% of women using a high-performance test by the age of 35, and again by the age of 45.⁴ The largest group (41%; 130/316) of our responders believe that under current prevailing conditions, there was a 51 to 75% chance of achieving this World Health Organization (WHO) target (→Fig. 1).

Question 2: The global burden of disease 2019 study shows that in India, incidence of cervical cancer declined by 21% from 1990 to 2019. Also, the mortality due to cervical cancer has reduced by 32% in the same period. The decline was not uniform over time across various

Table 1 Survey multiple-choice questionnaire

| |
|---|
| 1. On November 17, 2020, the World Health Assembly (WHA) announced its target by 2030 of screening 70% of women using a high-performance test by the age of 35, and again by the age of 45. Current screening rate in India is less than 30%. In your opinion, what are the chances of achieving this in India? |
| a) 76–100% |
| b) 51–75% |
| c) 26–50% |
| d) 25% or less |
| 2. The Global Burden of Disease 2019 study shows that in India, incidence of cervical cancer has declined by 21% from 1990 to 2019. Also, the mortality due to cervical cancer has reduced by 32% in the same period. Do you see a similar reduction in incidence and mortality in your practice? |
| a) Yes |
| b) No |
| 3. What do you think is the cause for decline in cervical cancer rates? |
| a) Increased awareness and hence increased screening |
| b) Increased vaccination |
| c) Higher number of hysterectomies |
| d) Less reporting |
| 4. What do you think is most important to prevent cervical cancer? |
| a) Screening for all females |
| b) Vaccination for all girls |
| c) Screen all mothers and vaccinate their daughters |
| d) safe sexual practices |
| 5. When do you recommend cervical cancer screening to eligible women in your outpatient department? |
| a) To all asymptomatic eligible patients |
| b) To all symptomatic eligible patients |
| c) Only to those who specifically ask for it |
| d) Only to high-risk women |
| 6. Which test do you recommend for cervical cancer screening in eligible patients? |
| a) Human papillomavirus (HPV) DNA and cytology |
| b) Cytology alone |
| c) HPV DNA alone |
| d) Visual inspection with acetic acid/ visual inspection with Lugol's iodine (VIA/VILI) |
| 7. Department of Health Research released a Health Technology Assessment for early diagnosis of cervical cancer. It concluded that among various screening strategies, VIA every 5 years is the most cost-effective screening method in the context of India. As a clinician how confident are you in performing VIA/VILI for your patients routinely |
| a) I am not aware about it |
| b) Need some training |

Table 1 (Continued)

| |
|---|
| c) Well versed with technique but do not do it routinely for my patients |
| d) Well versed with technique and do it routinely |
| 8. What do you think is the most important barrier (from the doctors' point of view) in the real-world practice in recommending cervical cancer screening test? |
| a) Lack of awareness among clinicians about need of test/ who are eligible women |
| b) Time constraints |
| c) Cost of the test |
| d) Not sure which is the most appropriate test |
| 9. When the test is recommended, how receptive are your eligible patients in getting the test done? |
| a) 76–100% |
| b) 51–75% |
| c) 26–50% |
| d) 25% or less |
| 10. What do you think is the most important barrier (from patient point of view) in getting the test done |
| a) Asymptomatic, so don't want to get tested |
| b) Fear of pain and discomfort |
| c) Feeling shy/embarrassed—so not willing for examination |
| d) Fear about being diagnosed with cancer |
| e) Cost |
| f) lack of easy availability of test |
| 11. As a doctor how do you think you can help in removing patient-related barriers? How to increase awareness among general public for cervical cancer screening (select as many as applicable) |
| a) Creating awareness about myths and facts in schools/teenagers |
| b) Creating awareness about myths and facts among parents |
| c) Social media promotion |
| d) Appropriate counselling to individuals |
| 12. Do you think our country has enough facilities in public and private sector offering cervical cancer screening tests? |
| a) Yes |
| b) No |
| 13. What steps should govt take to improve screening rates in our country (select all that apply)? |
| a) Promote National Cervical Cancer Screening Program |
| b) Strengthen infrastructure for existing screening programs |
| c) Train primary health workers |
| d) Enhance focus on schools/colleges |
| 14. Along with screening, treatment of screen detected lesions is equally important. What method do you follow after screening? |

