Original Article

Cost savings in colonoscopy with artificial intelligence-aided polyp diagnosis: an add-on analysis of a clinical trial

Running title: Cost reduction for colonoscopy using AI

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Conflict of interest disclosure

YM, SK, and MM are inventors of the patented "Image-processing instrument and method" (No. 6059271 in Japan), with inventors' premiums paid by Showa University. YM and MM have received speaking honoraria from Olympus Corp. AR have received a research grant from Olympus Corp. AR is the consultant of Cook Medical and Boston Scientific Corp. KM received research funding from Cybernet Corp. JEE: consultant/shareholder Satisfai Health. None of the other authors have conflicts of interest relating to the present study.

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ABSTRACT

Background and Aims: Artificial intelligence (AI) is being implemented into colonoscopy practice, but no study has investigated whether AI is cost-saving. We quantified the cost reduction from using AI as an aid in the optical diagnosis of colorectal polyps.

Methods: This study is an add-on analysis of a clinical trial that investigated the performance of AI for differentiating colorectal polyps (i.e., neoplastic versus non-neoplastic). We included all patients with diminutive (≤5 mm) rectosigmoid polyp for analyses. The average colonoscopy cost was compared for two scenarios: A) a diagnose-and-leave strategy supported by the AI prediction (i.e., diminutive rectosigmoid polyps were not removed when predicted as non-neoplastic), B) a resect-all-polyps strategy. Gross annual costs for colonoscopies were also calculated based on numbers and reimbursement of colonoscopies conducted under public health insurances in four countries.

Results: Overall, 207 patients with 250 diminutive rectosigmoid polyps (104 neoplastic, 144 non-neoplastic, and two indeterminate) were included. AI correctly differentiated neoplastic polyps with 93.3% sensitivity, 95.2% specificity, and 95.2% negative predictive value. Thus, 105 polyps were removed while 145 were left under the diagnose-and-leave strategy, which was estimated to reduce the average colonoscopy cost and the gross annual reimbursement for colonoscopies by 18.9% and 149.2 million dollars in Japan, 6.9% and 12.3 million dollars in England, 7.6% and 1.1 million dollars in Norway, and 10.9% and 85.2 million dollars in the United States, respectively, compared to the resect-all-polyps strategy.

Conclusions: The use of AI to enable the diagnose-and-leave strategy results in substantial cost reductions for colonoscopy.

KEY WORDS

Cost effectiveness, endocytoscopy, optical biopsy, computer-aided diagnosis, computer-aided detection

INTRODUCTION

Colonoscopy screening decreases the incidence and mortality of colorectal cancer and is implemented in many countries[1-3]. The main benefits of colonoscopy screening are based on its ability to detect and remove neoplastic, premalignant colorectal polyps. A challenge of colonoscopy is its limited ability to adequately distinguish between neoplastic and non-neoplastic polyps, especially when they are small in size. Therefore, with conventional colonoscopy today, many polyps are removed which could have been left in situ with better tools to distinguish between neoplastic and non-neoplastic lesions. Current practice of removing all polyps is resource-demanding, cost-driving, and increases the risk of complications and adverse events.

To address this challenge, the use of artificial intelligence for optimal polyp diagnosis and classification into neoplastic versus non-neoplastic polyps is catching considerable attention [4-7]. We have recently shown that a real-time AI tool can distinguish neoplastic from non-neoplastic diminutive (≤5 mm) polyps during colonoscopy compared with pathologic diagnosis[8] and multiple studies reported that the performance of AI for optical diagnosis for diminutive adenomas exceeded the negative predictive values (NPV) of 90%, meeting the consensus threshold for a diagnose-and-leave strategy for rectosigmoid polyps known as the Preservation and

Incorporation of Valuable Endoscopic Innovations-2 (PIVI-2) threshold [7-18]. Furthermore, several AI tools for colonoscopy have been approved by regulatory bodies [12, 19, 20]. However, the use of AI for optical diagnosis is not widespread, partly because there is no reimbursement from the public payers or health insurance systems due to lack of evidence regarding the AI's cost-saving.

The present study is the first to quantify the cost reduction attained from AI combined with the diagnose-and-leave strategy in colonoscopy. We used actual data obtained from a clinical trial for the cost calculation to avoid making misleading assumptions.

