RESEARCH COMMUNICATION

# Comparing Endoscopy and Upper Gastrointestinal X-ray for Gastric Cancer Screening in South Korea: A Cost-utility Analysis

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## Abstract

**Background: There are limited data evaluating the cost-effectiveness of gastric cancer screening using endoscopy or upper gastrointestinal x-ray in the general population. Objective: To evaluate the cost-effectiveness of population-based screening for gastric cancer in South Korea by decision analysis. Methods: A time-dependent Markov model for gastric cancer was constructed for healthy adults 30 years of age and older, and a deterministic sensitivity analysis was performed. Cost-utility analysis with multiple strategies was conducted to compare the costs and effects of 13 different screening alternatives with respect to the following eligibility criteria: age at the beginning of screening, screening interval, and screening method. The main outcome measurement was the incremental cost-effectiveness ratio. Results: The results revealed that annual endoscopic screening from ages 50-80 was the most cost-effective for the male population. In the females, biennial endoscopy screening from ages 50-80 was calculated as the most cost-effective strategy among the 12 screening alternatives. The most cost-effective screening strategy may be adjustable according to the screening costs and the distribution of cancer stage at screening. The limitation was that effectiveness data were obtained from published sources. Conclusions: Using the threshold of $19,162 per quality-adjusted life year on the basis of the Korean gross domestic product (2008), as suggested by the World Health Organization, endoscopic gastric cancer screening starting at the age of 50 years was highly cost-effective in the Korean population. The national recommendation for gastric cancer screening should consider the starting age of screening, the screening interval, and the screening modality.**

**Key words:** Stomach neoplasms - mass screening - endoscopy - quality-adjusted life years - Korea

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## Introduction

The incidence of gastric cancer has gradually declined, but it remains one of the leading causes of cancer death worldwide (Parkin et al., 2001; Ferlay et al., 2004). In South Korea, the age standardized incidence of gastric cancer is 65.7 per 100,000 people for men and 26.0 per 100,000 people for women, which are among the world's highest incidences (Shin et al., 2007). The 5-year survival rate of early gastric cancer (EGC) exceeds 90% (Kunisaki et al., 2006), but that of metastatic cancer is less than 5% (Yeh et al., 2010). Therefore, the early detection and treatment of gastric cancer are important priorities. In 1996, the first "10-Year Strategy for Cancer Control" was established in Korea, and organized cancer screening for gastric cancer was started as a National Cancer Screening (NCS) program in 1999 (Kim et al., 2011). Currently, the NCS program in Korea recommends biennial gastric cancer screening for people older than 40 years via direct upper-gastrointestinal x-ray (UGI series) or endoscopy (or both) (Kim et al., 2011). The median doubling time of gastric cancer is estimated as 2–3 years (Fujita, 1978). Therefore, the optimal interval of screening for gastric cancer is proposed as less than 3 years (Dan et al., 2006). The annual participation rate for gastric cancer screening in 2002 was 9.6% for men and 12.9% for women, and 5 years later, the rate increased to 18.7% for men and 24.7% for women (Choi, 2009). Only 43% of people screened for gastric cancer in 2007 underwent endoscopy, whereas 57% of people underwent UGI series with low sensitivity for EGC (Choi, 2009) consequently decreasing the effectiveness of EGC detection.

If the gastric cancer screening strategy uses inappropriate methods or does not consider the prevalence or incidence of gastric cancer in the target population, false positivity or false negativity will occasionally occur and can result in unnecessary costs or decreases

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in the cure effect. Establishing a strategic early cancer screening method that considers medical and economical aspects is important for increasing the health of the population and effective allocation of resources. To create an effective early cancer screening strategy, a rational standard considering methods of examination, target ages, ending ages, and period of examination must be established, and the effectiveness of increasing the early cancer screening participation rate and cancer screening must be evaluated and administrated continuously. Korea is the only nation other than Japan to implement mass screening programs for gastric cancer. However, there is a paucity of data evaluating the cost-effectiveness of gastric cancer screening using endoscopy or UGI series for the general population.

This study aimed to explore the cost-effectiveness of various gastric cancer screening programs using endoscopy or UGI series in Korea relative to no screening (investigating only when there are clinical symptoms) and determine the most favorable screening alternative for gastric cancer with regard to starting age and screening interval.

