RESEARCH ARTICLE

Cost-Effectiveness of Korea's National Cervical Cancer Screening Program

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Abstract

Background: Cervical cancer, which is common in developing countries, is also a major health issue in Korea. Our aim was to evaluate the cost-effectiveness of Korea's National Cancer Screening Program (NCSP), implemented in 1999. Materials and Methods: The target population was Korean women 30 years or over who were invited to take part in the NCSP in 2002–2007. By merging NCSP records with Korean Central Cancer Registry data, patients diagnosed with cervical cancer who had been screened were assigned to a "screened group," while patients diagnosed elsewhere were assigned to a "non-screened group." Clinical outcomes were measured in terms of life-years saved (LYS), derived from 5-year mortality rates supplied by the Korean National Health Insurance Corporation and National Statistical Office. Direct and travel costs associated with screening were evaluated from the perspective of the payer, the NCSP. Results: A diagnosis via screening was associated with 2.30 LYS, and the incremental cost-effectiveness ratio (ICER) estimate for screening was 7,581,679 KW/LYS (6,727 USD/LYS). ICER estimates were lower for older patients (≥ 50 years) than younger patients (4,047,033 KW/LYS vs 5,680,793 KW/LYS). The proportion of early-stage cancers detected was 16.3% higher in the screened group. Conclusions: In light of Korea's per capita gross domestic product (32,272 USD in 2012), the current NCSP's incremental cost per LYS appears acceptable.

Keywords: Cost-effectiveness - mass screening - cervical cancer - pap smear - Korea

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Introduction

The annual incidence of cervical cancer worldwide has increased by 0.6%, from 378,000 cases in 1980 to 454,000 cases in 2010 (Forouzanfar et al., 2011). It is one of the most common cancers in developing countries, and it also represents a major health issue in Korea and Japan, economically developed Asian nations (Konno et al., 2008; Razak et al., 2013). In Korea, cervical cancer accounted for 9.8% of new cancer cases in 2002, although the age-standardized incidence has steadily declined from 19 per 100,000 women in 1993-1995 to 15 per 100,000 women in 1999-2002 (Chung et al., 2006; Shin et al., 2007).

In Japan, the Papanicolaou (Pap) smear, the conventional cytological method for cervical cancer mass screening, is used in an organized cervical cancer screening program (Konno et al., 2008). In Korea, a National Cancer Screening Program (NCSP) including the Pap smear was established in 1999, and, since 2002, coverage has included all National Health Insurance (NHI) beneficiaries and Medical Aid recipients (Cho et al., 2013).

Several studies have reported beneficial outcomes associated with cervical cancer screening. For instance, in one Japanese prefecture, screening participation increased from 0.2% in 1961 to 30.4% in 1991, and cervical-cancer related mortality fell from 12.1 per 100,000 in 1961 to 4.0 per 100,000 in 1994 (Sato et al., 1998). Similarly, a cohort study found that Korean women who had been screened more than once had a significantly reduced risk of invasive cervical cancer or carcinoma *in situ* compared to unscreened women (Jun et al., 2009). Studies of the cost-effectiveness of Pap screening strategies have also been conducted in Asian countries. However, most of them have used hypothetical economic evaluation models rather than assessing empirical data (Koong et al., 2006; Woo et al., 2007; Chen et al., 2011; Zhao et al., 2012).

The purpose of the present study was to use empirical data to investigate the life years saved (LYS) by cervical cancer diagnosis through the Korean NCSP. In addition, the cost of administering the NCSP was examined in terms of LYS.

Materials and Methods

Study population and data sources

The target population was Korean women 30 years or older who were invited to participate in cervical cancer

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screening provided by the NCSP between 2002 and 2007. The NCSP's cervical cancer screening initially included all Medical Aid Program recipients, and, in 2002, it expanded to include all NHI beneficiaries as well (Jung et al., 2010; Han et al., 2012). However, because of the separation of administrative management for NCSP, the NCSP database used in this study included only a subset of the individuals covered according to screening years. For the years 2002-2004, only Medical Aid Program recipients were included in the NCSP database records. All Medical Aid Program recipients and National Health Insurance (NHI) beneficiaries were included in the NCSP database in 2005-2006. Finally, in 2007, Medical Aid Program recipients and NHI beneficiaries in the bottom 50% by income were included in the database.

The NCSP invited women to undergo cervical cancer screening at their even-numbed ages. Using NCSP records, individuals who had received cervical cancer screening were identified and assigned to the 'screened group.' Women who did not undergo screening were assigned to the 'non-screened group'.