MATERIALS AND METHODS

Study design

This is an add-on analysis of a previously conducted large-scale single-center clinical trial that investigated 791 patients with real-time use of AI to predict the pathology of diminutive colorectal polyps [8]. Figure 1 and Video 1 illustrates how the AI tool (EndoBRAIN, Cybernet System Corp. and Olympus Corp., Tokyo) works. It was designed to output a prediction of either neoplastic or non-neoplastic for polyps visualized during routine colonoscopy with the use of endocytoscopy (×520 ultra-magnification colonoscopes providing microvascular visualization under narrow-band imaging [NBI]; H290ECI, Olympus Corp., Tokyo). The NPV of the AI system for identifying diminutive rectosigmoid adenomas, which was the primary endpoint, was 95.2% (95% confidence interval [CI] 90.3% to 98.0%) under the most conservative scenario. The present study included all patients from the clinical trial, who had at least one diminutive (≤ 5mm) rectosigmoid polyp that was removed after AI assessment.

Outcome measures

The average cost of colonoscopy including pathological assessment was calculated according to the two scenarios described below. The main outcome measures were the reduction in cost per colonoscopy, and in the gross annual reimbursement for colonoscopies in Japan, England, Norway, and the United States.

Scenarios for polyp management

For the estimations of cost reductions from the use of AI in colonoscopy, the two following scenarios were compared: A) Use of AI combined with a diagnose-and-leave strategy; B) No use of AI; resect-all-polyps strategy.

In the former scenario, diminutive rectosigmoid polyps that were predicted as non-neoplastic by the AI system were assumed not to be removed but left in situ, while all remaining polyps were assumed to be removed. In the latter scenario, all polyps were assumed to be removed.

Costs

We calculated the average costs per colonoscopy including pathological assessment of polyps based on the reimbursement rates of the public insurance systems of Japan, England (National Health Service [NHS]), Norway, and the US (Medicare). We examined the raw data from the clinical trial regarding the number, distribution, size, and AI prediction of polyps to figure out the cost of each colonoscopy of all the subject under both the diagnose-and-leave strategy supported by the AI prediction and the resect-all-polyps strategy, which were used to calculate the average cost per colonoscopy. Additional costs for anesthesia or sedation were not included. In this study, we did not account for the need to re-evaluate the left polyps at a shorter interval under the diagnose-and-leave strategy, which may require additional costs and time.

Supplementary Tables 1, 2, 3, and 4 illustrate the reimbursement rates used for the cost calculation for the four countries. Based on the calculated average cost per colonoscopy, gross annual reimbursement for colonoscopies per country was calculated using updated annual number of colonoscopies under public insurance systems (3,636,623 in Japan in 2014 [21], 693,000 in England in 2017[22], 95,000 in Norway in 2018[23], and 1,972,424 in the US in 2015[24]), prevalence of diminutive rectosigmoid polyps in the clinical trial (34.3% (271/791) of colonoscopies [8]), and assuming that AI was implemented in 100% of colonoscopy procedures. (e.g., Gross annual reimbursement for colonoscopies in Japan was calculated as follows: [Average colonoscopy cost]×3,636,623×0.343×1.00)

Implementation cost of the AI tool

The initial purchase fee, implementation fee, and annual maintenance fee of EndoBRAIN for an endoscopy unit in Japan were 46,119 dollars, 1,820 dollars, and 1,092 dollars, respectively (sum: 49,031 dollars). Assuming the use of EndoBRAIN on 1,000 cases annually for 5 consecutive years, its per-colonoscopy cost would be 10 dollars. This cost calculation in consideration of the fees required to implement the AI tool was conducted only for the Japanese simulation because EndoBRAIN is currently available only in Japan and has a fixed price.

Study registration and ethics

The ethics committee of Showa University Northern Yokohama Hospital approved the original clinical trial protocol on 10th May, 2017 and the present add-on analysis on 16th January, 2020 (No. 17H011; available as Supplementary document 1). The trial was registered as a UMIN clinical trial (UMIN000027360, registered on May 16th 2017). All patients gave informed consent for participation. The study was conducted in accordance with the Helsinki Declaration.

Statistical analysis

Statistical analyses of the main outcome measures were based on the worst case scenario. In the worst-case scenario, polyps lacking either AI diagnosis or pathology were treated as false-positive or -negative. Measures of sensitivity, specificity, and NPV are expressed with 95% CI using an exact binomial method (command “binom.test” in R). As all continuous variables were non-normally distributed, they are expressed as medians [interquartile range (IQR)]. All statistical analyses were performed using R version 3.4.1. (The R Foundation for Statistical Computing. http://www.R-project.org/. Accessed June 30, 2017).

RESULTS

Patient and polyp characteristics

A total of 207 patients with 250 diminutive rectosigmoid polyps removed after assessment with AI were included in the study. The median age was 67 years (IQR 59–73 years), with 152 being male and 55 female. The indications for colonoscopy were surveillance after polypectomy (75 patients), diagnostic colonoscopy (68 patients), therapeutic colonoscopy for polyps larger than 5 mm (38 patients), screening colonoscopy (25 patients), and one other reason. The 250 polyps had a median size of 3 mm (IQR 2–4 mm). Based on histopathologic assessment after removal, 104 polyps were neoplastic, 144 were non-neoplastic, and two were indeterminate due to missing of specimens. One hundred and thirteen polyps were located in the rectum and 137 in the sigmoid colon. Analysis of their morphologies according to the Paris classification showed that 198 were type IIa, 46 type Is, and 6 type Ip [25].