## Materials and Methods

*Markov model structure*

A time-dependent Markov model was used to compare hypothetical cohorts of Korean people in which one was followed without screening and the others underwent different screening strategies for gastric cancer. The perspective for the evaluation was societal, and the time horizon covered the full lifetime or up to the age of 99 years for the patients beginning screening at the age of 30 years. This cohort simulation approach with a cycle length of 1 year was used for running the Markov model. The gastric cancer incidence and mortality due to other causes of death (excluding gastric cancer) were modeled as time-dependent transition probabilities.

Patients moved across 10 health states. These health states were (1) asymptomatic healthy, (2) test-positive EGC, (3) test-negative EGC, (4) symptom-positive EGC, (5) symptom-negative EGC, (6) test-positive advanced gastric cancer (AGC), (7) test-negative AGC, (8) symptom-positive AGC, (9) symptom-negative AGC, and (10) dead. The probability of a patient's transition from one state to another state each year was obtained from previously published studies. According to these studies, the median duration of remaining in the early stage is approximately 44 months, and the cumulative 5-year risk for progressing from EGC to AGC is 63% (Tsukuma et al., 2000). One of the assumptions for the screening was that endoscopy and UGI series would make it possible to capture a sizable amount of cancer cases that would otherwise have gone undiagnosed until alarming symptoms developed. Thus, the model needed to incorporate an estimate of sojourn time when the cancer is screen-detectable but displays no clinical symptoms. We assumed a sojourn time of about 5 years from the previous literature (Tsukuma et al., 2000; Hamashima et al., 2006; ).

*Alternative screening programs*

Because there are two available screening methods (endoscopy and UGI series) for gastric cancer in Korea, we considered different screening alternatives with regard to the following eligibility criteria: age at the beginning of screening and the interval between two screenings. All combinations of starting ages (30, 40, or 50 years with an ending age of 80 years) and screening intervals (1 and 2 years) were considered, giving 12 different screening alternatives in addition to the no-screening option. The screening was stopped when the gastric cancer was detected, a participant died, or participants reached the age of 80 years.

*Major assumptions*

The incidence of gastric cancer is assumed to be similar between the screened and unscreened groups (Tsubono and Nishino, 2000). In the screened pathway, suspicious lesions detected by endoscopy were biopsied. If there were suspicious lesions in UGI series, then those people were followed by endoscopy and biopsied on another screening day.

The overall mortality and gastric cancer mortality were estimated using the vital statistics of Korea for 2008 (Korea National Statistical Office, 2010). Patients who survived for 5 years after undergoing EGC treatment are assumed to have the same age- and gender-specific death rates as healthy people. We used the tunnel state to reflect the probability applied differently throughout the period (Hawkins et al., 2005). Stage-specific survival was applied differently according to the receipt of treatment. When the person did not undergo treatment due to undetected gastric cancer, his or her mortality was decided by the stage-specific survival rate in the unscreened population from the published data (Babazono & Hillman, 1995; Kubota et al., 2000; Kunisaki et al., 2006). The treatment costs of gastric cancer were determined according to the cancer stage. All patients who were diagnosed with gastric cancer were assumed to receive the same treatment, to pay the same treatment price, and to not participate in future gastric cancer screening.

*Incidence and prevalence rates*

The gender-specific gastric cancer incidence of the population was obtained from Korea Central Cancer Registry data reported in 2008 (Korea Central Cancer Registry, 2010). Mortality according to age and gender was assessed using National Statistical Office 2008 data (Korea National Statistical Office, 2010). The stage distribution and the survival outcomes in the unscreened population were projected on the basis of local studies (Hansson et al., 1999; Kubota et al., 2000; Dan et al., 2006; Kunisaki et al., 2006; Miyamoto et al., 2007; Nam et al., 2009). The corresponding outcomes for the