Cervical cancer diagnoses in the study population were identified using Korean Central Cancer Registry (KCCR) data. The detected cancers were classified by cervical intraepithelial neoplasia (CIN) stage and spread: CIN 1/2, local (CIN 3), regional, and distant. Cervical cancer-related mortality was determined by merging databases from the Korea National Health Insurance Corporation and the National Statistical Office. Cost data relevant to screening participation were obtained directly, from the internal accounts of screening units, and indirectly, from published studies and national statistics.

Cost-effectiveness analyses

Cost-effectiveness outcomes were examined from the perspective of the payer, the NCSP. The information used in the cost-effectiveness models is presented in Table 1. In the COST I model, which dealt with direct costs, expenditures related to screening and follow-up examinations were considered. Follow-up examination costs were included only for patients for whom the screen yielded a false positive, as follow-up examinations for true-positive cancer patients can be viewed as a part of the treatment course instead.

The costs associated with traveling to attend screening or follow-up examinations may also be considered screening costs, so the COST II model consisted of the data included in COST I as well as these indirect costs. Because screening and travel costs occurred only if people utilized NCSP cervical cancer screening, the COST I and COST II models were only applied to individuals who had been screened. All costs were inflated to 2009 values using the National Consumer Indices (Statistics Korea, 2012).

To measure the effectiveness of the national cervical cancer screening program, we examined 5-year survival rates and LYS, starting from the year of diagnosis. In determining LYS, people with no mortality record during the 5-year follow-up period were assumed to live until the last year of their life expectancy (Korean Statistical Information Service: KOSIS, 2012).

Individuals in both the screened and non-screened groups were divided into 5-year age groups according to their age at screening or diagnosis. Both effectiveness outcomes and costs were presented per 100,000 people, stratified by age group, to facilitate comparison of the screened and non-screened groups. Outcome information for the total sample was age-adjusted to match the age distribution in Korea as a whole (KOSIS, 2012).

To determine cost-effectiveness of NCSP cervical cancer screening, cost and effectiveness outcomes associated with cervical cancer diagnoses in the screened and non-screened groups were compared. The sums obtained in COST I and COST II were divided by the number of cervical cancer cases diagnosed via screening. Then, the incremental costs attributable to the screening program were evaluated based on the LYS from 2002-2007. In addition, the incremental costs needed to detect additional early-stage cervical cancer cases via screening were examined by considering diagnoses of CIN 1/2 or local-stage cervical cancer. Data management and analyses were performed using Microsoft Excel™ and SAS 9.2 software.

Results

Study population

According to our database, the average cervical cancer screening participation rate in 2002-2007 was 20.2% (Table 2). Women 55-59 years old had the highest rate of participation, at roughly 30%. Women in their early 30s and women over 75 years of age had the lowest NCSP participation rates (Table 2).

Table 1. Costs Relevant to Participation in Korea's National Cervical Cancer Screening Program

Cost type	Amount (KW)	Source
Cost I Model: Direct screening costs		
(1) Cost of screening test: Pap smear+consultation	10,880 KW (5,760+5,120)	National Cancer Screening Program guidebook. 2002-2011. Division of Cancer Policy, Ministry of Health and Welfare
(2) Costs of follow-up testing caused by false-positive screening results: (a) Colposcopy+ (b) biopsy+(c) histopathologic exam+ (d) consultation+(e) specialty consultation fee	511,704 KW (6,390+17,970+ 19,690+16,880+ 50%*5,648)	(b) (c): National Cancer Center Hospital, Goyang (d) (e): Division of Medical Information and Technology, Yonsei University Health System, Seoul
Cost II Model: Cost I+travel costs		
Round-trip travel costs	23,404 KW (11,702*2)	Third Korea National Health and Nutrition Examination Survey (KNHANES III), 2005

*All unit costs were inflated to 2009 values; [a]The cost for the specialty consultation fee was multiplied by 50% for this analysis, under the assumption that half of the participants with false-positive screening results received a specialty consultation and the remaining half were retested by a general physician; KW, Korean Won

Table 2. The Proportion of Korean Women Who Participated in Cervical Cancer Screening in 2002–2007

Age group (years)	Screened	Non-screened
30–34	6.30%	93.80%
35–39	10.10%	90.00%
40–44	20.70%	79.30%
45–49	23.70%	76.30%
50–54	28.60%	71.40%
55–59	30.30%	69.70%
60–64	28.10%	71.90%
65–69	21.30%	78.70%
70–74	14.50%	85.50%
75–79	7.80%	92.20%
≥80	2.50%	97.50%
Total	20.20%	79.80%