Performance of AI in identification of polyps

Table 1 shows the performance of AI in identifying neoplastic change in 250 diminutive rectosigmoid polyps. AI differentiated diminutive neoplastic rectosigmoid polyps with sensitivity 93.3% (95% CI 86.7%–97.3%), specificity 95.2% (90.3%–98.0%), and an NPV of 95.2% (90.3%–98.0%). Under the diagnose-and-leave strategy supported by AI-based optical diagnosis, 105 polyps would have been removed, while 145 would have been left. This would have resulted in 58.0% (51.6%–64.1%) reduction of polyp removal.

Cost reduction from the use of AI

Table 2 and Figure 3 illustrate the results of calculation of the average colonoscopy cost and gross annual reimbursement for colonoscopies in the four countries under the two strategies. In Japan, the average colonoscopy cost under the diagnose-and-leave strategy (supported by AI prediction) was 119 dollars lower than that under the resect-all-polyps strategy (515 dollars versus 634 dollars), in consideration of the implementation cost of the AI tool. The expected gross annual reimbursement savings for colonoscopies would be 149,220,133 dollars.

In England, the colonoscopy cost under the diagnose-and-leave strategy was 52 dollars lower than that under the resect-all-polyps strategy 701 dollars versus 753 dollars) based on NHS reimbursement rates. The expected gross annual reimbursement savings for colonoscopies would be 12,360,348 dollars.

In Norway, the colonoscopy cost under the diagnose-and-leave strategy was $34 lower than that under the resect-all-polyps strategy (414 dollars versus 448 dollars). The expected gross annual reimbursement savings for colonoscopies would be 1,114,733 dollars.

In the US, the colonoscopy cost under the diagnose-and-leave strategy was 125 dollars lower than that under the resect-all-polyps strategy (1,020 dollars versus 1,246 dollars) based on Medicare reimbursement rates. The expected gross annual reimbursement savings for colonoscopies would be 85,244,220 dollars.

Overall, the diagnose-and-leave strategy was calculated to reduce the gross annual reimbursement for colonoscopies by up to 18.9%, 6.9%, 7.6%, and 10.9% in Japan, England, Norway, and the US, respectively (Figure 3).

DISCUSSION

This is the first study to analyze cost reductions resulting from the use of AI combined with the diagnose-and-leave strategy for diminutive colorectal polyps based on the real data obtained from a prospective trial. The study results showed that the use of AI could save 119 dollars, 52 dollars, 34 dollars, and 125 dollars per colonoscopy, and up to 149.2 million dollars, 12.4 million dollars, 1.1 million dollars, and 85.2 dollars for the gross annual reimbursement for colonoscopies conducted under public health insurances in Japan, England, Norway, and the United States, respectively. Given that the required cost of AI implementation (10 dollars) was much lower than the reduced per-colonoscopy cost (129 dollars) in Japan, and as the AI tool had performance exceeding the threshold proposed in the PIVI-2 initiative, we consider that clinical implementation of AI-assisted optical biopsy should be encouraged, together with reimbursement support from public/private health insurance bodies under a fee-per-use scenario.

The clinical application of optical diagnosis for diminutive polyps is increasingly being endorsed because it will save a large amount of money being spent on needless polypectomies and pathological examinations [26-28]. The National Institute for Clinical and Healthcare Excellence (NICE), which defines clinical standards in England and Wales, officially approved the optical diagnosis of diminutive colorectal polyps with the use of narrow-spectrum endoscopy in 2017, moving us a significant step forward towards its implementation in clinical practice [29]. However, this clinical procedure has not yet been widely adopted, mainly because of a lack of accuracy in non-experts. We, however, consider the use of AI to be a solution to overcome this unfavorable situation; AI can guarantee standardization in the quality of optical diagnosis, consequently accelerating dissemination of the PIVI and NICE implementations, which will ultimately contribute to a considerable cost reduction for colonoscopy. Moreover, the recently published guideline of the British Society of Gastroenterology considered narrowing the subject of the optical diagnosis; “DISCARD-lite”, one of the encouraged strategies, targets only diminutive rectosigmoid polyps for optical diagnosis, which are exactly the same subjects of the present study[30, 31].

The strength of the present study is that we used actual data to calculate the estimated cost reduction, rather than constructing a microsimulation model. This helped avoid having to make a large number of assumptions, which could sometimes mislead study results. In the present study, we did not evaluate the cost-effectiveness of the AI tool, but focused mainly on the cost reduction, because the AI model could be assumed to have encouraging effectiveness (i.e., > 90% NPV for diminutive rectosigmoid adenomas) according to the previous prospective study [8].