**Table 1. Results of the Base Case Analysis**

| Strategy of Screening for Gastric Cancer (Male) | Cost ($) | Incremental Cost ($) | Effectiveness (Utility) | Incremental Effectiveness | C/E | Incremental C/E (ICER) |
|---|---|---|---|---|---|---|
| M_30_99_No screening | 1,619 | | 22.262 | | 72.758 | |
| M_50_80_2yr_Endoscopy | 1,815 | 196 | 22.3 | 0.038 | 81.422 | 5,116 |
| M_50_80_2yr_UGI | 1,836 | 20 | 22.297 | -0.003 | 82.35 | (Dominated) |
| M_50_80_1yr_Endoscopy | 1,975 | 159 | 22.333 | 0.033 | 88.457 | 4,820 |
| M_40_80_2yr_Endoscopy | 1,977 | 2 | 22.308 | -0.025 | 88.663 | (Dominated) |
| M_50_80_1yr_UGI | 2,009 | 34 | 22.324 | -0.009 | 90.037 | (Dominated) |
| M_40_80_2yr_UGI | 2,017 | 42 | 22.305 | -0.029 | 90.466 | (Dominated) |
| M_30_80_2yr_Endoscopy | 2,206 | 230 | 22.313 | -0.02 | 98.878 | (Dominated) |
| M_30_80_2yr_UGI | 2,278 | 303 | 22.307 | -0.026 | 102.143 | (Dominated) |
| M_40_80_1yr_Endoscopy | 2,295 | 320 | 22.349 | 0.016 | 102.721 | 20,490 |
| M_40_80_1yr_UGI | 2,369 | 74 | 22.337 | -0.011 | 106.087 | (Dominated) |
| M_30_80_1yr_Endoscopy | 2,760 | 464 | 22.355 | 0.006 | 123.485 | 81,294 |
| M_30_80_1yr_UGI | 2,890 | 129 | 22.342 | -0.012 | 129.364 | (Dominated) |
| Without dominated options (simple or extended) | | | | | | |
| M_30_99_No screening | 1,619 | | 22.262 | | 72.758 | |
| M_50_80_1yr_Endoscopy | 1,975 | 355 | 22.333 | 0.071 | 88.457 | 4,979 |
| M_40_80_1yr_Endoscopy | 2,295 | 320 | 22.349 | 0.016 | 102.721 | 20,490 |
| M_30_80_1yr_Endoscopy | 2,760 | 464 | 22.355 | 0.006 | 123.485 | 81,294 |
| **Strategy of Screening for Gastric Cancer (Female)** | **Cost ($)** | **Incremental Cost ($)** | **Effectiveness (Utility)** | **Incremental Effectiveness** | **C/E** | **Incremental C/E (ICER)** |
| F_30_99_No screening | 774 | | 23.81 | | 32.515 | |
| F_50_80_2yr_Endoscopy | 977 | 202 | 23.828 | 0.018 | 41.005 | 11,378 |
| F_50_80_2yr_UGI | 999 | 22 | 23.827 | -0.002 | 41.936 | (Dominated) |
| F_40_80_2yr_Endoscopy | 1,109 | 132 | 23.834 | 0.006 | 46.543 | 21,014 |
| F_40_80_2yr_UGI | 1,146 | 37 | 23.832 | -0.002 | 48.121 | (Dominated) |
| F_50_80_1yr_Endoscopy | 1,164 | 55 | 23.844 | 0.009 | 48.839 | 6,073 |
| F_50_80_1yr_UGI | 1,206 | 42 | 23.839 | -0.004 | 50.624 | (Dominated) |
| F_30_80_2yr_Endoscopy | 1,290 | 125 | 23.84 | -0.004 | 54.13 | (Dominated) |
| F_30_80_2yr_UGI | 1,352 | 187 | 23.836 | -0.007 | 56.722 | (Dominated) |
| F_40_80_1yr_Endoscopy | 1,425 | 261 | 23.855 | 0.012 | 59.766 | 22,283 |
| F_40_80_1yr_UGI | 1,499 | 73 | 23.849 | -0.006 | 62.871 | (Dominated) |
| F_30_80_1yr_Endoscopy | 1,791 | 365 | 23.863 | 0.007 | 75.055 | 50,033 |
| F_30_80_1yr_UGI | 1,908 | 117 | 23.856 | -0.007 | 80.004 | (Dominated) |
| Without dominated options (simple or extended) | | | | | | |
| F_30_99_No screening | 774 | | 23.81 | | 32.515 | |
| F_50_80_2yr_Endoscopy | 977 | 202 | 23.828 | 0.018 | 41.005 | 11,378 |
| F_50_80_1yr_Endoscopy | 1,164 | 187 | 23.844 | 0.015 | 48.839 | 12,188 |
| F_40_80_1yr_Endoscopy | 1,425 | 261 | 23.855 | 0.012 | 59.766 | 22,283 |
| F_30_80_1yr_Endoscopy | 1,791 | 365 | 23.863 | 0.007 | 75.055 | 50,033 |

C/E, cost effectiveness ratio; ICER, incremental cost effectiveness ratio; UGI, upper-gastrointestinal x-ray.

screened population were projected from clinical studies conducted in Korea or Japan (Kubota et al., 2000; Han et al., 2003; Nam et al., 2009).