(Continued)

Table 1 (Continued)

| |
|---|
| a) Screen and treat approach in single visit |
| b) Screen, triage, and treat (treatment based on second test after first screen positive) |
| c) Based on patient profile and willingness to follow |
| d) Based on infrastructure available |
| 15. The World Health Organization 2030 call for elimination of cervical cancers targets fully vaccinating 90% girls by 15 years of age with two doses of HPV vaccine. In your opinion, what are the chances of achieving this in India? |
| a) 76–100% |
| b) 51–75% |
| c) 26–50% |
| d) 25% or less |
| 16. In your practice how often do you recommend HPV vaccine? |
| a) Offered to females who ask for it |
| b) Offer to all females irrespective of age |
| c) All females between 10 and 26 years |
| d) All females between 10 and 45 years |
| e) I am not much in favor, so discourage |
| 17. Do you think boys should also be vaccinated for HPV? Only eligible girls |
| a) Not required |
| b) Required to increase herd immunity |
| c) Required to protect boys from HPV-related diseases |
| d) No, as it will decrease vaccination rates in females as in our society priority will be given to males |
| 18. Do you think cervical cancer vaccination should be included in national Immunization schedule? |
| a) Yes |
| b) No |
| 19. State of Sikkim has completely vaccinated (with HPV vaccine) all their girls in the age group of 9 to 14 years. What do you think are the barriers in replicating this across India? |
| a) Lack of sufficient long-term safety data |
| b) Risk of potentially serious side effects |
| c) High cost |
| d) Sociocultural |
| e) Lack of healthcare infrastructure |
| 20. If HPV vaccine is made available in India at Rs 250 per dose, would you recommend to all eligible patients? |
| a) Yes |
| b) No |
| 21. Do you think if we are able to vaccinate majority of the girls with HPV vaccine, we can avoid screening strategies in future? |
| a) Yes |
| b) No |

316 responses

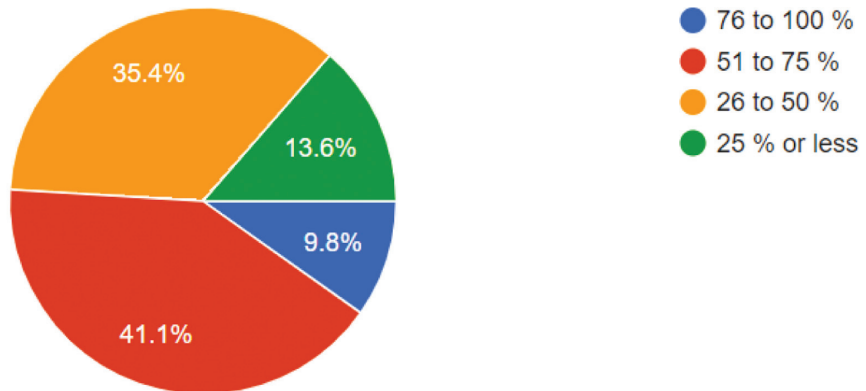


Fig. 1 Response analysis of question 1: On November 17, 2020, the World Health Assembly (WHA) announced its target by 2030 of screening 70% of women using a high-performance test by the age of 35, and again by the age of 45. Current screening rate in India is less than 30%. In your opinion, what are the chances of achieving this in India?

states with highest decrement seen in the state of Jharkhand.⁵ In the real world, majority of the professionals (75%; 237/316) have seen a fall in incidence and mortality in their clinical practice.

Question 3: A total of 67.4% (213/316) of responders believe that increased awareness among general public and wider acceptability of cervical screening is the most important cause of fall in cervical cancer incidence. This has specifically been seen in urban population. A significant portion of responders (13.3%; 42/316) were of opinion that increases in number of hysterectomies also contributed to this fall (–Fig. 2).

