

Special Report



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National screening programs for cervical cancer in Asian countries

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ABSTRACT

Cervical cancer is still one of the most common female cancers in Asia and the leading cause of cancer-related deaths in low- and middle-income countries. Nowadays, national screening programs for cervical cancer are widely provided in Asian countries. We reviewed the National Cancer Screening Program (NCSP) in China, India, Indonesia, Japan, Korea, and Thailand. The NCSP were established at varying times, from 1962 in Japan to 2014 in Indonesia. The primary screening method is based on cytology in all countries except for India and Indonesia. In India and Indonesia, visual inspection of the cervix with acetic acid (VIA) is mainly used as a primary screening method, and a “see and treat” strategy is applied to women with a positive VIA result. The starting age of NCSP ranges from 18 years in China to 30 years in Thailand. The screening interval is 2 years in all countries except for China and Indonesia, in which it is 3 years. Uptake rates of NCSP vary from 5.0%–59.7%. Many women in low- and middle-income countries still do not participate in NCSP. To improve uptake rates and thereby prevent more cases of cervical cancer, Asian countries should continue to promote NCSP to the public using various approaches.

Keywords: Cervical Cancer; Cancer Screening; National Health Programs; Asia

INTRODUCTION

Globally, there were 885,193 new cases and 311,365 deaths from cervical cancer in 2018. In Asia, there were 315,346 new cases and 168,411 deaths [1]. Cervical cancer is the 3rd most common type of cancer in women in Asia, and is the leading cause of female cancer deaths

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Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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in low- and middle-income countries to this day. Many Asian countries have been trying to prevent cervical cancer for some time, using various methods. One method is screening, which aims to detect precancerous changes that, if not treated, may lead to cervical cancer. There are now several tests that can be used in screening for cervical cancer. Cytology (conventional or liquid-based) is the most commonly used test that has been shown to dramatically reduce cervical cancer incidence and cancer-related deaths worldwide [2-4]. Scientific evidence for the diagnostic and preventive value of the human papillomavirus (HPV) test has also been established [5-7]. Visual inspection of the cervix with acetic acid (VIA) and visual inspection of the cervix with Lugol's iodine (VILI) show promise [8-10], but there is as yet insufficient evidence for their effectiveness. Whatever the test used, one of the keys to an effective screening program is to reach as many women at risk of precancerous lesions or invasive cancer as possible. In this respect, well-organized screening programs, designed and managed by the government, are preferable to opportunistic screening. Here, we review national screening programs and discuss ways forward to eliminate cervical cancer in Asian countries.

CERVICAL CANCER SCREENING IN ASIAN COUNTRIES

1. China

China is a country with a vast territory, a large population, complex landforms, and unbalanced economic development. Cervical cancer is the 3rd most common female cancer in women aged 15–44 years in China. In 2018, a total of 106,430 (10.7 per 100,000) new cervical cancer cases were diagnosed in China [11]. There has been an increase in the incidence of cervical cancer in younger women in recent years.

The All-China Women's Federation and the Ministry of Health launched the “Two Cancers” (cervical cancer and breast cancer) examination project in July 2009, which has implemented a free screening program for rural women aged 18–65, involving publicity, health education, and examinations [12]. The cervical cancer screening in this project is performed using cytology, at 3-year intervals. If women have a positive result using the Pap test or VIA, a colposcopy-directed biopsy is recommended to confirm the diagnosis. By the end of 2014, cytology and HPV tests had been used to provide free cervical cancer screening for 42,870,000 rural women. The 2011–2020 Women's Development Program proposes that cervical cancer screening coverage should reach 80%. However, screening coverage in 2010 was only 29.1% in urban areas and 16.9% in rural areas [12].

To standardize screening for cervical cancer, the China Society for Colposcopy and Cervical Pathology of the China Healthy Birth Science Association was established in 2015, and the “Expert Consensus on China's Cervical Cancer Screening and Abnormal Management Issues” was launched in 2017. National training in colposcopy and cervical cytology standardized systems was carried out. Although the basic principles of the Expert Consensus refer to the recommendations of the 2016 American College of Obstetricians and Gynecologists “Cervical Cancer Screening and Prevention” guidelines [13], China lacks the best screening techniques and strategies for their national conditions at present. A great effort should be made to educate the public and improve their medical knowledge. We hope to accumulate enough large-scale Chinese data in the near future to develop guidelines for cervical cancer screening that are more relevant to the Chinese population.