*Characteristics of the screening tests*

Every person not previously diagnosed with gastric cancer was eligible for screening. Non-participants in screening and people with false-negative screening results were assumed to be diagnosed after the sojourn time had passed, and were more likely to be diagnosed with AGC. Based on public cancer screening data in Korea, the sensitivities of UGI series and endoscopy were 42.1 and 59%, respectively, and their specificities were 89.8 and 96.3%, respectively (Lee et al., 2010). However, a study of private screening programs reported the sensitivity of endoscopy was 85.4–98.8% and the specificity was 100% (Yeun, 1992). Therefore, we analyzed the sensitivity and specificity of each test by using the recent participation rates of private programs (37.1%) and public programs (62.9%) (Yeun, 1992; National Cancer Center, 2008; Lee et al., 2010).

*Cost and effectiveness*

Costs were categorized as screening costs, initial treatment costs (first year), follow-up treatment costs (2–5 years, after 5 years), and terminal care costs (Park, 2006). Screening costs included direct medical costs, nonmedical direct costs, incurred transport costs, and costs related to lost productivity. The treatment cost data for this study were obtained from a survey study in Korea (Table 1). The treatment costs by stage were assumed to be same for the unscreened and screened

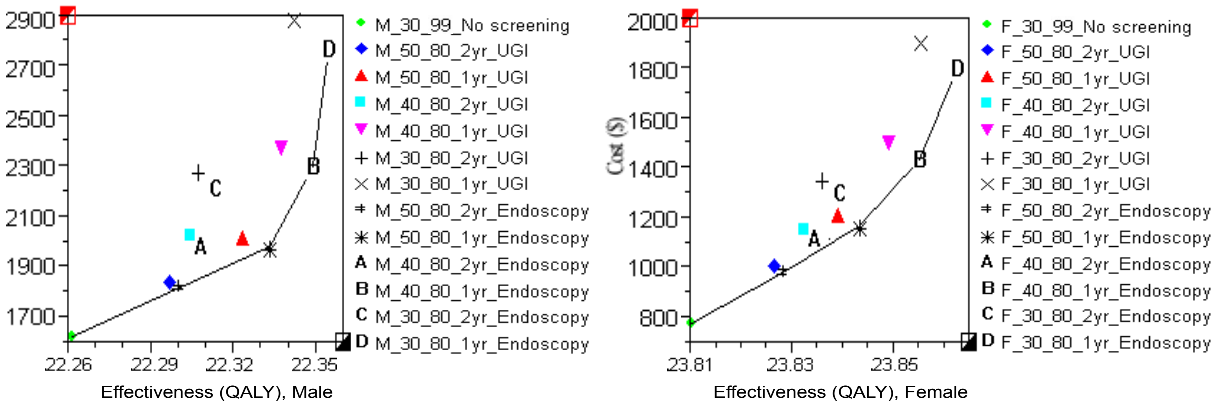


**Figure 1. Comparing Different Alternatives of Gastric Cancer Screening**

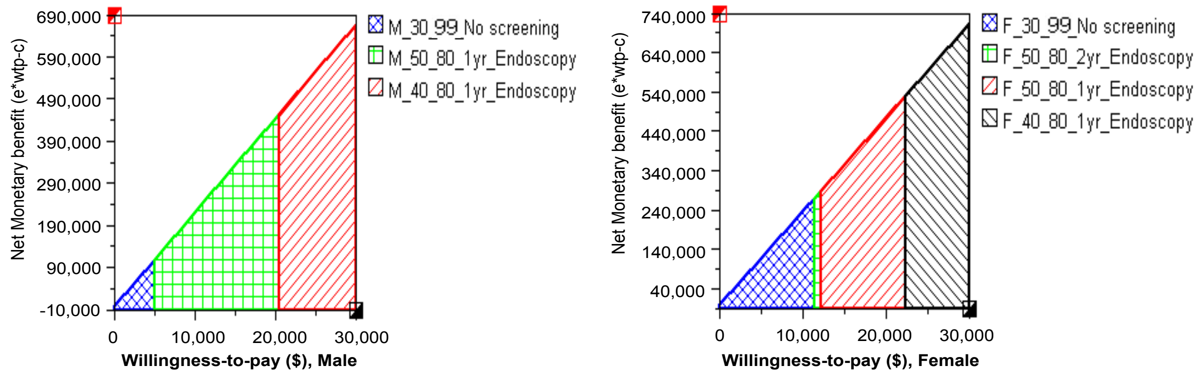


**Figure 2. Gastric Cancer Screening Strategy Graph on Willingness-to-Pay**

populations. All estimated costs are expressed using an exchange rate of 1103 Korean won to 1 United States dollar, which was the annual exchange rate in 2008. To capture both the mortality and morbidity outcomes due to gastric cancer screening, health improvement was measured in quality-adjusted life years (QALYs). The quality of life according to gastric cancer stage was obtained from several published articles (Dan et al., 2006; Hanmer et al., 2006). The survival rate according to stage was calculated using the 5- or 10-year survival rates from a synthesis of published studies (Babazono & Hillman, 1995; Kim et al., 2000; Kunisaki et al., 2006; Miyamoto et al., 2007).

*Statistics and sensitivity analysis*

Comparisons were made between the reference strategy of no screening for the population and different screening strategies using endoscopy or UGI series. A discount rate of 3% for costs and effects was applied to the analyses. Final outcome measures were incremental cost-effectiveness ratios (ICERs) expressed as $/QALY. All of the base case estimates including the sensitivity and specificity of each screening program were varied over a wide range during the sensitivity analyses. The ranges for sensitivity analysis were based on the range of variables in all relevant studies. When published data were not available, base case estimates were halved and doubled, with additional adjustment made by author consensus. One-way sensitivity analysis was applied to the base case population of Korea to identify the factors that had the greatest impact on cost-effectiveness and to determine the impact of assumptions and estimations for all variables used. Analysis was performed using Data 2009 (Treeage Software Inc, Williamstown, MA).

## Results

*Base case results*

The 1-year-interval UGI series screening strategy from ages 30 to 80, calculated through the Markov model, resulted in the highest cost of $2890 for males and $1908 for females, and utility was highest for annual endoscopy from ages 30 to 80 with 22.355 QALY for males and 23.863 QALY for females (Table 1).

Compared to the no screening alternative, the ICER of the endoscopic screening alternative with a 2-year interval from ages 40 to 80 for the male population was $7673/QALY. Additionally, compared to the no screening alternative, the ICER of UGI series from ages 40 to 80 with a 2-year interval was estimated to be $9292/QALY for the male population. The cost-effectiveness results are displayed graphically in Figure 1.

Based on commonly accepted thresholds of society's willingness to pay per QALY of $19,162, the endoscopic gastric cancer screening at the starting age of 50 years may be highly cost-effective in the Korean population. Comparing the net health benefit among these strategies, annual endoscopic screening for Korean men from ages 50 to 80 was the most cost-effective strategy for the defined willingness-to-pay threshold (Figure 2). The ICER of this strategy over no screening was $4979/QALY.

