J Korean Med Sci. 2025 Feb 17;40(6):e43
https://doi.org/10.3346/jkms.2025.40.e43
eISSN 1598-6357·pISSN 1011-8934

JKMS

Original Article
Medicine General & Health Policy

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Cost Utility Analysis of National Cancer Screening Program for Gastric Cancer in Korea: A Markov Model Analysis

Seowoo Bae[1,2] **Hyewon Lee**[1] **Eun Young Her**[1] **Kyeongmin Lee**[3] **Joon Sung Kim**[4] **Jeonghoon Ahn**[2] **Il Ju Choi**[5] **Jae Kwan Jun**[1,3] **Kui Son Choi**[1,3] **and Mina Suh**[1,3]

[1]National Cancer Control Institute, National Cancer Center, Goyang, Korea
[2]Department of Health Convergence, Ewha Womans University, Seoul, Korea
[3]Graduate School of Cancer Science and Policy, National Cancer Center, Goyang, Korea
[4]Division of Gastroenterology, Department of Internal Medicine, Incheon St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea
[5]Center for Gastric Cancer, National Cancer Center, Goyang, Korea

Received: Feb 15, 2024
Accepted: Oct 7, 2024
Published online: Dec 5, 2024

Adress for Correspondence:
Mina Suh, MD, PhD
National Cancer Control Institute, National Cancer Center, 24 Jungbalsan-ro, Western Tower 4, 24 Jeongbalsan-ro, Ilsandong-gu, Goyang 10403, Republic of Korea.
Email: omnibus@ncc.re.kr

ORCID iDs
Seowoo Bae
https://orcid.org/0000-0002-8123-388X
Hyewon Lee
https://orcid.org/0000-0001-6915-329X
Eun Young Her
https://orcid.org/0000-0001-7195-5718
Kyeongmin Lee
https://orcid.org/0000-0002-2629-6669
Joon Sung Kim
https://orcid.org/0000-0001-9158-1012
Jeonghoon Ahn
https://orcid.org/0000-0002-0177-0192

ABSTRACT

Background: The Korean National Cancer Screening Program (NCSP) for gastric cancer requires economic evaluation due to the low sensitivity of upper gastrointestinal series (UGIs) and the associated low cancer survival rate. This study aimed to ascertain the most cost-effective strategy for the NCSP.
Methods: The hypothetical target population of this study was aged 40 years or older, and no actual participants were involved. Markov simulation models were constructed for 25 strategies, combinations of 1) screening methods (UGIs or endoscopy vs. endoscopy-only), 2) screening intervals (one, two, or three-year), and 3) upper age limit of screening (69, 74, 79 years old, or "no limit"). Costs, utility, and other input parameters were extracted from various databases and previous studies. Cost-utility, sensitivity, and scenario analyses were conducted.
Results: The endoscopy-only strategy with a three-year interval with an upper age limit of 69 was the most cost-effective strategy with an incremental cost-utility ratio of KRW 13,354,106 per quality-adjusted life years. According to the probabilistic sensitivity analysis, the uncertainty of the result was significantly small. Scenario analysis is showed that as the screening rate increased, the endoscopy-only strategy saved more costs compared to the current NCSP. Therefore, it is important to maintain a high screening rate when altering the NCSP strategy.
Conclusion: Endoscopy-only screening was more cost-effective method than UGIs for the NCSP. Furthermore, a three-year interval with an upper-age limit of 69 years was the most cost-effective strategy. Efforts to improve cost-effective screening guidelines will support the efficient use of medical resources. Additionally, maintaining a higher screening rate may maximize the impact of the modification in strategy on cost-effectiveness.

Keywords: Incremental Cost-Utility Ratio; Endoscopy; Sensitivity and Scenario Analysis; Gastrointestinal Cancer

Il Ju Choi
https://orcid.org/0000-0002-8339-9824
Jae Kwan Jun
https://orcid.org/0000-0003-1647-0675
Kui Son Choi
https://orcid.org/0000-0001-5336-3874
Mina Suh
https://orcid.org/0000-0001-8101-7493

Funding
This research was supported by Grant-in-Aid for Cancer Research and Control from the National Cancer Center of Korea (Grant No. 2210850-3).

Disclosure
The authors have no potential conflicts of interest to disclose.

Author Contributions
Conceptualization: Suh M, Jun JK, Choi KS. Data curation: Lee H, Her EY, Lee K. Formal analysis: Suh M. Funding acquisition: Suh M. Investigation: Bae S, Lee H, Her EY, Lee K. Methodology: Suh M, Ahn J, Bae S. Project administration: Suh M. Software: Bae S. Validation: Suh M, Kim JS, Choi IJ. Writing - original draft: Bae S. Writing - review & editing: Suh M, Bae S, Ahn J, Kim JS, Choi IJ, Jun JK, Choi KS.

INTRODUCTION

Gastric cancer is the sixth most prevalent malignancy and ranks third in cancer-related deaths worldwide. It accounts for 5.6% of all cancer incidences and 7.7% of all cancer-related deaths.[1] Therefore, there is global interest in improving the survival rate of gastric cancer. The prognosis of cancer is known to be closely related to its stage at the time of the initial diagnosis.[2] Early detection is crucial for reducing mortality, as endoscopic screening lowers the risk of gastric cancer death by 40.0%.[3]

To improve five-year survival, the probability of finding tumors at an early stage with a good prognosis should be increased. In cases of early gastric cancer, the prognosis is exceptionally good, with the five-year survival rate exceeding 90%.[4] However, for distant-stage gastric cancer, the five-year survival rate drops sharply to below 5.0%.[5] This large survival gap indicates the importance of reducing morbidity and mortality via "early detection" using optimal screening methods.[6] Furthermore, patients with early-stage gastric cancer have a high likelihood of improving their long-term quality of life through treatments such as endoscopic mucosal resection or endoscopic submucosal dissection,[7] indicating a strong chance of recovery with early diagnosis.