Question 4: Screening the mothers and vaccinating eligible daughters are considered by majority (65.8%; 208/316) as the most important strategy for preventing cervical cancer. Other options selected were screening of all women (15.5%; 49/316), vaccination of all girls (13.9%; 44/316), or following safe sexual practices (4.1%; 13/316). Question 5: Majority of clinicians (79%; 250/316) offered screening to all asymptomatic eligible females. Another

11.1% (35/316) were offering screening to symptomatic females. Smaller fractions offered screening to high-risk females (4.1%; 13/316) and to those who specifically asked for it (3.5%; 11/316).

Question 6: For screening, 55.4% (175/316) offered both HPV and cytology as the primary test. Cytology alone was being used by 26.9% (85/316). Smaller fractions used HPV DNA alone, visual inspection with Lugol's iodine/visual inspection with acetic acid (VILI/VIA), or none of these options (–Fig. 3).

Question 7: Department of Health Research released a Health Technology Assessment for early diagnosis of cervical cancer. It concluded that among various screening strategies, VIA every 5 years is the most cost-effective screening method in the context of India.⁶ In real world, the preferences were highly variable among doctors in India. Maximum doctors (30.7%; 97/316) were well trained in VIA/VILI but did not routinely apply it. There was almost equal distribution between those who wanted to get trained in VIA/VILI

316 responses

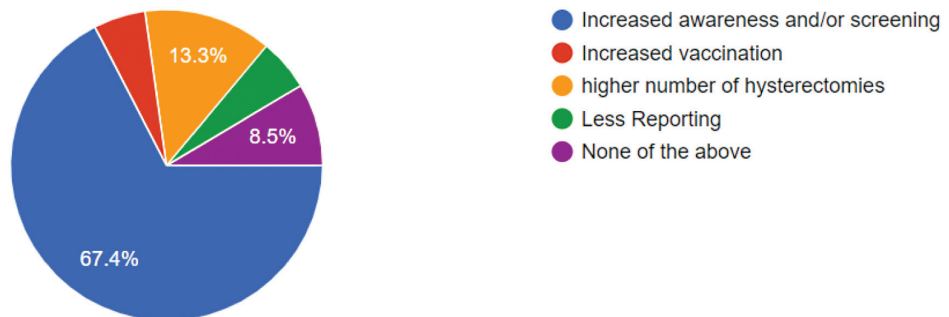


Fig. 2 Response analysis of question 3: What do you think is the cause for decline in cervical cancer rates?

316 responses

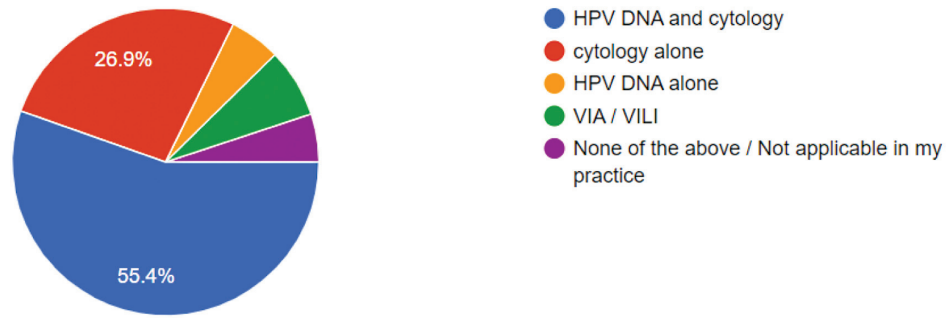


Fig. 3 Response analysis of question 6: Which test do you recommend for cervical cancer screening in eligible patients?

(25.3%; 80/316) and those who actually used their training routinely (22.2% (70/316)). A smaller but significant percentage (21.8%; 62/316) did not believe in this approach/ methodology.

Question 8: The most important barrier in better implementation of cervical cancer screening programs in India was attributed to lack of clarity among colleagues regarding the need for testing or its eligibility criteria (51.6%; 163/316) (→ Fig. 4). The second most common deterrent was the cost of the test (25.9%; 82/316). Other barriers included time constraints (17.7%; 56/316) and not being sure about the most important test (4.7%; 15/316).

Question 9: When the test is recommended, receptiveness of patients was between 51 and 75% (35.1%; 111/316). Only 12% (38/316) experienced less than 25% of their patients willing to undergo testing.