**Table 3. Sensitivity Analysis (Korean Population Screening)**

| | Sensitivity analysis range | | 50 to 80 years, Endoscopy ICER (Male) | | | | 50 to 80 years, Endoscopy ICER (Female) | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | 2-yr interval | | 1yr interval | | 2-yr interval | | 1-yr interval | |
| | Min | Max | Min | Max | Min | Max | Min | Max | Min | Max |
| Endoscopy + Consultation cost ($) | 19.68 | 78.72 | (Ext Dom) | 6,558 | 3,307 | 18,695 | 7,618 | 14,733 | 7,828 | 17,968 |
| UGI + Constulation cost ($) | 18.57 | 74.28 | (Ext Dom) | (Ext Dom) | 8,303 | 4,979 | (Ext Dom) | 11,378 | 18,9181 | 2,188 |
| Biopsy cost ($) | 12.27 | 49.08 | (Ext Dom) | (Ext Dom) | 4,955 | 5,028 | 11,328 | 11,480 | 12,122 | 12,321 |
| EGC first year treatment cost ($) | 2,996 | 11,982 | (Ext Dom) | (Ext Dom) | 4,595 | 5,748 | 11,050 | 12,036 | 11,865 | 12,836 |
| EGC first year productivity loss cost ($) | 0 | 9,301 | (Ext Dom) | (Ext Dom) | 3,786 | 4,979 | 10,358 | 11,378 | 11,183 | 12,188 |
| EGC 2-5 year treatment cost ($) | 369 | 1,476 | (Ext Dom) | (Ext Dom) | 4,853 | 5,232 | 11,268 | 11,599 | 12,079 | 12,407 |
| EGC 2-5 year productivity loss cost ($) | 0 | 3,825 | (Ext Dom) | (Ext Dom) | 3,671 | 4,979 | 10,236 | 11,378 | 11,058 | 12,188 |
| AGC first year treatment cost ($) | 5,817 | 23,270 | (Ext Dom) | (Ext Dom) | 5,382 | 4,174 | 11,688 | 10,759 | 12,582 | 11,400 |
| AGC first year productivity loss cost ($) | 0 | 18,773 | 6,268 | (Ext Dom) | 6,292 | 4,979 | 12,378 | 11,378 | 13,460 | 12,188 |
| AGC 2-5 year treatment cost ($) | 1,690 | 6,760 | (Ext Dom) | (Ext Dom) | 5,202 | 4,535 | 11,550 | 11,035 | 12,416 | 11,733 |
| AGC 2-5 year productivity loss cost ($) | 0 | 10,398 | 6,303 | (Ext Dom) | 6,400 | 4,979 | 12,435 | 11,378 | 13,590 | 12,188 |
| After 5 year treament cost ($) | 636 | 2,543 | (Ext Dom) | (Ext Dom) | 5,037 | 4,864 | 11,416 | 11,303 | 12,261 | 12,042 |
| After 5 year productivity loss cost ($) | 0 | 5,136 | (Ext Dom) | (Ext Dom) | 5,446 | 4,979 | 11,683 | 11,378 | 12,778 | 12,188 |
| Treatment cost for last one year ($) | 3,980 | 15,921 | (Ext Dom) | (Ext Dom) | 5,261 | 4,417 | 11,639 | 10,857 | 12,423 | 11,718 |
| Productivity loss cost for last 1 year (male) | 0 | 8,049 | (Ext Dom) | (Ext Dom) | 5,548 | 4,979 | - | - | - | - |
| Productivity loss cost for last 1 year female) | 0 | 4,829 | - | - | - | - | 11,695 | 11,378 | 12,474 | 12,188 |
| Endoscopy sensitivity (%) | 59.00% | 98.80% | (Ext Dom) | (Ext Dom) | 5,241 | 4,492 | 11,945 | (Ext Dom) | 13,812 | 10,267 |
