Review

National Cancer Screening Programs and Evidence-Based Healthcare Policy in South Korea

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\textbf{A B S T R A C T}

\textbf{Background:} South Korea has managed its National Cancer Screening Program (NCSP) since 1999 with free cancer screenings for the five major types of cancer (stomach, liver, colorectal, breast, and cervical cancer). Despite the tremendous amount of government funding, the necessity of this policy and scientific evidence pertaining to it have been questioned.

\textbf{Objective:} This study reviewed the NCSP’s effectiveness and its evidence.

\textbf{Findings:} First, the lead-time bias of diagnosis and the length-time bias regarding the average survival time may increase the misunderstanding that the early detection of cancer will contribute to lower mortality rates and higher survival rates. Second, the positive predictive values (PPVs) of the five major types of cancer checked by the NCSP have remained at 0.6–5.7%. The sensitivity of the screening programs also stood at less than 50% on average.

\textbf{Conclusion:} This study showed that the NCSP program has been less effective, as shown by its low PPVs and sensitivity values, and that its anticipated contribution to lowering the number of cancer-related deaths may have been a product of biased reasoning. To develop the NCSP, adequate explanations of the benefits and potential risks of cancer examinations as well as the accuracy of examinations need to be provided to patients.

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1. Introduction

Cancer is the leading cause of death in South Korea. In 2011 alone, 71,000 people succumbed to cancer, which caused approximately 27% of the 257,000 deaths that year\textsuperscript{[1]}. Approximately 305 of 100,000 people got cancer in 2010, almost one-and-a-half times compared to 220 in 1999\textsuperscript{[2]}. Compared to other industrialized countries, the age-standardized cancer incidence rate per 100,000 in South Korea is 333.6 for males and 297.0 for females, which is higher than those of the UK (male: 280.8; female: 260.5) and Japan (male: 247.3; female: 167.6)\textsuperscript{[3]}. The benefit rate – the ratio covered by health insurance out of the total medical cost except for non-payment items – was almost 90% in South Korea, which means an amount of 4.2 trillion won was nationally spent on cancer treatments\textsuperscript{[4]}. This is the reason behind the emergence of national efforts to reduce the incidence of cancer and the number of deaths caused by cancer as political challenges in the public healthcare field. The World Health Organization has encouraged the creation of national cancer control programs in order to help combat the disease, reduce the loss of life, and enhance the quality of life for patients and families\textsuperscript{[5]}.

However, South Korea and Japan have National Cancer Screening Programs (NCSPs) in place as a cancer-management policy at the national level. South Korea has

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operated its NCSP since 1999, providing medical aid beneficiaries who have less accessibility to healthcare services with free cancer screening for stomach, breast, and cervical cancers. Since its establishment, the services offered by the program have gradually expanded to accommodate those in low-income brackets who fall below the 20% healthcare premium criterion set in 2002, with colorectal cancer screening added to this service in 2004 [6]. Currently, adults who fall below the 50% criterion pay no deductible for the top five cancer checkups (stomach, liver, colorectal, breast, and cervical cancer), and only 10% of the early screening bill is charged for those at the 50% level or higher [7]. Despite the generous amount of government funding and efforts to increase the exam reception rate, the validity of and scientific evidence pertaining to this policy have been questioned [7]. In other words, it is necessary to prove the effectiveness of the objectives of the NCSP, which is to promote early detection, and to provide treatment in an effort to increase the survival rate and lower the mortality rate.

This study reviewed scientific evidence concerning whether the NCSP can lower cancer mortality rates and raise cancer survival rates while remaining effective and avoiding causality bias. This study also looked at problems and remedies pertaining to the NCSP, during which we explored the implications of the South Korean case for other advanced nations.