Korea, along with Japan and Mongolia, has some of the highest incidence rates of gastric cancer in the world, which is approximately 10 times that of the United States.[8] To prevent this high incidence from leading to serious severity or death, the Korean government implemented the National Cancer Screening Program (NCSP) in 2002, starting with breast, cervical, and gastric cancer screening. Currently, the NCSP facilitates adults aged 40 years or older to undergo upper gastrointestinal series (UGIs) or endoscopy as primary gastric cancer screening every two years.

Nonetheless, controversy remains over the inclusion of UGIs in the NCSP owing to their poor accuracy compared to endoscopy (positive predictive value 0.008 vs. 0.061).[9] The economic feasibility and effectiveness in improving the prognosis of patients with gastric cancer has been questioned, and several related studies had reported that those who chose UGIs as their primary screening had poorer survival results than those who used endoscopy, and that UGIs were less cost-effective.[10,11] Additionally, patient who underwent UGIs incurred higher healthcare costs per tumor detected.[9] However, these studies were conducted in the early 2010s; therefore, they are outdated and cannot confirm whether the screening strategy is currently cost-effective or not. This evaluation is critical, as the unit costs of UGIs and endoscopy, as well as the screening accuracy of UGIs, have changed over the past decade. According to the National Health Insurance Service (NHIS) Cancer Screening database and the Korea Central Cancer Registry database, UGIs sensitivity declined from 26.2% in 2010 to 19.5% in 2019.

Other than the aforementioned studies, no cost-effectiveness analysis of gastric cancer screening had been conducted in Korea. To confirm the validity of the current screening strategy, a greater discussion of the cost-effectiveness of the NCSP based on the latest data is essential. In addition to screening method selection, considerations of upper age limits and years of screening interval are necessary.

This study aimed to identify the most cost-effective screening strategy among various combinations of 1) screening methods, 2) screening intervals, and 3) upper age limits for examination. The primary outcome of the study was the incremental cost-utility ratio (ICUR), and we further performed sensitivity and scenario analyses to confirm how variations affect the result.

METHODS

Population

The target hypothetical population for this cohort simulation included men and women aged 40 years or older. They were classified as unscreened or screened, and those who were screened were asymptomatic adults. The analysis covered the entire lifespan until death, with a maximum age of 120 years and a total of 81 cycles. The baseline year was 2021; if data were not unavailable, the most recent values were used.

Model construction

We constructed Markov simulation models (**Supplementary Fig. 1**) using Tree-Age PRO Healthcare version 2020, based on the natural history model of gastric cancer, as shown in **Fig. 1**. In this model, everyone starts with a completely healthy status or pre-cancerous stages, such as atrophic gastritis, intestinal metaplasia, and dysplasia. They can then progress to local, regional, and metastatic cancer stages. Patients at each cancer stage received treatment and followed up for one to five years. After treatment, patients could return to the atrophic gastritis state, and at the end of each cycle, those in the termination stage would proceed to the next cycle unless they had died. The analysis cycle of the Markov model was set to 1 year.

We constructed 25 Markov models including a “no screening” arm and arms of combinations of 1) screening methods, 2) screening intervals, and 3) upper age limits for examination. Two screening methods were considered: 1) either endoscopy or a UGIs as the initial screening (with proportions detailed in **Supplementary Table 1**), followed by endoscopy if UGIs results were positive; or 2) endoscopy-only without UGIs. Three screening intervals were considered: 1-year, 2-year, and 3-year. The screening intervals were based on a 2-year interval (as recommended in the 2015 Gastric Cancer Screening Guideline), with variations of ± 1 year. Finally, we considered four upper age limits for examination: (69, 74, 79 years, and

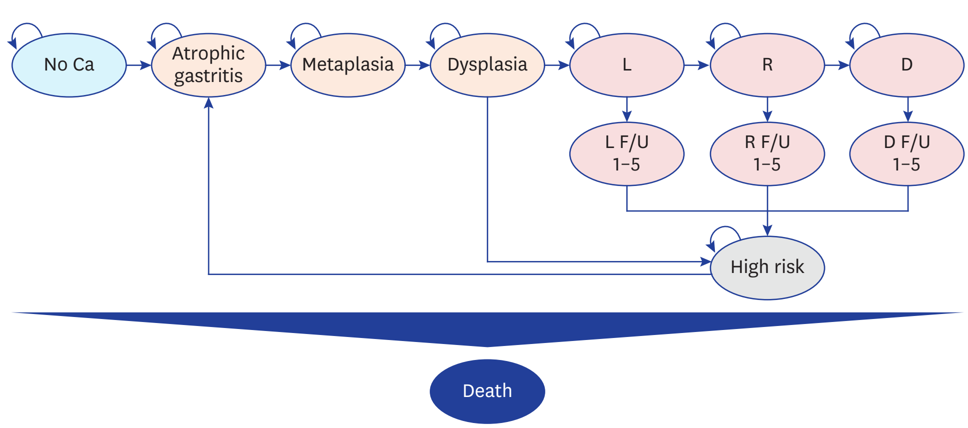

Fig. 1. Natural history of gastric cancer.
No Ca = No cancer, L = Local cancer, R = Regional cancer, D = Distant cancer, F/U 1–5 = Follow up for 1–5 years.