*The study population included (1) Medical Aid Program recipients from 2002–2004; (2) the entire national population in 2005–2006; and (3) Medical Aid Program recipients and the bottom 50% of NHI beneficiaries by income in 2007. Total participation rate was age-adjusted

Table 3. Number of Cervical Cancer Cases Detected per 100,000 Korean Women and 5-year Mortality

	Cervical cancer diagnoses per 100,000 women		5-year mortality rate of patients with cervical cancer	
	Screened	Non-screened	Screened	Non-screened
Screening year				
2002	145.9	67.4	5.20%	35.90%
2003	185.6	59.6	12.60%	31.20%
2004	168.8	52.2	11.10%	31.30%
2005	118.2	48.5	5.90%	15.30%
2006	111.9	48	4.40%	12.70%
2007	102.7	49.3	2.80%	16.20%
Total	114.5	49.5	4.90%	16.60%

*The total frequency values were age-adjusted. Cervical cancers in the screened

In 2002, the age-adjusted rate of cervical cancer diagnosis via the NCSP was 146 per 100,000 screening participants (Table 3). The detection rate peaked in 2003-2004, at 186 cancers per 100,000 screenings. Then, the NCSP detection rate gradually decreased; by 2007, it had fallen to 103 cervical cancer diagnoses per 100,000 screenings. The incidence of cervical cancer diagnoses among non-NCSP participants was 49.5 per 100,000 in 2002-2007, accounting for roughly 30% of cervical cancers diagnosed in Korea (Table 3). Overall, the rate of cervical cancers diagnosed was more than twice as high in the screened group. During 2003 and 2004, the NCSP rate of cervical cancer diagnosis was more than triple that in the non-screened group (Table 3).

Incremental clinical and cost outcomes

Among cervical cancer patients screened by the NCSP in 2002-2007, 4.9% died within 5 years. At 16.6%, the 5-year mortality for patients diagnosed with cervical cancer though a route other than the NCSP was more than triple that (Table 3). Although the 5-year mortality rate among screened cancer patients was over 10% in 2003-2004, by 2007 it had dropped to 2.8%. Likewise, the mortality rates among non-screened cervical cancer patients in 2005 and 2006, which were 15.3% and 12.7%, respectively, were half those seen in the previous years (Table 3). Mortality in this group did increase slightly in 2007, however, to 16.2%.

Table 4. Total Direct and Indirect Screening Costs per Cervical Cancer Diagnosis in the Screened Group, 2002-2007

	Cost I (KW)/diagnosis	Cost II (KW)/diagnosis
Age group (years)		
30–34	7,789,196	17,856,498
35–39	6,661,463	15,295,865
40–44	7,043,672	16,782,755
45–49	7,142,240	17,111,208
50–54	9,415,293	22,731,449
55–59	8,447,979	20,335,036
60–64	7,318,320	17,616,911
65–69	7,059,043	16,947,479
70–74	4,803,405	11,559,339
75–79	6,179,769	14,732,680
≥80	7,013,513	16,561,384
Total	7,323,019	17,721,662

*Cost I includes direct screening costs for cervical cancer. Cost II includes direct plus indirect (i.e. travel) costs. Total costs were age-adjusted and inflated to 2009 values

Table 5. Incremental Life Years Saved (LYS) and Incremental Cost-Effectiveness Ratios (ICERs) for Cervical Cancer Screening: 2002–2007

	LYS/diagnosis	ICER	
		Cost I (KW)/LYS	Cost II (KW)/LYS
Age group (years)			
30–34	0.2	38,694,716	88,706,474
35–39	0.88	7,582,464	17,410,642
40–44	1.96	3,586,190	8,544,713
45–49	2.1	3,405,098	8,157,851
50–54	3.14	3,000,149	7,243,295
55–59	2.98	2,837,704	6,830,606
60–64	2.42	3,019,387	7,268,372
65–69	3.18	2,222,291	5,335,317
70–74	2.86	1,681,717	4,047,033
75–79	2.59	2,382,865	5,680,793
≥80	2.5	2,799,933	6,611,631
Total	2.31	3,175,535	7,581,679

*Total LYS and ICERs were age-adjusted. The LYS outcomes were derived from the 5-year period following diagnosis. All cost estimates were adjusted to 2009 values

Based on the expenditures associated with screening listed in Table 1, direct and indirect costs per cervical cancer diagnosis were estimated using the COST I and COST II models (Table 4). In 2002-2007, the average direct cost of screening was 7,323,019 Korean Won (KW) (equivalent to 6,498 US Dollars, USD; exchange rate May 2013 1 USD=1,127 KW) per cervical cancer diagnosis, while the average total cost was roughly two times greater (17,721,662 KW; 15,725 USD).