| Endoscopy specificity (%) | 96.30% | 100.00% | (Ext Dom) | (Ext Dom) | 5,008 | 4,932 | 11,444 | 11,271 | 12,264 | 12,064 |
| UGI sensitivity (%) | 42.10% | 90.80% | (Ext Dom) | (Ext Dom) | 4,979 | 4,979 | 11,378 | 11,378 | 12,188 | 12,188 |
| UGI specificity (%) | 81.20% | 90.10% | (Ext Dom) | (Ext Dom) | 4,979 | 4,979 | 11,378 | 11,378 | 12,188 | 12,188 |
| Endoscopy compliance (%) | 45.00% | 85.00% | 5,234 | (Ext Dom) | 5,273 | 4,707 | 11,405 | 11,354 | 12,507 | 11,914 |
| UCI compliance (%) | 45.00% | 85.00% | (Ext Dom) | (Ext Dom) | 4,979 | 4,979 | 11,378 | 11,378 | 12,188 | 12,188 |
| 5 yr progression risk from EGC to AGC | 48.10% | 77.90% | (Ext Dom) | (Ext Dom) | 4,958 | 5,067 | 11,575 | 11,277 | 12,271 | 12,123 |
| No screen : EGC proportion | 7% | 39% | (Ext Dom) | (Ext Dom) | 2,067 | 5,237 | 7,475 | 11,714 | 7,592 | 12,606 |
| No screen : AGC proportion | 61% | 93% | (Ext Dom) | (Ext Dom) | 5,237 | 2,067 | 11,714 | 7,475 | 12,606 | 7,592 |
| Screen : EGC proportion | 52% | 86% | 15,349 | (Ext Dom) | 16,021 | 4,622 | 25,762 | 10,884 | 29,096 | 11,640 |
| Screen : AGC proportion | 14% | 48% | (Ext Dom) | 15,349 | 4,622 | 16,021 | 10,884 | 25,762 | 11,640 | 29,096 |
| No screen : survival data (EGC) | 78.2%(5yrs) | 92.6%(5yrs) | (Ext Dom) | (Ext Dom) | 4,729 | 4,981 | 11,035 | 11,381 | 11,418 | 12,194 |
| No screen : survival data (AGC) | 24.5%(5yrs) | 35.1%(10yrs) | (Ext Dom) | (Ext Dom) | 6,290 | 4,577 | 11,912 | 11,243 | 12,647 | 12,082 |
| Screen : survival data (EGC) | 93.9%(5yrs) | 98.4%(5yrs) | (Ext Dom) | (Ext Dom) | 5,099 | 4,845 | 11,595 | 11,134 | 12,481 | 11,862 |
| Screen : survival data (AGC) | 60.1%(5yrs) | 61.8%(10yrs) | (Ext Dom) | (Ext Dom) | 4,817 | 5,393 | 11,322 | 11,507 | 12,155 | 12,260 |
| EGC symptom develop probability | 10% | 40% | (Ext Dom) | (Ext Dom) | 4,676 | 5,149 | 10,655 | 11,784 | 11,302 | 12,684 |
| AGC symptom develop probability | 56% | 90% | (Ext Dom) | (Ext Dom) | 5,424 | 2,776 | 11,705 | 9,759 | 12,528 | 10,526 |
| Normal utility (QALY) | 0.782 | 0.918 | (Ext Dom) | (Ext Dom) | 4,979 | 4,979 | 11,378 | 11,378 | 12,188 | 12,188 |
| EGC utility (QALY) | 0.65 | 0.85 | (Ext Dom) | (Ext Dom) | 6,551 | 4,698 | 14,817 | 10,755 | 16,009 | 11,502 |
| AGC utility (QALY) | 0.17 | 0.7 | (Ext Dom) | (Ext Dom) | 4,368 | 5,483 | 10,213 | 12,300 | 10,729 | 13,383 |
| Discount rate (%) | 1% | 5% | (Ext Dom) | (Ext Dom) | 3,544 | 6,791 | 8,393 | 15,141 | 8,922 | 16,322 |