2. Backgrounds of the Korean National Cancer Screening Program

In 2012, the NCSP recorded an examination reception rate of 63.4% [8]. Here, the examination reception rate refers to the percentage of people who receive cancer screening through the NCSP among those eligible for the five cancer screening programs included in the NCSP. The aforesaid figure is almost 25% jump from 38.3%, the examination reception rate for the year 2004. This resulted from the government’s efforts to encourage cancer screening through media publicity and from the incentive of free screening. Co-developed by the National Cancer Center of Korea and relevant societies in 2001, the five cancer screening programs were revised and supplemented based on recommendations pertaining to the five cancer screening programs suitable for mass screening [8]. The program budget was financed from the National Health Promotion Fund (50%), national taxes (25%), and local taxes (25%). The program is now spearheaded by community health centers. At the beginning of the year, the Ministry of Health and Welfare formulates a program plan and directs it together with the budget to community health centers. After undertaking such a screening program according to the program plan for one year, community health centers report their program output to the Ministry of Health and Welfare at the end of the year. Those eligible for cancer screening are directly notified by the National Health Insurance Corporation (NHIC), and examinees receive screening at a medical institution mandated by the NHIC. Regarding the screening of stomach cancer, breast cancer, and colorectal cancer, the program includes verifications of cancer through an additional inspection in case any disease is detected during the inspection of the first screening (Table 1). However, only few studies reviewed the effectiveness of the NCSP and the number of cancer patients detected by the NCSP over the last years. This program is currently based on the hypothesis that cancer screening can lower cancer mortality rates and raise cancer survival rates, but scientific evidence in support of this has yet to be fully discussed. Accordingly, this study examined whether such a hypothesis about the NCSP is unbiased and effective.

3. Review of the National Cancer Screening Program: Bias and effectiveness

3.1. The two plausible biases inherent in the assumptions of the National Cancer Screening Program

The early detection of cancer makes use of screening tests. Referring to primary tests conducted to determine quickly and clearly those who are likely to have the disease regardless of the existence of symptoms, these are distinguished from diagnostic tests, whose aim is to discover the symptoms or causes of cancer. However, screening tests can contain two biases leading to the misunderstanding that these tests are effective.

The first one is the lead-time bias of the diagnosis (Fig. 1). This refers to the inference that cancer screening helps to prolong patients’ survival time even in cases where screening does not at all help to reduce the mortality rate of the disease because an effective treatment does not exist despite the discovery of cancer through early detection strategies [4]. Let us suppose that stomach cancer takes three years from the onset to death and that a patient is screened for the disease six months after its onset. In such a case, this patient will survive for two and a half years. However, for a stomach cancer patient who has not been screened at all starts to show symptoms only two years after onset, if he or she is screened at that moment, the survival time will amount to one year. Thus, according to these results, screened patients survive a year and a half longer than unscreened patients. In reality, however, there has been no gain whatsoever from earlier detection. Furthermore, if the progress of the disease does not improve, the

Table 1
Guidelines of the National Cancer Screening Programs in South Korea.

<table>
<thead>
<tr>
<th>Target populations</th>
<th>Frequency</th>
<th>Types of test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stomach</td>
<td>40 yrs or over</td>
<td>Endoscopy or upper gastrointestinography</td>
</tr>
<tr>
<td>Liver</td>
<td>40 yrs or over</td>
<td>Liver sonography and alpha fetoprotein</td>
</tr>
<tr>
<td>Colorectal</td>
<td>50 yrs or over</td>
<td>Fecal occult blood test</td>
</tr>
<tr>
<td>Breast</td>
<td>40 yrs or over (female)</td>
<td>Mammography and clinical breast examination</td>
</tr>
<tr>
<td>Cervix</td>
<td>30 yrs or over (female)</td>
<td>Pap smear</td>
</tr>
</tbody>
</table>

* 40 yrs and over with HBsAg-positive, anti-HCV-positive or liver cirrhosis results.
period in which the individual lives as a cancer patient will be prolonged for a year and a half instead, thus increasing the attendant mental pain and medical expenses.