Question 10: The most important barrier in screening tests for cervical cancer was females not wanting to be tested because they were asymptomatic (43.3%; 137/316) (→ Fig. 5). Another 20.6% (65/316) did not want to undergo test because of being shy or embarrassed. The third most common reason was the fear of being detected to have cancer (10.4%; 33/316).

Question 11: Suggested remedy for overcoming barriers included creating awareness about myths and facts about cancer screening and vaccination in schools/among teenagers (68.45; 216/316), doing the same among parents (55.5%; 176/316), by use of social media promotion (53.8%; 170/316), or by appropriate counselling of individuals (49.4%; 156/316).

Question 12: Responders were equally divided when asked the question about adequacy of screening facility in public and private sectors, while 50.3% (159/316) did not agree, and 49.7% (157/316) agreed.

Question 13: Suggestions to improve screening rates in government programs included promoting national cervical cancer screening program (67.7%; 214/316), strengthening infrastructure for existing screening programs (62%; 196/316), training of primary healthcare workers (57.6%; 182/316), and enhancing awareness in schools and colleges (57.9%; 183/316).

Question 14: Regarding treatment strategy along with screening, 59.5% (188/316) followed screen, triage, and treat method, 19.9% (63/316) tailored the strategy to fit individual patient preference, 13.6% (43/316) opted to screen and treat in a single visit, and 7% (22/316) would follow whatever was possible based on the infrastructure available.

316 responses

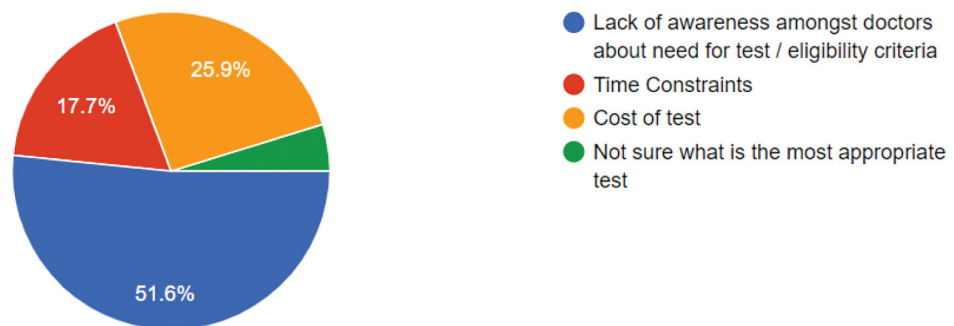


Fig. 4 Response analysis of question 8 : What do you think is the most important barrier (from the doctors' point of view) in the real-world practice in recommending cervical cancer screening test?

316 responses

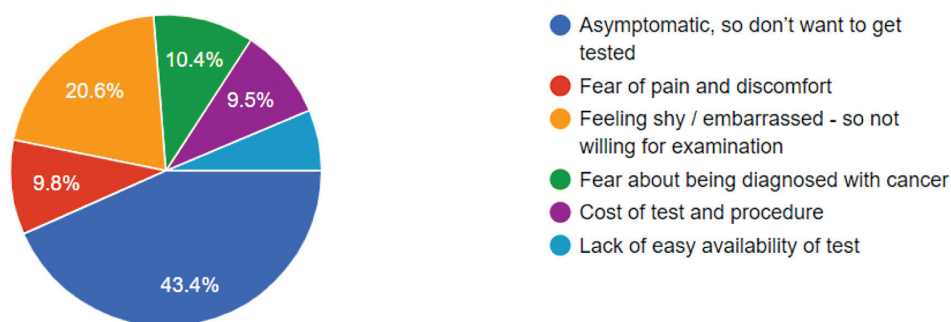


Fig. 5 Response analysis to question number 10: *What do you think is the most important barrier (from patient point of view) in getting the test done.*

Question 15: A total of 38.3% (120/316) believed there is a 51 to 75% chance of fulfilling WHO's goal by 2030 of vaccinating 90% of girls before they attained the age of 15 years. Another 28.5% (90/316) gave it a 26 to 50% chance of successful completion.