Note: Sensitivity analysis was performed to cover the widest reasonable range of variables in the literature; ICER, incremental cost effectiveness ratio; Min, minimum value; Max, maximum value; Ext Dom, extended dominated; UGI, upper-gastrointestinal x-ray; EGC, early gastric cancer; AGC, advanced gastric cancer; QALY, quality-adjusted life year.

The cost for a woman in the unscreened population was $774, and the effect was 23.810 QALY. Compared to the no screening alternative, the ICER of the endoscopic screening alternative with a 2-year interval from the age of 40 to 80 for females, which is one of the national guidelines for gastric cancer screening, was $13,892/QALY. Compared to the no screening alternative, the ICER of UGI series from the age of 40 to 80 with a 2-year interval for the female population was estimated to be $16,844/QALY. The 2-year-interval endoscopic screening of Korean women from the age of 50 to 80 was the most cost-effective screening strategy for the defined willingness-to-pay threshold (Figure 2). The ICER of this strategy over no screening was $11,378/QALY.

*Sensitivity analysis*

One-way sensitivity analyses were performed with a maximum value and minimum value for each parameter, with discounting rates of 1 and 5% and varying the screening and treatment costs by 50 or 200%. Cost-effectiveness was most sensitive to the cost of endoscopic screening or UGI series and the distribution of cancer stage at screening (Table 2). When the cost of endoscopic screening was doubled, the most cost-effective alternative for males was UGI series screening with a 2-year interval from the age of 50 to 80, and compared to the no screening alternative, the ICER of that strategy was $6558/QALY. In the same condition for females, the UGI series screening with a 2-year interval from the age of 50 to 80 was the most cost-effective alternative, and the ICER of this strategy was $14,733/QALY compared to the no screening alternative. The cost-effectiveness ratio of gastric cancer screening from ages 50 to 80 using endoscopy appeared to be acceptable as a public policy.

## Discussion

The NCS program was started in Korea under an initiative of the Ministry of Health and Welfare (Ministry of Health and Welfare Republic of Korea, 2004). However, there is a paucity of information regarding the cost-effectiveness of a mass screening program for gastric cancer using endoscopy or UGI series. Therefore, this research evaluated the cost and utility of mass gastric cancer screening programs to help plan gastric cancer screening strategies.