The second is length-time bias regarding the average survival time (Fig. 2). This can arise when there are cases of cancer with favorable or unfavorable progress [4]. Using cervical cancer as an example, let us suppose that there are cases in which the average survival times are two years and six months in all cases. If an individual undergoes cervical cancer screening every two years, cases of cancer with bad progress, leading to death within six months, will both develop symptoms and end in death promptly. Therefore, they are likely not to be diagnosed through detection. However, a type of cancer with an average survival time of two years is more likely to be discovered through detection. In this case, there is the possibility that those whose cancers have been discovered through early detection will be seen consequently as having had their survival time prolonged in comparison with a patient group for which the onset of cancer has not undergone early detection. These two biases create vague expectations that the early detection of cancer will contribute to lower mortality rates and higher survival rates. However, to grasp whether the early detection of cancer has actually been effective for achieving such a goal, far stricter scientific evidence is necessary.

3.2. Effectiveness of the National Cancer Screening Program

To identify the effectiveness of the NCSP, we evaluated the positive predictive values (PPV) pertaining to people who received cancer screening under the NCSP in 2010.
using data from the NHIC [6]. The PPV are the proportions of positive results in statistics and diagnostic tests that are true positive results [9]. It means that the PPV show the likelihood of having an invasive cancer if one is recalled for assessment (true positive cases divided by the sum of the true positive and false positive cases). We estimated the PPV as the number of screen-detected cancer cases diagnosed per 100 positive screenings. We also evaluated sensitivity as a performance measure for the cancer screening method. Sensitivity measures the proportion of actual positives which are correctly identified as such (e.g., the percentage of sick people who are correctly identified as having the condition) [9]. We defined sensitivity as the probability of a positive screening result, given a finding of cancer within one year of screening (true positive/[true positive + false negative]). Sensitivity and PPV are expressed as percentages. A high result can be interpreted as indicating the accuracy of such a statistic.

According to the results of NHIC’s statistical analyses, the PPVs of the five aforementioned cancer screening programs all ranged from 0.6% to 5.7% (Fig. 3). For instance, the PPV of stomach cancer stood at 3.3%, which meant that only 3.3 people relative to total stomach cancer screening examinees proved to be actual stomach cancer cases among those diagnosed with suspected cases of stomach cancer during cancer screening. In other words, as South Korea’s stomach cancer screening examinees totaled 4,915,858 people and 18,654 people were hence diagnosed as suspected cancer cases in 2010, 3.3% of suspected cancer cases (611 people) turned out to be actual cancer cases while the remaining 96.7% (18,043 people) illustrated that the early detection of cancer was incorrect. Other types of cancer also showed low PPVs. In particular, the PPV of breast cancer stood at 0.6%. This meant that less than one person proved to be an actual cancer case among those women diagnosed as suspected cases of breast cancer during cancer screening.

**Fig. 3.** Positive predictive values of the Korean National Cancer Screening Programs, 2010 (%). Source: National Health Insurance Corporation, 2011.

**Fig. 4.** Sensitivity levels of the Korean National Cancer Screening Programs, 2010 (%). Source: National Health Insurance Corporation, 2011.
under the NCSP. Such findings raise doubts about whether the NCSP is actually helpful for health promotion and life extension. Furthermore, there is a high likelihood that numerous non-cancer patients rush into surgery simply because they were diagnosed as suspected cancer cases through the early screening program. Although there is no statistical evidence of this, a high number of patients may come under physical, mental, and economic duress due to such surgery based on inaccurate screening results given that Korean doctors often practice defensive medicine.

Meanwhile, it is also problematic when cancer screening fails to detect actual cancer cases. According to screening sensitivity calculations of the NCSP based on the aforesaid data, 45.3% of total stomach cancer patients were correctly detected through cancer screening (Fig. 4). Simply put, cancer screening failed to detect more than half of actual stomach cancer cases which were supposed to be detected during the course of cancer screening. The sensitivity of cervical cancer stood at a relatively favorable level of 77.1%. However, the sensitivity of breast cancer was low, at 34.8%, which is insufficient to support the effectiveness of the NCSP.