"no limit"). The upper age limit for screening was set to 74 years (as recommended), with variations of ± 5 years. A discount rate of 4.5% was incorporated for both cost and quality adjusted life year (QALY), and the healthcare system perspective was applied.

Variables

Prevalence

The prevalence of atrophic gastritis, metaplasia, and dysplasia were included as input variables. For atrophic gastritis and metaplasia, 32.7% and 17.7%, respectively, were extracted from the domestic study of Hwang et al.[12] (2018). For dysplasia, an 8.0% prevalence was used based on Korean-American data from Shah et al.[13] (2020).

Transition probability

The annual transition probabilities were also extracted from several domestic and foreign studies as a reference. Transition probability from normal to atrophic gastritis was 1.3% (Xie et al.[14], 2007), and from atrophic gastritis to metaplasia was 5.1% (Lee et al.[15], 2007). The transition probabilities from metaplasia to dysplasia, dysplasia to local cancer, local to regional cancer, and regional to distant cancer were 0.2%, 2.4%, 14.8%, and 3.3%, respectively, as calculated from Korean-American data in Shah et al.[13] (2020).

Mortality

The mortality rate was divided into the death rate of the general population and deaths due to gastric cancer among individuals over 40 years of age. The mortality rate of general population was taken from Statistics Korea (2021), excluding deaths due to gastric cancer. The 40–44 age group had the lowest mortality rate at 0.10%, and the mortality rate increased with age, reaching 8.98% in the 80–89 age group.

For deaths due to gastric cancer, the mortality rate from the first year of occurrence to fifth year of treatment, was calculated by SEER stage for each age group. Data from the Korea Central Cancer Registry (1993–2018) was used. In most cases, the mortality rate increased with age. For local, regional, and distant cancers, the mortality rate was highest in the first year of occurrence and gradually decreased as the number of years of treatment increased.

Cost

The screening costs were extracted from the 2021 NCSP Guide.[16] Specifically, endoscopy screening cost included endoscopic examination cost (KRW 78,390) and biopsy cost (KRW 33,270), which was adjusted by the biopsy implementation rate. The UGI examination cost (KRW 59,970) was input for the UGIs strategy.

In the case of local, regional, and distant cancers, treatment costs were input from the first year of occurrence to the fifth year of follow-up observation. Since a health care system perspective was taken, only direct costs were included. Direct costs (hospitalization, outpatient, and drug costs) for each stage and follow-up years were referenced from the cancer patient database of the 2010–2016 NHIS. The average cost was calculated by dividing the total annual medical expenses (outpatient, hospitalization, and pharmacy costs) by the number of survivors. The price index for 2021 was applied.

Utility

In this study, QALY was used as a utility outcome. For age-specific utility weights of the general population, the scores extracted from the EQ-5D survey of the Korea National Health and Nutrition Examination Survey in 2020 were used. The utility weights for each gastric cancer state were based on the average quality-of-life utility weights calculated using the standard gambling method of Lee et al.[17] (2018). The utility weights of the general population decreased with age but were generally distributed between 0.8 and 1.0. By contrast, the utility weights for each cancer stage were in the order of local cancer (0.773), regional cancer (0.589), and distant cancer (0.404). In our study, in the fifth year of follow-up, the utility weight was considered to be the same as that of the general population.

Sensitivity and specificity

According to the integrated data of the NHIS Cancer Screening database and the Korea Central Cancer Registry database of 2019, the sensitivity of endoscopy ranged from 65% to 74% and was much higher than that of UGIs (average of 19.49%). In the case of specificity, both exceeded 99% for all age groups.

Screening rate

According to the NHIS Cancer Screening database, the annual screening rate of endoscopy ranged from 40% to 60% in most age groups. However, UGIs showed a very low rate of average of 6.28%.

Analysis

Base case analysis

We conducted a long-term cost-utility analysis from a healthcare system perspective. Direct costs related to screening and treatment were included. The QALYs were used as utility outcome. Cost-utility analysis of 25 strategies, including "no-screening" as comparator (**Table 1**), were implemented. Dominated strategies were excluded, and ICURs were calculated only for non-dominated ones.

Table 1. Twenty-four strategies of gastric cancer screening

Strategy	Screening method	Screening interval	Screening age
No screening	-	-	-
S1	Endoscopy	1 yr	40–69 yr
S2			40–74 yr
S3			40–79 yr
S4			40–∞ yr
S5		2 yr	40–69 yr
S6			40–74 yr
S7			40–79 yr
S8			40–∞ yr
S9		3 yr	40–69 yr
S10			40–74 yr
S11			40–79 yr
S12			40–∞ yr
S13	Endoscopy or UGI	1 yr	40–69 yr
S14			40–74 yr
S15			40–79 yr
S16			40–∞ yr
S17		2 yr	40–69 yr
S18			40–74 yr
S19			40–79 yr
S20			40–∞ yr
S21		3 yr	40–69 yr
S22			40–74 yr
S23			40–79 yr
S24			40–∞ yr

UGI = upper gastrointestinal series.

The ICUR threshold was set at KRW 50 million per QALY saved. In the past, many countries used GDP per capita (1 to 3 GDP for severe diseases) as the ICUR threshold in the health care sector. However, due to controversy over its validity and the need to accept flexible threshold that reflects reality, the standards are not been explicitly stated at present.[18] In Korea, the Health Insurance Review and Assessment Service (2008) had determined that if the severity of the disease is high, ICUR threshold may be allowed over 1 GDP per capita (GDP per capita in South Korea is about KRW 40,000,000 in 2022).[18] Additionally, there is the result of the study that the public is willing to pay an average of KRW 40,280,000 for a year's extension of life in case of severe diseases.[19] Based on the above evidence, in this study, we considered KRW 50 million as the ICUR threshold.