Question 16: The real-world offering of HPV vaccination was 42.7% (135/316) as being offered to all girls between the age of 10 and 26 years; 23.7% (75/316) being offered to all females between the age of 10 and 45 years; 20.3% (64/316) of giving to those ladies who ask for it; 10.4% (33/316) not offering it to anyone/ not being in favor of HPV vaccination; and 2.8% (9/316) offering to all females irrespective of age.

Question 17: Regarding HPV vaccination of boys, 55.7% (176/316) felt they should be vaccinated to protect them from HPV-related diseases; 22.8% (72/316) wanted them to be vaccinated to improve herd immunity; 11.7% (37/316) felt vaccinating boys will reduce the chance of girls receiving vaccination (gender bias in families); and 9.8% (31/316) felt HPV vaccination was not required for boys.

Question 18: An overwhelming majority (93%; 294/316) wanted HPV vaccination to be part of the national immunization schedule.

Question 19: Barriers in replicating the success of Sikkim in complete HPV vaccination included high vaccine cost (46.5%; 147/316) lack of appropriate infrastructure (24.7%; 78/316); insufficient long term safety data (4.7%; 15/316); and risk of potentially serious side effects (1.3%; 4/316).

Question 20: If the HPV vaccine was available for Rs 250 per dose, 96.8% (306/316) respondents would recommend it for all eligible patients.

Question 21: Whether successful implementation of HPV vaccination can eliminate the need for cervical cancer screening remains an open issue with 47.5% (150/316) agreeing with it and 52.5% (166/316) disagreeing.

Discussion

Cervical cancer is one of the very few cancers that can be eliminated. With effective screening, vaccination, and concerted efforts, many developed countries have been success-

ful in bringing down cervical cancer rates drastically. However, it is still a big challenge for developing countries. Realizing the urgent need to eliminate cervical cancer, in May 2018, the WHO Director-General announced a global call for action. This was adopted by the WHA in 2020 announced. Their target aims at bringing the threshold of cervical cancer to 4 per 100 000 women-years and thus eliminate it as a public health problem. Three key pillars were proposed: (i) vaccinating 90% of girls fully with HPV vaccine by 15 years of age; (ii) screening 70% of women using a high-performance test by the age of 35, and (iii) treating 90% of women with invasive and preinvasive cervical cancer. These goals need to be fulfilled by 2030 to eliminate this disease by next century and save the future generations.⁴

A national family health survey conducted in 2015 to 2016 estimated lifetime cervical cancer screening prevalence in India to be as low as 29.8%. Screening rates varied among different geographic region from 10.0% in the Northeast Region to 45.2% in the Western Region.⁷ However, the data published in WHO—Cervical Cancer Country Profiles estimates that fewer than one in ten women have been screened in India in past 5 years, averaging the screening rates to be less than 2%.⁸ In our study less than 10% of responders feel that there is a 76 to 100% of achieving this target. A diligent effort by the government, healthcare authorities, doctors and general public would be required for realization of this target in countries like India.

A variety of tests are available for screening including conventional cytology, VIA, VILI, and HPV testing. Newer and more precise tests include HPV mRNA, p16 immunohistochemistry staining, and DNA methylation. A cluster randomized trial by Sankaranarayanan et al compared the impact of screening by all three modalities in India. The detection rate for high grade lesions was same in all groups. They recommended that VIA can be used as a useful test in low-resource countries after appropriate training and quality control.⁹ Indian national guidelines by Federation of Obstetrics and Gynaecology society of India (FOGSI) also recommend co-testing by HPV DNA and cytology as the primary screening tests in good-resource settings, while in poor-resource settings VIA is the test of choice.¹⁰ For successful implementation of a screening program it is not only important to choose the right test but also

appropriate training of healthcare professionals, quality assurance and multilevel coordination between healthcare systems is required. In our study, majority prefer recommending HPV DNA and cytology as primary test, but only 20% doctors are well trained in VIA and do it routinely in practice. However, many are willing to get trained.