2. India

India contributes one-third of the cervical cancer burden in Asia, with 96,922 new cases and 60,078 deaths in 2018 [14]. Implementation of an organized screening program is essential, but in a resource-constrained diverse setting is challenging. Although the National Cancer Control Program, which provided cytology-based screening, was launched in 1975, its coverage was poor and limited to tertiary centers and the private sector.

After the feasibility and efficacy of VIA were established by several large randomized controlled trials [9,15,16], a VIA-based national program was proposed in 2006 for women aged 30–59 years. In 2007, Tamil Nadu started a pilot screening program for cervical cancer in 2 major rural districts to proactively identify potential problems with the program, and their solutions, before a state-wide expansion [17]. VIA-based cervical screening and clinical breast examination were offered to women at health facilities in 2 districts, along with testing of blood pressure and blood sugar. The program was scaled up to all 32 districts in the state. From 2012 to 2014, a total of 7,420,556 women (52% of the target population) received VIA screening, with 3.8% of results positive. However, compliance with colposcopy and biopsy was only 47.3% and 34.6%, respectively.

Universal cervical cancer screening in India remains an unmet need. According to the National Family Health Survey (NFHS-4), only 22.3% of eligible women received cervical cancer screening during 2015–2016 [18]. In 2016, the Ministry of Health and Family Welfare launched a mobile technology platform for cervical cancer screening [19]. This mobile healthcare system supports the implementation and continuous monitoring of the screening program in each state. National level training for the mobile healthcare system was widely implemented in April 2018, with approximately 12,000 healthcare providers being trained across 24 states. Training modules and linkages are now being developed and piloted in a six-district program, which will eventually be scaled up to over 700 districts in the country.

The Federation of Obstetric & Gynaecological Societies of India (FOGSI) developed resource-based guidelines in 2018 [20]. These advise the best screening strategy according to the available resources and provide guidance on follow-up and management of screen-positive cases. This enables providers to choose from the available options to provide the best care possible in all situations.

3. Indonesia

In Indonesia, cervical cancer occurs in 24.5 per 100,000 women annually [21]. The Ministry of Health started the Cervical and Breast Cancer Prevention (CECAP) project in January 2007 [22]. This project aimed to develop a national model for the prevention of the 2 main female cancers over 5 years. The cervical cancer arm of the project had a goal of implementing cost-effective methods for early detection at public health centers. From the beginning, the CECAP project has worked toward the development of policies and dissemination of training guidelines on cervical cancer screening nationwide.

Cervical cancer screening programs in Indonesia target married women aged 30 to 50 years old [23]. Women are counseled about cervical cancer and afterward VIA is performed [24]. According to the regulations released by the Ministry of Health of the Republic of Indonesia in 2017 (PERMENKES No. 15/2015), women with a negative VIA result should be reexamined within 3–5 years. Meanwhile, women with a positive VIA result should undergo cryotherapy. Cryotherapy will be performed by a trained and qualified doctor in screening program

locations or primary health care facilities. The Cervical Cancer Management Guideline published by the Ministry of Health of the Republic of Indonesia also recommends the use of cytology as a screening tool for cervical cancer [23]. At present, cervical cancer screening tests (VIA and cytology) are both provided for free, as they are covered by National Health Insurance [25].

At the end of 2018, almost 5 years after the government launched the cervical cancer screening program, Indonesian cervical cancer screening coverage was only 7.3% of the target population, which is around 37 million women aged 30–50 years old [26]. The 5th Indonesian Family Life Survey, in 2014–2015, which included 5,397 female respondents aged 40 years and older without any history of cancer, revealed that only 20% of those women were aware of cytology and cervical cancer screening [27]. The lack of cervical cancer screening awareness and participation among Indonesian women, combined with the problem of socioeconomic disparities, needs well-targeted innovation in health promotion and a better strategy to increase cervical cancer screening coverage. The affordable cervical cancer screening program, led by the government, was only available in 8 of 34 provinces in Indonesia until 2018, which is another aspect that should be of concern to the government of Indonesia [27].

4. Japan

In Japan, the incidence of cervical cancer has increased since the late 1990s, in contrast to the decreasing trend observed in most developed countries [28]. The age-standardized incidence rate decreased by 1.7% per year until 1997, and thereafter increased by 2.6% per year. This trend may be due to increased HPV infection among young women, the absence of national HPV vaccination, or an inadequate screening program.