Sensitivity analysis

A one-way sensitivity analysis was performed to determine the most sensitive variable for cost-effectiveness results. A tornado diagram was drawn to identify the most influential variable on ICUR, and how the ICUR between the strategies changed when the value of the variable varied ± 20%. In addition, a probabilistic sensitivity analysis (PSA) was conducted to explore the uncertainty of the model. The distribution of the variables used is illustrated in **Supplementary Table 2**.

Scenario analysis

A scenario analysis was performed to confirm how the ICUR changes as the screening rate varies. First, we assessed whether the probability of choosing UGIs for the first screening (0–30%) had a significant impact on the results or not. Second, we examined how the primary cancer screening rate (either UGIs or endoscopy) affected the results when it varied from 40% to 100%.

Ethics statement

This study received Institution Review Board (IRB) approval from the Cancer Prevention and Control Central IRB of the National Cancer Institute and the requirement for informed consent was waived (IRB No. NCCNC08129).

RESULTS

ICUR

Once the ICUR curve was connected to the strategies with the lowest slope of incremental cost and utility, four strategies (S9, S5, S1, and S4) were selected. All of these were endoscopy-only strategies. The shorter the screening interval and the higher the upper age limit, the higher the cost and utility. Among the four, the endoscopy-only strategy with a three-year interval and an upper age limit of 69 (S9) was the most cost-effective strategy.

According to the results, all four strategies were cost-effective within the threshold (KRW 50 million). The ICURs of S9, S5 (2y, age 40–69 years, endoscopy), S1 (1y, age 40–69 years, endoscopy), and S4 (1y, age 40–∞ years, endoscopy) compared to "no screening" were KRW 13,354,106/QALY, KRW 18,041,634/QALY, KRW 31,771,404/QALY, and KRW 35,508,558/QALY, respectively (**Table 2**). The ICUR values including dominated strategies were presented in **Supplementary Table 3**.

Table 2. ICUR results of cost-utility analysis

Strategy	Cost, KRW	Incremental cost, KRW	Utility, QALY	Incremental utility, QALY	ICUR, KRW/QALY
No screening (ref)	177,213		18.5100		
S9 (3y, age 40–69 yr, endoscopy)	437,081	259,868	18.5295	0.0195	13,354,106
S5 (2y, age 40–69 yr, endoscopy)	576,826	399,613	18.5322	0.0221	18,041,634
S1 (1y, age 40–69 yr, endoscopy)	1,006,194	828,981	18.5361	0.0261	31,773,404
S4 (1y, age 40–∞ yr, endoscopy)	1,124,929	947,716	18.5367	0.0267	35,508,558

QALY = quality adjusted life year, ICUR = incremental cost-utility ratio.

The current NCSP strategy (S20, 2y, age 40–∞, endoscopy+UGIs) was dominated. Compared to S9, it had slightly higher QALY (S20 18.5320 vs. S9 18.5295), but the cost was much greater (S20 KRW 617,323 vs. S9 KRW 437,081), resulting ICUR of KRW 72,096,800 per QALY.

Sensitivity analysis

One-way sensitivity analysis

The most sensitive variables to ICUR between S9 and "no screening" were utility of patients with local cancer and the general population, prevalence of dysplasia, and cost of endoscopic screening (**Fig. 2**). The red bar indicates when the variable increases, and the blue for decreases. As utility of patients with localized cancer increased, the ICUR between the two strategies also increased. On the other hand, as utility of general population increased, the ICUR decreased. In case of cost of endoscopy screening, as the cost increased, the ICUR also increased. By the way, there were no variables which had an overwhelmingly noticeable effect on the results.