World Health Organization choosing interventions that are cost effective (WHO-CHOICE) suggested the very cost-effective threshold would be less than gross domestic product income per capita in relevant population(World Health Organization, 2001). Using this threshold of $19,162 per person in Korea (2008) (International Monetary Fund (IMF), 2011), the mass screening strategy of endoscopy for both men and women over 50 is very cost-effective in Korea. In our base case model, we demonstrated that gastric cancer screening from the age of 50 to 80 in males via annual endoscopy is the most cost-effective with an ICER of $4979/QALY. The ICER of the screening strategy for women from the age of 50 to 80 using biennial endoscopy was $11,378/QALY. Based on our results, the optimal age (40 years old) to initiate screening should be reconsidered, as the cost-effectiveness was improved for older people because the incidence of gastric cancer increases rapidly with increasing age.

A previous study in Japan demonstrated that an indirect X-ray method ($29) was more cost-effective than direct radiography ($96) and endoscopy ($80) in 1995 (Babazono & Hillman, 1995). This study also reported that screening 40-year-old men and women was less cost-effective than beginning screening at the age of 50, consisting with our findings. The cost of endoscopy may be different in different countries: $80 in Japan (1995), approximately $150 (2006) in Singapore, and approximately $300 (2006) in the USA. These costs were almost 3- to 9-fold higher than that in Korea. Endoscopic screening exhibited more sensitivity and specificity than UGI series in Korea, with a positive predictive value of 98-99.8% (Kim et al., 2000). Although UGI series may have clinical utility as an alternative method of gastric cancer screening and endoscopy has a weakness in terms of discomfort during the procedure, UGI series strategies were dominated by endoscopic screening strategies in our results. Thus, in our model, endoscopy is more cost-effective than UGI series despite their approximately equal costs. Endoscopy appears to be optimal as the first-line method for gastric cancer screening in Korea. Our results recommend that the current national guideline for the use of UGI series to screen people 40 years old or older should be re-evaluated in Korea.

The costs, availability, and accessibility of endoscopy are very different in different countries. Although endoscopy is widely available in major cities in China, its availability and accessibility are limited in rural areas (Leung et al., 2008). By contrast, mass screening using endoscopy was reported to be unfeasible in Japan because of a lack of experienced endoscopists and the insufficient governmental support system (Leung et al., 2008). A study in Singapore suggested endoscopic screening only for moderate-to-high-risk groups (Yeh et al., 2010). The cost of endoscopy is the major modifiable factor that affects the cost-effectiveness of a screening program. As this study is a country-specific economic evaluation, the interpretation and generalization of our results to other countries should be cautiously approached. Whether such mass screening programs for gastric cancer using endoscopy or UGI series are cost-effective and actually reduce the mortality of gastric cancer in other countries remains to be researched.

We made conservative estimates to decrease the bias relative to the screened group. For example, previous research reported that repetitive cancer screening increases the likelihood of detecting EGC; however, we applied the same gastric cancer stage distribution in the screening arms. In reality, some cases of EGC can be treated via endoscopic mucosal resection, which would result in lower costs and a higher quality of life (Probst et al., 2009). The costs of treatment according to cancer stage were assumed to be similar without considering whether screening was performed.

Several limitations for this research should be mentioned. First, the results of this study were produced by a computer simulation program, which uses many assumptions. For instance, effectiveness data were obtained from reports from others (Dan et al., 2006; Hanmer et al., 2006). However, to qualify the uncertainty of the utility of the health status, we analyzed sensitivity over a wide range of effectiveness. Second, the infrastructure for mass gastric cancer screening is already in place in Korea, so the cost of installing a screening program was not considered in this research. However, if a new gastric cancer screening program is implemented by a government, the cost of establishing the basic infrastructure should be considered. In addition, the cost of lost productivity per case of gastric cancer should be considered from the societal or national perspectives of the patient group. In this study, the outcomes were not considered heterogeneous in regards to economic status, which requires additional study. Finally, the additional changes in the cost-effectiveness due to examining the incidence of reflux esophagitis, gastritis, and *Helicobacter pylori* infection (Gersonet al., 2004) which can be detected coincidently by these gastric cancer screening strategies, were not considered. However, we do not believe that including these factors would significantly change the risks according to the use of screening.

Screening for gastric cancer using endoscopy from ages 50 to 80 may be very cost-effective in the Korean population. The cost-effectiveness of gastric cancer screening was most sensitive to the cost of endoscopic screening and the distribution of cancer stage diagnosis. It is important that policymakers monitor the cost-effectiveness of several alternatives according to gender, starting age of screening, screening interval, and screening method. Additional studies are needed to confirm these findings before a widespread change in clinical practice can be recommended.

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