The target age for population-based screening in Japan is 20 years and older, with no upper limit. Screening with cytology is provided for free every 2 years. If the cytology result is not negative for intraepithelial lesion or malignancy, women should receive a confirmatory test of a colposcopy with or without biopsy, performed by a gynecologist, according to the screening program. HPV triage can be performed for women with abnormal squamous cells of uncertain significance (ASCUS) as a screening result. The results from all Japanese local governments are tabulated into a report every year.

There are 3 approaches to cervical cancer screening today: 1) population-based screening for residents, provided by local governments; 2) screening provided by employers or private insurance providers; and 3) opportunistic screening without any funding. Only population-based screening has a legal framework and quality assurance provided by the government. However, screening provided by employers or private insurance providers has recently been recognized to have similar quality assurance control to population-based screening. According to the population-based cancer screening report in 2016, referral rates were 1.3% and 2.4%, follow-up rates were 84.1% and 72.4%, detection rates for invasive cancer were 0.03% and 0.04%, and positive predictive values were 2.2% and 1.8% in women in population-based screening and private practice, respectively. There is no data regarding quality assurance of opportunistic screening in Japan, and establishing a system for quality assurance is also necessary for opportunistic screening, not only for population-based screening.

The participation rate in cervical cancer screening is quite low: approximately 40% [29]. Since 2013, the HPV vaccination program has been suspended by the Ministry of Health, Labour and Welfare, due to potential adverse events. Awareness of the increasing incidence of

cervical cancer in Japan in the current clinical situation and national promotion of screening programs and HPV vaccination are necessary to effectively decrease future morbidity and mortality from cervical cancer. Although the HPV test has recently been declared to be an acceptable screening method, there is still a lack of clinical guidance for screening using HPV tests that reflects Japanese socioeconomic situations, including insurance coverage and quality assurance.

5. Korea

In Korea, cervical cancer is the 7th most common malignancy in women, and the incidence rate is still higher than that in other developed countries [30]. Since the introduction of the NCSP in 1999 in Korea, the incidence rate of cervical cancer has gradually decreased from 16.3/100,000 to 9.1/100,000 in 2015 [31].

Both organized and opportunistic cancer screening programs are available in Korea, and the organized cancer screening program is provided by the government. Since its launch in 1999, the NCSP has provided cancer screening to Medical Aid recipients and National Health Insurance beneficiaries. Korea has a single-payer public health insurance system with universal coverage which is operated by the National Health Insurance Service (NHIS). The Medical Aid program is also operated, for those with the lowest income levels who are unable to pay for health care. Currently, the NCSP provides screening for stomach, liver, colorectal, breast, cervical, and lung cancers. Within the NCSP, the national cervical cancer screening program provides free screening using cytology every 2 years to women aged 20 years or older [32]. The target population for cervical cancer screening was women aged 30 years or older until 2015, but it was expanded to women 20 years or older in 2016.

According to the NCSP protocol, the NHIS invites all eligible women for cervical cancer screening each year by mail: those born in odd years are invited to be screened in odd years and those born in even years are invited to be screened in even years. Women with an invitation letter can visit a nearby cervical cancer screening institution. The cervical cancer screening program is mostly offered by private providers, primarily obstetrics and gynecology clinics or dedicated health-screening centers. The screening institution sends the results to the examinees by mail and is reimbursed by the NHIS upon submission of the results. In contrast, opportunistic cancer screening programs vary in terms of screening method and interval, depending on individuals' decisions or the recommendations of health care providers.

Although the participation rate increased by 0.9% annually (95% confidence interval=−0.7, 2.5) from 2002 to 2012, the participation rate in cervical cancer screening in Korea was still only 40.9% in 2012 [33]. In the NCSP, any health care centers which have a screening facility can be certified as a cancer screening unit, and women invited to undergo cervical cancer screening can visit any of these certified health care centers. Because of this, there is a potential risk of underestimation in the participation rates. Nevertheless, the actual number of participants has more than doubled compared to that of 2002. In 2013, the performance parameters in NCSP were evaluated as follows: cancer detection rate of 1.16 per 1,000, positive predictive value of 5.2%, sensitivity of 87.4%, and specificity of 97.9%. The positive predictive value and specificity have gradually increased since 2005.