Based on a 5-year follow-up of all patients diagnosed with cervical cancer, the number of incremental LYS by screening was 2.31 years (Table 5). The number of LYS was greatest for the age groups 65-69 years (3.18 per diagnosis) and 50-54 years (3.14 per diagnosis). By contrast, in women in their 30s, the incremental LYS was less than 1 year (Table 5).

Using the COST I model, the incremental cost-

Table 6. Incremental Detection Rate of Early-Stage Cancer (ESC) by Screening and Incremental Cost-Effectiveness Ratios (ICERs) for Detection of ESCs: 2002–2007

	Incremental detection rate of ESC	ICER	
		Cost I (KW)/LYS	Cost II (KW)/LYS
Age group (years)			
30–34	4.00%	1,945,194	4,459,298
35–39	9.90%	675,382	1,550,794
40–44	9.20%	766,537	1,826,405
45–49	12.40%	575,045	1,377,678
50–54	19.40%	485,457	1,172,044
55–59	24.10%	351,086	845,096
60–64	20.40%	358,339	862,607
65–69	28.20%	250,770	602,052
70–74	33.50%	143,216	344,648
75–79	24.50%	252,252	601,374
≥80	34.60%	202,889	479,093
Total	16.30%	418,901	1,000,138

*Total incremental detection rate of ESCs and ICERs were age-adjusted. ESC includes cervical intraepithelial neoplasias (CIN) of grade 1/2 and local stage (CIN 3) cervical cancers. All cost estimates were adjusted to 2009 values

effectiveness ratio (or ICER, obtained from the ratio of incremental cost:LYS) was 3,175,535 KW/LYS (2,818 USD/LYS) per cervical cancer patient (Table 5). Using the COST II model, the ICER was 7,581,679 KW/LYS (6,727 USD/LYS). With regard to age, the ICER associated with the cervical cancer screening program was lowest (4,047,033-5,680,793 KW/LYS) in the 65-79 year-old age group and highest (17,410,642-88,706,474 KW/LYS) in the 30-39 year old age group (Table 5).

In 2002-2007, the NCSP for cervical cancer was associated with a 16.3% increase in early-stage detection relative to the non-screened group (Table 6). The difference in the proportion of early-stage cancers diagnosed was roughly 20% in patients over the age of 50. By contrast, among women aged 30-34 years, the increase in the early-stage detection rate associated with screening was only 4.0%.

For each 1% increase in the early-stage cervical cancer detection rate via screening, the associated direct costs were 418,901 KW (372 USD, Table 6). When both direct and indirect costs were considered, the ICER for the same increase was 1,000,138 KW (887 USD). The age groups 55 years and over had ICER estimates below the age-adjusted average for the sample as a whole (Table 6).

Discussion

The 5-year survival rate for cervical cancer patients in 1993-2002 was reported to be 78.7% (Jung et al., 2007). This estimate is significantly lower than that identified in our research (95.1% in the screened group; 83.4% in the non-screened group), which focused on patients diagnosed from 2002-2007. It is likely that the introduction of the NCSP in 1999 and the gradual expansion of beneficiaries have partially contributed to increased cervical cancer survival rates. Indeed, our results reveal a trend of decreasing 5-year mortality rates, with the exception of the baseline year 2002 (Table 3). The 5-year mortality estimate for cervical cancers identified in 2005-2007 was less than half the estimate for cancers identified in 2003-2004.

We found that the average incremental direct screening cost was 3,175,535 KW/LYS (2,818 USD/LYS). When travel costs associated with screening were considered, the incremental cost doubled. From the perspective of the payer, the NCSP, the costs associated with adding one year to a cervical cancer patient's life seem reasonable. In its early years, the absence of empirical data on the cost-effectiveness of screening was considered one of the NCSP's major challenges (Kim et al., 2011). By demonstrating superior cost-effectiveness and survival outcomes, our research reveals that Korea's NCSP for cervical cancer is beneficial.

When ICER values were compared according to age group, women aged 30-34 years required the greatest incremental costs per LYS. This age group also had the fewest LYS (0.20) per diagnosed patient (Table 5). It is possible that women in their early 30s had never undergone cervical cancer screening before attending the NCSP; thus, if they did have cervical cancer, it may have been more likely to reach an advanced stage relative to the cancers detected in other age groups. In addition, with the exception of women aged 80 years and older, the participation rate in the NCSP was lowest in women aged 30-34 years (6.3%, Table 2). This suggests that women in their early-to-mid 30s who underwent cervical cancer screening may be different from the average woman in this age group. Indeed, the increase in early-stage cancers detected via screening was lowest for the 30-34 year-old age group (4.0%). By contrast, ICER estimates per LYS were lowest for patients older than 50 years. In this age range, 20-35% of cervical cancers were detected at an early stage (Table 6), which contributed to the favorable ICER values.