For the success of cervical screening program, it is imperative that screen positive patients are diligently followed up and they get appropriate treatment. A study by Vidhubala et al from South India evaluated a community-based screening program in rural setting (Tirunelveli and Tuticorin districts).¹¹ They observed 2,192 screened women, in which 807 were referred, of which 74 (9.2%) visited the referral center for treatment, indicating a poor follow-up. They concluded that the success of screening program depends on the completion of care continuum. Screen positive patients can be treated immediately in the same sitting (screen and treat approach) or triaged by a second test before referral (Screen-triage-treat) or referred directly for colposcopy (traditional practice). Although, WHO recommended screen and treat approach method, being single visit has the highest compliance rate, it leads to overtreatment in many.¹² Excision and ablative methods can be used for treatment. In our study, majority of the clinicians prefer screen-triage-treat approach, which is the preferred modality if appropriate follow-up is feasible. Many would like to base their treatment upon the infrastructure available and patient's willingness to follow up.

HPV vaccination is the next important component of prevention of cervical cancer. Sixty-five percent drop in cervical cancer incidence has been reported from United States from 2012 to 2019 among women in their early 20s, the first cohort to receive the HPV vaccine, predicting the usefulness of this vaccine in elimination of cervical cancer.¹³ However, since the recommendation of vaccine by WHO in 2009, till June 2020, only 107 of 184 countries have included vaccine nationwide or partially in their national immunization schedule. In spite of high uptake of the vaccine in high-income countries, globally only approximately 15% girls and 4% boys have been fully vaccinated by 2019.¹⁴ This is because 70% of the girls live in most populous countries of the world (including India) that have not yet introduced the vaccine widely and systematically. Considering the current scenario WHO 2030 target of fully vaccinating 90% girls below 15 years of age seems quite ambitious. We found that 42.4% clinicians offer vaccination to eligible age group. Incorporation of the vaccine as a part of national immunization schedule and bringing down the cost are shown as the two most important steps toward improving vaccination rates in our study. This would lead to wider acceptability rates among the clinicians in counseling and motivating the eligible age group.

Government must take swift and concerted action to fulfil this herculean task. Strengthening of both screening and vaccination programs is the need of the hour. Cancer control programs in different states need to be synergized by improving upon the cancer registries, strengthening of infrastructure, training of primary health workers, digitali-

zation of the program, incorporation of task shifting, and supporting other programs for women welfare.¹⁰ There is an urgent need of development of low-cost HPV tests and HPV vaccine and their successful implementation through nationwide program. Success of government in coronavirus disease 2019 pandemic through testing and vaccination is an example and a motivation to achieve the WHO target for cervical cancer prevention. Successful delivery of vaccine program can be achieved by involvement of schools, health centers, and use of campaign approaches done in other low- and middle-income countries (LMICs). As learnt from Sikkim model, vaccination target does not seem impossible. Involving public private partnership and nongovernment organizations (NGOs) can further help in achieving the target.

Many high-income countries with low incidence of cervical cancer are planning to limit their screening activities to nonvaccinated females, to better utilize their funds and sources. Brisson et al in their mathematical model analysis also suggested that even most LMICs can eliminate cervical cancer within a century by just increasing the vaccination coverage to 90%. But, in high-incidence countries like India this may not be sufficient.¹⁵ In our study also we got a divided opinion. As of now in India it seems reasonable to promote both screening and vaccination.

Fortunately for our country (and other nations), Serum Institute of India and Department of Biotechnology, Govt. of India have collaborated to make available a tetravalent HPV vaccine (that covers serotypes 6,11,16,18—i.e., 90% of HPV types found in LMIC). This is expected to be sold at INR 250 per dose.¹⁶ This will go a long way in controlling cervical cancer in a cost-effective manner. It will also be a boon to other LMICs, especially in the South Asia Association for Regional Cooperation region.

Conclusions

There are huge global disparities in uptake of HPV screening and vaccination. Our study indicates the challenges faced in the real world and the plausible solutions. Increasing awareness among clinicians about the right test, right time and providing adequate training at healthcare facilities are required. Screening eligible mothers and vaccinating their daughters seem to be a reasonable approach. Making the public aware about related myths and facts by involving schools, colleges, and social media promotion is the way forward. Public-private partnership, NGOs, and development of low-cost vaccine and HPV DNA test may help in overcoming the barriers. Effective, accessible, and quick implementation of cervical cancer screening and vaccination strategies are required to bring an end to enormous sufferings caused by this disease.

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Nil.

Conflict of Interest

None declared.

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