6. Thailand

Cervical cancer is the 2nd most common cancer among women in Thailand, with an estimated 8,622 new cases in 2018 [34]. Opportunistic cytology-based screening for cervical

cancer has been ongoing since 1985. In 2005, the Ministry of Public Health and National Health Security Office began providing nationwide cervical screening at 5-year intervals to all Thai women aged 35–60 years, under the universal health care coverage insurance scheme and integrated into the routine health services of Thailand [35]. Consequently, cervical cancer incidence has steadily decreased from 24.7 to 14.4 per 100,000 over the last 2 decades [36]. Cytology and VIA screening methods are covered by the universal health care plan. HPV vaccination was introduced in 2017, as a school-based National Immunization Program only for 5th grade girls, aged 11–12 years. Two national surveys reported that the coverage rates for cervical cancer screening were 46.3% and 59.7% in 2007 and 2009, respectively [37].

The challenges in introducing high-quality, frequently repeated cytology screening and the low sensitivity of cytology in detecting cervical cancer and high-grade cervical intraepithelial neoplasia (CIN) lesions in various settings have led to the evaluation of alternative screening approaches such as HPV test-based screening. A cost-effectiveness analysis study in Thailand also supported the full-scale implementation of the HPV test as a primary cervical cancer screening method [38]. In this analysis, high-risk HPV testing decreased costs by 1,523,011 USD and detected 506 more cases of high-grade CIN, compared with cytology. Self-collected HPV tests can also be used as an alternative option for the unscreened or under-screened population and has shown reliability and good acceptability in Thai women [39]. Recently, the Ministry of Public Health agreed to move forward to a paradigm change of “National Cervical Cancer Screening 2020” starting in October 2020, by implementing primary HPV screening with partial genotyping for HPV 16 and 18 for all Thai women aged 30–60 years at 5-year intervals. Women positive for HPV 16 and 18 will be directly referred for colposcopy, while those positive for other oncogenic types will be advised to undergo cytology triage and will be referred for colposcopy only if the cytology is abnormal, with a threshold of ASCUS. Another alternative strategy, p16/Ki-67 dual staining, for triage of HPV-positive women has been shown to have higher specificity and be more cost-effective in Thailand, compared with cytology [40].

CONCLUSION

The Asian countries included here are trying to establish optimal screening programs for cervical cancer and to improve their coverage rates of screening, in alignment with the national conditions and demands of each country. Unfortunately, other Asian countries that have a high burden of cervical cancer, including Nepal, Myanmar, and the Philippines, were left out of the discussion. Although primary screening methods, starting ages, and screening intervals vary a little from country to country (**Table 1**), almost all Asian national programs to date are based on primary cytology-based screening with HPV triage, as recommended by the American Society for Colposcopy and Cervical Pathology [41]. However, VIA remains an alternative to cytology in middle-income countries.

Table 1. National cancer screening programs for cervical cancer in Asian countries

Country	Nationwide screening	Beginning of the national screening program	Primary screening method	Targeted age	Interval	Uptake rates	Confirmatory tests
China	Available	2009	Cytology, HPV test	18–65	3 year	16.9%–29.1%	Colposcopy
India	Partially available	2007	VIA	30–59	2 year	5%	See and treat
Indonesia	Available	2014	VIA, cytology	30–50	3–5 year	7.3%	See and treat
Japan	Available	1962	Cytology	>20	2 year	30%	Colposcopy
Korea	Available	1999	Cytology	>20	2 year	53.5%	Colposcopy
Thailand	Available	2005	Cytology	35–65	2 year	46.3%–59.7%	Colposcopy

HPV, human papillomavirus; VIA, visual inspection of the cervix with acetic acid.

Based on several large-scale studies on primary HPV test-based screening, screening programs have begun to change in Europe. HPV testing every 5 years for women aged 30–60 years is now the primary screening method in the Netherlands [42], and HPV testing is performed every 5 years for women aged 25–74 years in Australia [43]. However, there are still big challenges in the introduction of HPV test-based screening in almost all Asian countries. There is a need for cost-effectiveness comparisons between cytology-based, HPV test-based, and co-testing screening, and comparative effectiveness studies regarding starting ages, screening intervals, and follow-up protocols, that take into account the national situations of each country. These studies may be time-consuming, so may be difficult to implement in the short-term.

Large numbers of women in low- and middle-income countries still do not have access to cervical cancer screening programs. To improve coverage rates and prevent cervical cancer, health care providers should actively promote national screening programs to the public. Proper follow-up management, quality control of screening tests, and feedback collection from participants are also needed. With our efforts, effective national screening programs with vaccination against HPV will lead to the elimination of cervical cancer in Asia.

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