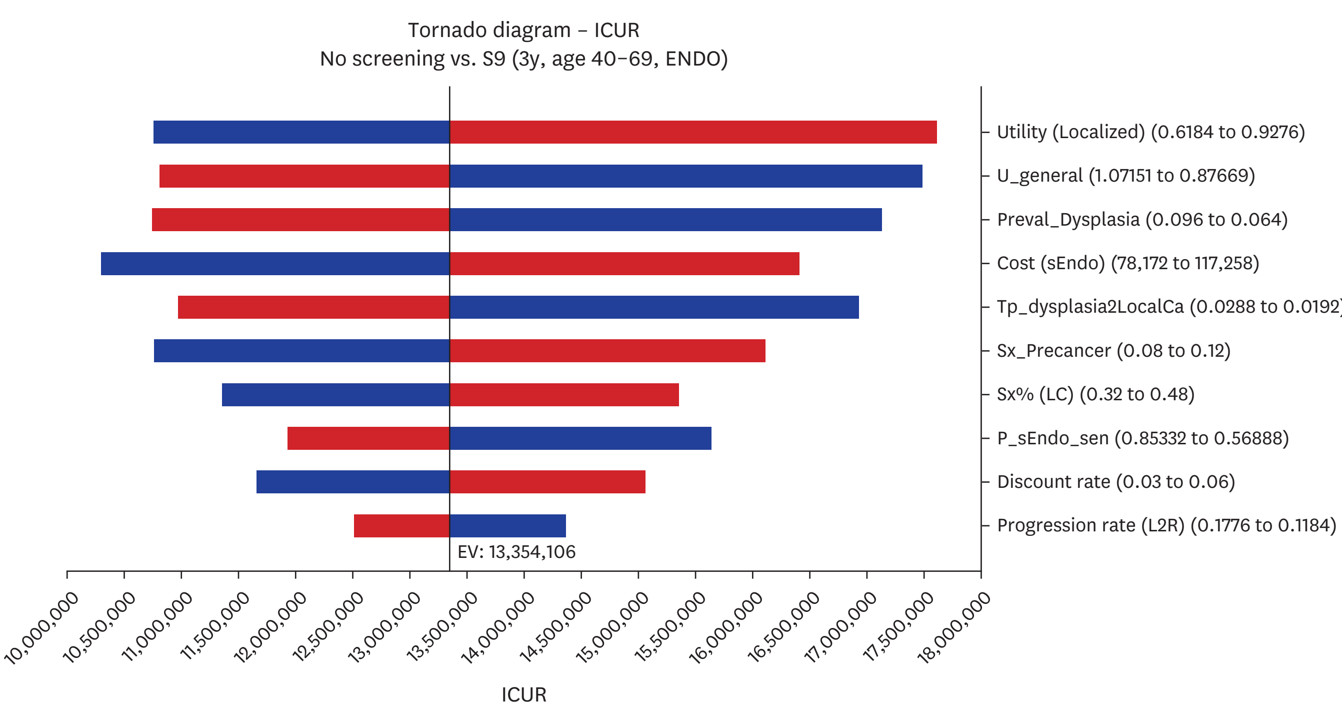

Fig. 2. One-way sensitivity for No screening vs. S9 – Tornado diagram. The red bar indicates when the variable increases, and the blue for decreases. For example, as endoscopy screening cost increases, the ICUR between "no screening" and S9 also increases.
ICUR = incremental cost-utility ratio, ENDO = endoscopy, Utility (localized) = utilities for local cancer patients, U_general = utilities for general population, Preval_Dysplasia = prevalent rate of dysplasia, Cost(sEndo) = endoscopy screening cost, Tp_dysplasia2LocalCa = transition rate from dysplasia to local cancer, Sx_Precancer = symptom rate of precancer, P_sEndo_sen = sensitivity of endoscopy screening, Sx_LC = symptom rates for local cancer, Progression rate (L2R) = transition rate from local cancer to regional cancer.
This diagram was created using Tree-Age PRO Healthcare version 2020.

As this study took a health care system perspective and only included direct costs, so non-reimbursed sedation costs were not included in the basic analysis. When sedation costs were increased from KRW 0 to KRW 100,000, the S9 strategy was still cost-effective within the threshold in all ranges (ICUR KRW 13,354,106–28,989,103) (**Supplementary Table 4**).

PSA

We conducted 100,000 repeated Monte Carlo simulations to confirm the robustness of the model. Variables were assigned to triangular or gamma distributions. Among four strategies, only S9 and S5 had low uncertainties. The cost-effectiveness acceptability curves of S9 and S5 are shown in **Fig. 3**. Specifically, the probability of S9 being cost-effective compared to "no-screening" was approximately 80%, which was 60%p higher than that of "no screening" (**Fig. 3A**). The probability of S5 being cost-effective was 75%, which is 50%p higher than that of "no screening" (**Fig. 3B**).

Scenario analysis

Scenario analysis according to probability of UGI selection

We varied the probability of UGI selection in the first screening of S20 (current NCSP). As a result, ICURs between scenarios of various rates (0%, 10%, 20%, and 30%) were similar, which means that the probability of UGI selection is not an affective variable in the results. In other words, no improvement in cost-effectiveness was observed when the UGI selection rate alternated (either decreased or increased) (**Fig. 4**).

Scenario analysis according to primary screening rate

Fig. 4 shows the changing trend of ICURs between current NCSP and S9 (endoscopy-only) when the primary screening rate of each strategy varied from 40% to 100% in intervals of 10%. Observing the ICUR curves following the scenarios, both strategies had increased in utility and cost as the screening rate increased. When comparing the curves between the current NCSP strategy and S9, the latter was less costly at all screening rates. In addition, as the screening rate increased, the ICUR slope of the current NCSP strategy became steeper than S9. In other words, with a higher screening rate, the cost in the endoscopy-only strategy remained lower than in the current NCSP strategy, resulting in an increase in the ICUR difference between the two strategies (**Fig. 5**).

DISCUSSION

A Markov model is appropriate for predicting the cost-effectiveness of chronic diseases such as cancer because the progression of chronic diseases requires long-term observation. Markov model can describe this progression in a simple and effective way by implementing long-term simulation.[20,21] This study used a Markov model and constructed various scenarios to determine the most cost-effective screening strategy for gastric cancer. As the global economic burden of gastric cancer is greater than that of other cancers,[22] and its incidence in Korea is significantly higher compared to other countries,[8] economic evaluation studies on the domestic NCSP for gastric cancer have become vital. Although several cost-effectiveness analysis studies on gastric cancer screening have been recently conducted worldwide,[6,23,24] no related recent domestic studies are available.[9-11]