4. Discussion

Before the NCSP was adopted, sufficient scientific evidence and proven effectiveness had to be established. Unfortunately, that was not the case. This study showed that the NCSP program has been less effective, as demonstrated by the low PPV and sensitivity values, and that its anticipated contribution to lowering the number of cancer-caused deaths may have been merely biased reasoning. The global incidence of stomach cancer has been declining over the past decade. In South Korea as well, it had been decreasing before the NCSP was implemented [10]. Thus, it is difficult to conclude that the NCSP had a direct effect on the downturn. Rather, the decrease can be attributed to the fact that, thanks to environmental improvements and the evolution of the food industry, more people now have access to fresh food and are living in cleaner environments [10].

Some people claim, while the cancer screening program may not be resulting in as high a level of performance as was projected, that the program should be maintained because it helps detect cancer early. However, the amounts expended for these results should not be disregarded, because to provide early screening for people without disease requires a reliable medical, effective and ethical foundation [11,12]. In this study, the PPV of breast cancer was 0.6%, which means that 99.4% of people who were diagnosed as potential cancer patients turned out to be cancer-free in the final assessment, e.g., biopsy. Still, it is worth noting that the PPV can be low in early screenings because one aim is not to miss any possible cases. The American College of Radiology recommends a PPV of 5% or higher for early screenings [13]. Given that the breast cancer incidence rate in South Korea is a half of that in the US, the PPV of 0.6% here indicates that the early screening program is most likely creating a burden for program participants as well as a burden for the country overall in the form of budgetary waste.

Low PPVs and sensitivity levels are associated with not only the issue of effectiveness but also with the quality and appropriateness of the cancer screening tests [7]. In the case of cancer screening of the stomach, two initial screening tests, endoscopy and upper-gastrointestinal series (UGIS), are currently included in the NCSP, which has sparked fierce controversy between gastroenterologists and radiologists [14]. Endoscopy is ultimately necessary for verification because the screening rate of UGIS is comparatively low. However, there is controversy over whether it is necessary to include UGIS in the NCSP’s screening tests, as the inclusion of UGIS increases the level of inefficiency by doubling the number of examinations while also lowering the quality and reliability of the screening, though sensitivity is not the only criterion for the selection of screening tests in that the NCSP pertains to screening rather than verification. The PPV for endoscopy is higher than that of UGIS, and its sensitivity is better than that of UGIS [7,14,15]. In contrast, the cost of endoscopy is about one third that of UGIS [16]. Nevertheless, both screening tests are included in the NCSP, thereby perpetuating the cycle of a high cost with a low effect. The problem of low-quality devices for cancer screening is also related to a lack of well-trained personnel.

More fundamentally, the issue of effectiveness is potentially connected to the pain felt by patients. A low PPV of screening programs means that doctors operate on many patients for cancer who later turn out to be non-cancer cases. There is a high likelihood that some patients face physical, mental, and economic anguish due to excessive number of operations. In the same context, a low level of sensitivity of screening programs indicates that early screening at government-designated organizations construe patients as healthy, whereas they may die eventually due to detection of the terminal cancer. In 2013, national television news actually covered several cases of innocent victims of the NCSP [17]. When the cost outstrips the effect in terms of effectiveness, the government should not put it into practice. In the U.S., one report found that one third of operations following cancer screening is attributable to over-diagnosis. Bleyer and Welch investigated the effect of three decades of screening for mammography on breast-cancer incidence and indicated, although no one can say with certainty which women who have cancer are over-diagnosed, that these women undergo surgery, radiation therapy, chemotherapy, hormonal therapy or a combination of these treatments for abnormalities that otherwise would not have caused illness [18].