Recently, the prevalence of human papillomavirus (HPV) infection has increased in Korea, resulting in a continued, high burden of cervical cancer (Konno et al., 2008). Although two HPV vaccines are available in Korea, the cost of including them in the National Immunization program is prohibitive. Recent research on the implementation of wide-scale HPV vaccination in Asian countries has predicted beneficial clinical and cost-effectiveness outcomes (Ezat and Aljunid, 2010; Yamamoto et al., 2012). Nevertheless, from the payer's perspective, the expense associated with universal HPV vaccination may seem overwhelming (Praditsitthikorn et al., 2011; Sharma et al., 2012). For this reason, continuous efforts to expand participation in cervical cancer screening are still required. Increasing the uptake of cervical cancer screening is especially important because even though the ICER of adding vaccination to the Pap smear screening would be an cost-effective option, women of low socioeconomic status are less likely to participate in screening or to be able to afford the vaccination (Konno et al., 2008; Park et al., 2011; Praditsitthikorn et al., 2011; Yamamoto et al., 2012). The cost-effectiveness of vaccination in combination with frequent or infrequent screening by the NCSP needs to be evaluated, in light of young women's low screening participation rate and

increasing levels of HPV vaccination.

Recently, the HPV-DNA screening test has attracted public attention, especially in developing countries, as a potentially more cost-effective alternative to the Pap smear (Levin et al., 2010; Flores et al., 2011). It may not be feasible for all women to receive regular Pap smears throughout their lives. Moreover, although the Pap smear is inexpensive, it is less accurate than the HPV-DNA test; therefore, screening at wider intervals with the highly-sensitive HPV-DNA test may be more cost-effective than the current system (Gravitt et al., 2010; Levin et al., 2010; Chen et al., 2011; Flores et al., 2011; Shi et al., 2011). While HPV-DNA tests are not covered under the current NCSP, previous studies comparing screening methods have reported that the sensitivity of the Pap smear was improved markedly in combination with the HPV-DNA test (Kim et al., 2013). Further research examining the cost-effectiveness of single and combination test screening should be conducted to determine the most practical cancer screening strategy.

To the best of our knowledge, this is the first study to use empirical data to investigate differential outcomes for cervical cancer cases detected through Korea's NCSP vs other means. However, our study has several limitations. First, we did not consider treatment costs. Although cost-effectiveness analysis was conducted from the perspective of the NCSP, a substantial portion of the cost of cervical cancer treatment is paid by NHI, a resource available to the public. Treatment costs for cervical cancer are not expected to differ between the screened and non-screened groups, however, because patients' access to care is identical in terms of NHI coverage.

Second, we did not consider intangible costs and benefits, such as anxiety or discomfort associated with undergoing screening. In addition, we did not examine the utility assigned to a reduced risk of dying from cervical cancer via attending the screening program. Indeed, a Japanese study has shown that the most common reasons for screening refusal are inconvenience, inadequate time, cost, and feelings of shame associated with the procedure (Konno et al., 2008). Although we assume these factors are relatively minor, utility considerations could cause the cost-effectiveness of the NCSP to deviate from our results. Utility assessments should be reviewed thoroughly in future studies.

Third, although the NCSP is open to all Koreans, participation may be influenced by socioeconomic status or education level. Several studies of Korea's national gastric cancer screening program have reported that people with higher incomes, more education, and supplementary private health insurance tend to undergo screening at higher rates (Kim et al., 1994; Hahm et al., 2011; Lee et al., 2011; Park et al., 2011). These results suggest that the superior outcomes of patients diagnosed with cervical cancer by the NCSP may be influenced by the higher socioeconomic status of screening participants. This potential disparity implies that cervical cancer screening participation deserves attention from health social workers.

In conclusion, this analysis of Korea's national cervical cancer screening program demonstrates that, in 2002-2007, a higher rate of cancers was identified in the screened population, and the 5-year mortality was lower for cases that had been screened as well. The incremental direct costs related to screening were between 3,175,535 KW (2,818 USD) and 7,581,679 KW (6,727 USD) per LYS over a 5-year observation period, and, when evaluated in the light of Korea's per capita gross domestic product (32,272 USD in 2012), these estimates appear very cost-effective.

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