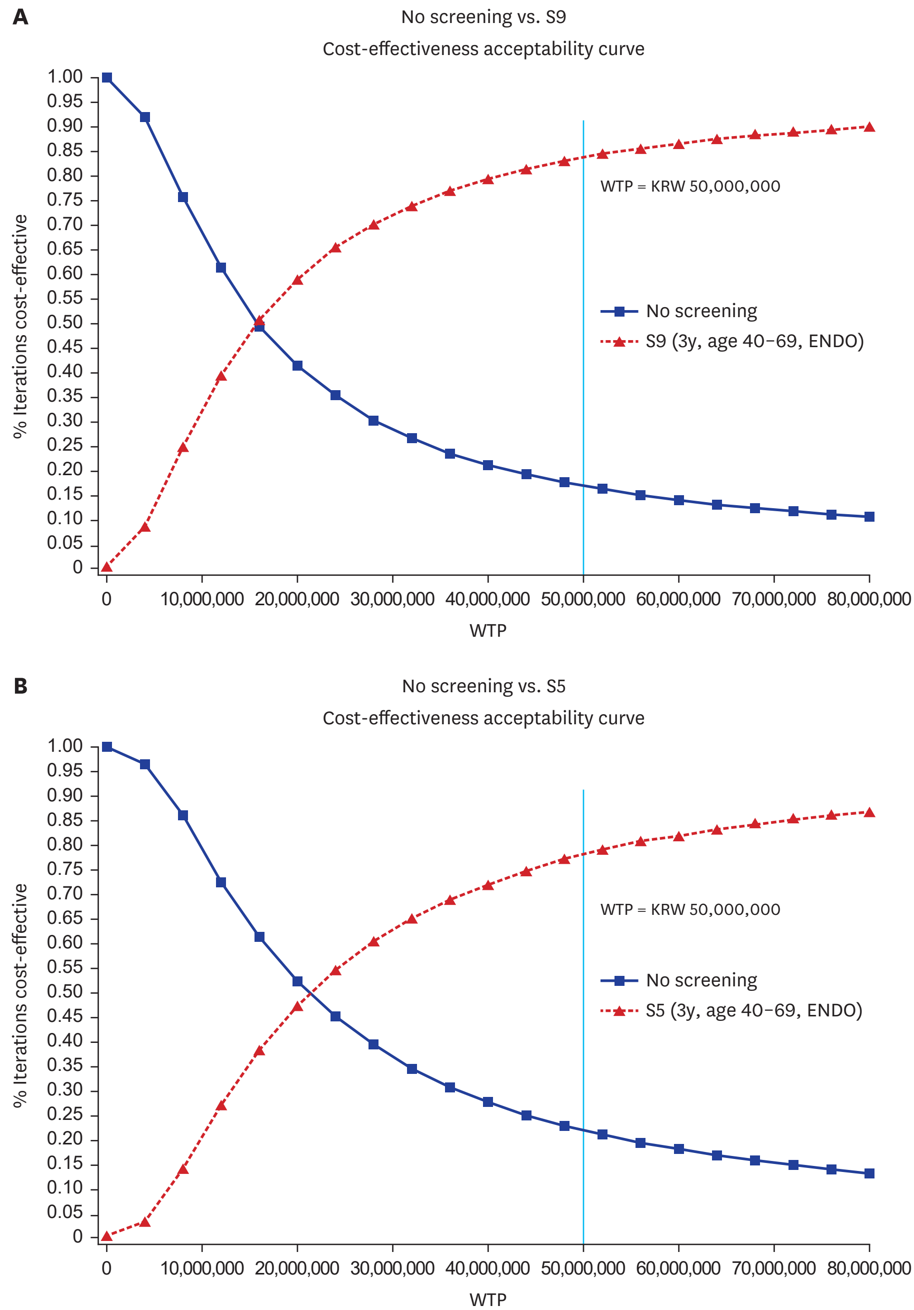

Fig. 3. Probabilistic sensitivity analysis–acceptability curve.
WTP = willingness-to-pay, ENDO = endoscopy.
The curves were created using Tree-Age PRO Healthcare version 2020.

In this study, we verified the cost-effectiveness of gastric cancer screening using recent data from three aspects (screening with or without UGIs, screening intervals, and screening upper age limits). Therefore, the results of this study can be interpreted in three ways.

First, it was more cost-effective to implement endoscopy-only than including UGIs. According to the results of the cost-utility analysis, all strategies selected as cost-effective were endoscopy-only strategies. Specifically, they can be interpreted in terms of cost and utility.

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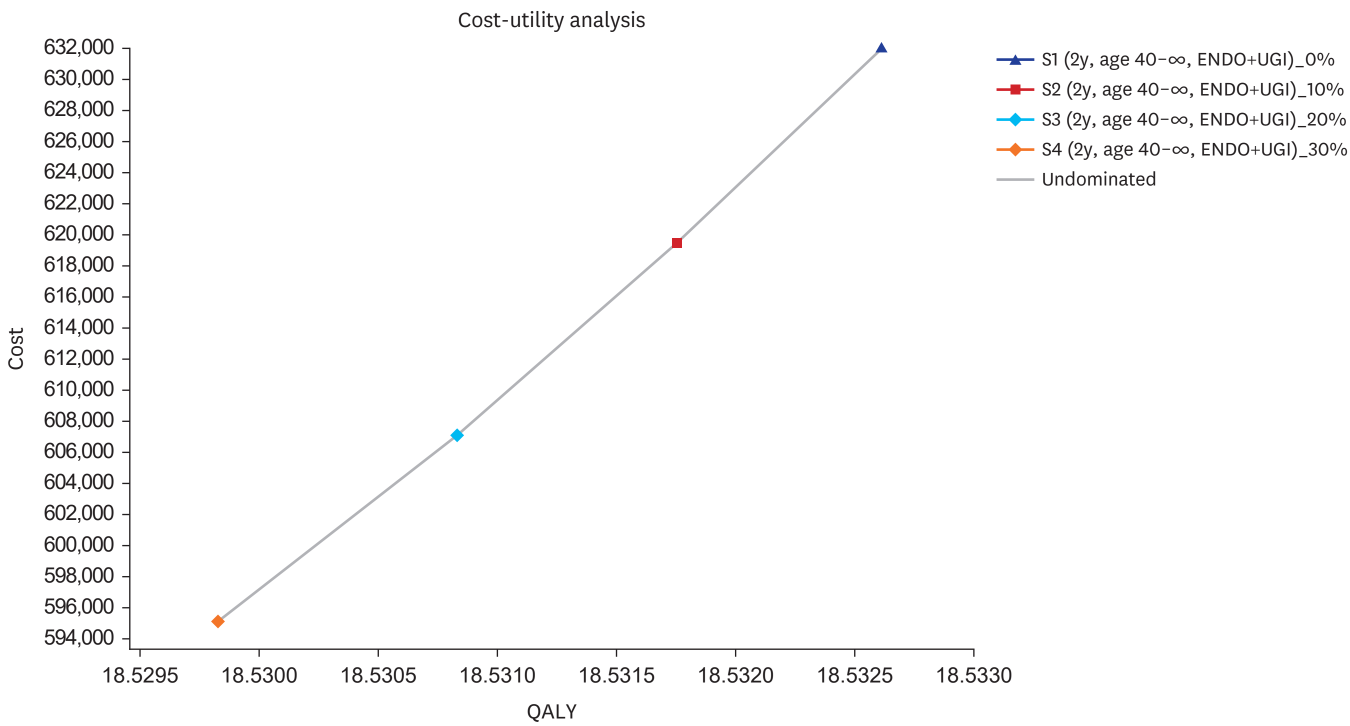