The NCSP in South Korea was initiated largely based on the fact that the Japanese government conducted a National Cancer Screening Project [6]. By that time, there was agreement reached among Japanese academics that a massive cancer screening for the entire population was necessary on the basis of several case–control studies [17]. According to the research, cancer screening is a preventive measure because it was found that patients with stomach cancer underwent fewer screening exams than those without. However, to prove scientifically the effectiveness of the NCSP, results from a Randomized Control Trial (RCT) are necessary. Assuming that there are 10,000 people randomly selected who had cancer screenings and another
10,000 who did not, if a significant difference is found in the screened group in terms of mortality a few years later, this would be evidence of an effective program. However, there have been no such studies conducted anywhere in the world that reviewed RCT-based research on the validity of such a program, as doing so requires extensive efforts and time. The USPSTF recommends cancer screenings only for breast and cervical cancers, which are considered effective only in a country where the incidence rate is above a certain level [5]. For this reason, in Japan large-scale screenings for early stomach cancer detection have led to lively discussions, and the claim that government-led stomach cancer screenings are based on a biased foundation is gaining dominance [19]. Thus, it is necessary to re-evaluate the need and validity of the NCSP in South Korea.

According to the guidelines for medical screenings from the U.S. Preventive Services Task Force (USPSTF) of the U.S. Department of Health & Human Services, scientific evidence of any benefits and risks should be compared and reviewed before adopting a certain method of screening [20,21]. If the risks outweigh the benefits, it cannot be regarded as effective and is therefore not recommended. Additionally, this applies when there is not enough scientific evidence published to be used for the comparison. It is likely that the most important issue that should be discussed before adopting any early detection program is to determine which is more effective: detecting the disease in a no-symptom preclinical phase and then treating, or treating after any symptoms have appeared. Based on the available scientific evidence, however, it is difficult to agree that the implementation of the NCSP is aligned with the USPSTF guidelines. With no RCT research performed, the assumption that the NCSP would have an impact on reducing death caused by cancer and on the incidence of cancer is likely to be an influence influenced by lead-time bias and length-time bias [22]. In general, population-based preventive intervention programs help to reduce medical expenses overall in a society [23], but when these are performed on every individual, costs can rise due to the need for 1:1 contact (e.g., cancer screening). In fact, a hypertension examination program for cardiac disorder and stroke prevention is merely one fourth as effective as a medical cost reduction compared to the possible savings resulting from an increase in the cigarette tax [24]. Therefore, with its effectiveness remaining unclear, it is difficult to say that the NCSP is an essential program [25].

To increase the effectiveness of the NCSP, first, the size of the disease burden and the possibility of treatment following examination, which are factors that influence the effectiveness of examinations, need to be reconsidered. If a program is effective, its impact would increase with increasing attendance rate and cancer incidence rate. Second, the cost of the examination method per cancer type, which is a factor that influences the cost as well as PPV, sensitivity and specificity should be evaluated. Low sensitivity reduces the cancer detection rate and the effectiveness of examinations due to false negatives. In contrast, low specificity reduces the PPV due to false positives and incurs additional costs [26,27]. Third, it should be discussed whether the NCSP ought to be a project directed at the entire nation. When high-risk groups are selected and examined in multiple steps, the effectiveness is likely to increase [28]. Finally, adequate explanations of the benefits and potential risks of cancer examinations as well as the accuracy of the examination in each case need to be provided to patients so that they may be informed in making decisions regarding their health [11,29]. For example, to prevent excessive examinations due to asymmetric information between physicians and patients, it is necessary to provide examinees with information such as the probability of detecting cancer through the current cancer examination as a percentage and of not being able to detect cancer as a percentage as well. This will help to prevent unnecessary surgery and medical malpractice which can arise due to the indiscriminate implementation of the NCSP. In addition, the government should be responsible by announcing the limitations, possible damages, and side effects of its policies instead of solely promoting their advantages. In the end, the NCSP can be effective when it is improved through consistent quality control.

Consequently, the NCSP is an example of a poorly-designed and inaccurately evaluated cancer screening programs and citizens must be informed about this. While the NCSP has been costly, it has been unclear whether strong evidence for this program’s effectiveness or cost-effectiveness exists. The present case, in terms of the scientific grounds and effectiveness of such examination programs, is expected to have important implications also for other advanced nations which are considering the introduction of massive cancer screening programs. Customized cancer communication may be a good alternative, instead of such a mass cancer screening [30].

References


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