Fig. 4. Scenario analysis according to proportion of selecting UGIs. The steepness of the slope of the line connecting each point is the ICUR values between each strategy. All slopes have similar steepness.
QALY = quality adjusted life years, ENDO = endoscopy, UGI = upper gastrointestinal series, ICUR = incremental cost-utility ratio.

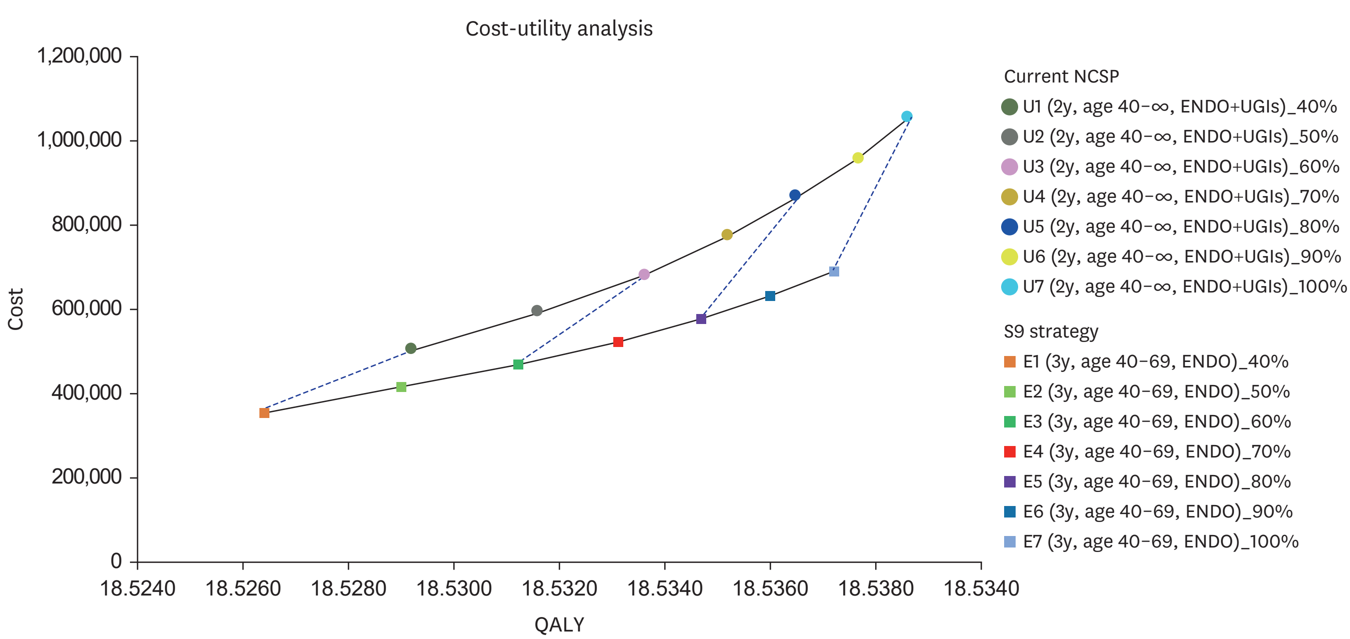

Fig. 5. Scenario analysis according to screening rates (current NCSP vs. S9). The slopes of the dotted lines are the ICURs between two connected strategies with the same screening rate.
QALY = quality adjusted life year, NCSP = national cancer screening program, ENDO = endoscopy, ICUR = incremental cost-utility ratio, UGI = upper gastrointestinal series.

In terms of cost, when comparing strategies with the same screening interval and the same upper age limit, those using UGIs cost less. Initially, receiving UGIs followed by an additional screening was expected to cost more. However, the actual analysis showed that it was rather cost saving. Primary causes of this phenomenon are 1) the insignificant impact of the additional secondary screening cost due to the low sensitivity of UGIs and 2) more than a two-fold difference in screening costs.[12] The cost of endoscopy is approximately KRW 70,000 and that of UGI is approximately KRW 50,000; however, after accounting for biopsy cost, the cost of the endoscopic strategy increases making more gap with the price of UGIs.

However, the overall utility of the UGI strategy was worse. The UGI had a higher probability of missing actual patients in the primary screening because of its low sensitivity. Patients who received false-negative results may have missed the chance for early detection, allowing for faster disease progression, which lowers the utility of the UGIs strategy. Cancer detection rates (CDR) are substantially higher in endoscopy than in UGIs (1.99 vs. 0.26 in 2015–2016).[25] In addition, endoscopy saves more life years and averts more gastric cancer deaths than UGIs.[11,26]

Overall, the UGI strategy was not cost-effective; therefore, it is necessary to reconsider whether it is reasonable to continue UGI implementation. In addition to being less cost-effective, it has a low sensitivity, CDR, and mortality reduction rate. A previous study reported that only 33% of participants who received NCSP for gastric cancer screening preferred UGIs as their future screening method.[27] UGIs were initially adopted as the screening strategy due to a lack of professionals, facilities, and equipment for endoscopy, but this has improved significantly over time, and endoscopic accuracy has increased. Consequently, the rate of endoscopy usage for gastric cancer screening has increased annually.[25]

In terms of age and screening interval, the strategy with an upper age limit of 69 years and a three-year interval was the most cost-effective. However, the two-year interval endoscopic strategy with the same upper age limit (S5) was also found to be cost-effective within willingness-to-pay, which can be chosen as the second-best strategy. Clinically, it has been reported that there is a significant reduction in gastric cancer mortality up to three years after the last screening.[26] While an upper age limit of 74 years is recommended for gastric cancer screening,[28] our analysis found 69 years to be the most cost-effective upper age limit. In addition, a higher upper age limit and shorter screening interval increase both the cost and QALY. This can be interpreted as both cost and QALY tend to increase as the number of examinations or their length increases.

According to the results of the scenario analysis, the probability of UGI selection did not significantly affect the cost-effectiveness. A scenario analysis was conducted to confirm whether the current low UGI screening rate (approximately 10%) had affected the low cost-effectiveness of the UGI strategy. However, the difference in the results according to various UGI selection rates was minor. Additionally, as the UGI selection probability increased, both cost and QALY decreased, again indicating that UGIs are cost-saving but inferior in improving quality of life.

For the primary screening rate in the current NCSP, as the screening rate increased, the slope of the graph (ICUR) tended to become steeper. However, when the strategy was converted to S9 (endoscopy, three-year interval, 69 years old as the upper age limit), the steepness of the slope became gentler. In other words, as the screening rate increased, the difference in QALY between the two became minimal, but at the same time, the cost was saved much more at S9. This suggests that when altering the NCSP system to S9, maintaining a high screening rate, may maximize the effect of the change.

The strengths of this study are as follows: firstly, a complex cost-utility analysis was performed considering not only the screening method but also the screening interval and upper age limit for various scenarios. In addition, long-term predictions were made using a Markov simulation model. Most previous domestic studies[9-11] compared only UGIs and endoscopy, and additionally analyzed either age or screening interval, or estimated for a short term. In this study, however, 25 scenarios were comprehensively designed across three aspects, allowing for a broader economic evaluation. Secondly, this study reflects real-world data by extracting screening indicators from the latest NCSP population data. Finally, we demonstrated the robustness of the model through PSA, accounting for parameter uncertainty in cost-effectiveness models in health economics by assigning a distribution to each parameter. Samples were drawn randomly from each distribution for a user-assigned number of times. This analysis is mandated by many health technology assessment agencies and guidelines internationally.[29] Our study guaranteed reliability by confirming the uncertainty of the cost-effectiveness results with PSA.

However, the study has some limitations. First, as with most economic evaluation studies, some variable data, such as epidemiological indicators, were obtained from previously published studies, making it unclear if the data perfectly suit for the target population. For example, although domestic research data was used in most cases, data from Korean Americans[13] was also included. Additionally, in case of PSA, some assumed values were input as distribution values. Second, since this study focused on age and screening intervals, it did not consider gender. For a follow-up study, additional analyses should account for gender. Third, since the study adopts a health care system perspective, indirect and non-medical costs, such as transportation, caregiver, and productivity loss costs, were excluded from the analysis. However, sedation cost, which can significantly impact screening expenses, were included in the sensitivity analysis. If the impact of other indirect cost is analyzed in future research, allowing for sufficient reflection of these, a more comprehensive cost-effectiveness analysis could be achieved. However, it is essential to carefully consider the range of costs to include, depending on the study's perspective. Finally, the study did not include *helicobacter pylori* infection status in the model. We included only the eradication treatment cost by adjusting the implementation rate without distinguishing additional states in the model. This was because the real-world implementation rate of *H. pylori* eradication treatment was low, and the focus of the study was on screening, not treatment. However, *H. pylori* remains a major cause of gastric cancer, with evidence indicating that infected individuals have a 3–6 times higher risk of developing gastric cancer compared to non-infected individuals.[30] Therefore, *H. pylori* treatment plays an important role in gastric cancer prevention.[31] Thus, a follow-up study focusing on the impact of *H. pylori* infection on gastric cancer incidence is recommended.

In conclusion, a three-year endoscopic screening with an upper age limit of 69 years was the most cost-effective strategy, and the uncertainty of the result was very low. The findings demonstrate that UGIs, as part of the current NCSP for gastric cancer, is not cost-effective compared to endoscopy. Our results can be used as scientific evidence if NCSP is revised in the future. Additionally, when altering the system, maintaining a higher screening rate is essential to maximize cost-effectiveness. Therefore, continuous efforts should be made to enhance the public's screening rate when shifting to a more appropriate system.

SUPPLEMENTARY MATERIALS

Supplementary Table 1
Examination proportion of endoscopy and UGIs in S13–S24

Supplementary Table 2
Input variables for probabilistic sensitivity analysis

Supplementary Table 3
ICURs for all 24 strategies (cost ascending)

Supplementary Table 4
One-way sensitivity analysis on sedation cost (No screen vs. S9)

Supplementary Fig. 1
Markov model. Model example: Strategy 9 (endoscopy-only, 40–69 years, 3-years cycle)–Local cancer.

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