This study has several limitations. First, we did not analyze the cost reduction from the use of AI in a resect-and-discard strategy (known as PIVI-1), which is estimated to be much greater than that from the diagnose-and-leave strategy, although very few endoscopists are actually adopting the PIVI-1 strategy. Such an analysis would be challenging, because AI-based prediction of the surveillance interval was not evaluated in the original prospective study [8]. Cost reduction under that strategy will be clarified in the ongoing international trial (UMINUMIN000035213), in which AI-assisted prediction of the surveillance interval is assessed as one of the outcome measures. Second, we did not separately evaluate the cost reductions resulting from AI and the diagnose-and-leave strategy, but instead performed a comprehensive analysis on the use of AI combined with the diagnose-and-leave strategy. This is because the diagnose-and-leave strategy alone cannot be widely implemented into practice because of the low performance of non-experts (in the original clinical trial, the non-experts' NPV for diminutive rectosigmoid adenomas was limited to 86.6% [82.1%–90.3%], which is in line with the results of a previous meta-analysis [32]). We believe that the combination of AI plus the diagnose-and-leave strategy as a comprehensive measure will solve the current problems of optical diagnosis. Thirdly, we investigated the cost reduction of colonoscopies conducted exclusively under public insurance systems, thus the amount of cost reduction could vary in consideration of procedures conducted under private insurance or without any insurance support. Fourth, we may have overestimated the AI performance described in the present study, which is a primary outcome measure of the initial study[8]. Post hoc analysis of the initial study revealed that the NPV of the AI tool was 91.4% (95% confidence interval, 85.7%–95.3%) when considering the presence of sessile serrated lesions (SSLs), which was a bit worse than the primary outcome measure of the initial study (95.2 % [90.3%–98.0%] NPV), in which the analysis of SSLs was excluded. However, we cited the data of the primary endpoint because the results of the primary endpoint were considered more reliable than those of the post hoc analysis. Fifth, the present study's data came from a single-center study, which can over-value the effects of the AI tool. To clarify the efficacy of AI in non-specialized settings, an international multicenter trial has been ongoing (UMINUMIN000035213). Finally, the endoscope used in the present study was an endocytoscope, which has lower availability than normal endoscopes, and may hinder the translation of our study results into routine practice. However, previous studies [7, 9] showed that AI tools designed for normal colonoscopes provided performance as excellent as that achieved with endocytoscopes, and therefore, the study results regarding the cost reduction could be generalized to other AI-colonoscopy tools.

In conclusion, use of AI combined with the diagnose-and-leave strategy can result in substantial cost reductions for colonoscopy. Considering that this technology provides even non-experts with the chance to achieve high-quality optical diagnosis, clinical implementation of this technology should be endorsed both on the clinical side and by public/private health insurance bodies.

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FIGURE LEGENDS

Figure 1 (A, B): A diminutive hyperplastic polyp (A) was predicted as having a 73% probability of being non-neoplastic by the artificial intelligence system (B) (EndoBRAIN, Cybernet Corp. Tokyo). EndoBRAIN works in conjunction with endocytoscopy (520-fold contact endomicroscopy; CF-H290ECI, Olympus Corp. Tokyo) combined with narrow-band imaging.

Figure 2: Overview of the study design. The average cost per colonoscopy was calculated under two scenarios; A) A diagnose-and-leave strategy supported by the artificial intelligence (AI) prediction; 2) a resect-all-polyps strategy.

Figure 3: Estimated gross annual reimbursement for colonoscopies under the diagnose-and-leave strategy supported by the artificial intelligence (AI) prediction and the resect-all-polyps strategy in Japan, England, Norway, and the United States. A percentage of the cost reduction by the use of AI in each country is also shown.

VIDEO LEGEND

Video 1: Multiple polyps diagnosed with the aid of artificial intelligence (AI). The AI tool (EndoBRAIN, Cybernet System Corp., Tokyo) automatically output the predicted pathology of the targeted polyp when an endoscopist contact the polyp with the tip of the endocytoscope (CF-H290ECI, Olympus Corp., Tokyo) and pushed the capture button of the endoscope. It correctly predicted the pathology of the first polyp as non-neoplastic with the probability of 91% and the second polyp as neoplastic with the probability of 99%.

TABLES

Table 1. Pathologic prediction of artificial intelligence for diminutive polyps in the rectosigmoid colon

	Pathology		
	Neoplastic polyps	Non-neoplastic polyps	Missing specimens
	N=104	N=144	N=2
Pathological prediction by AI			
Neoplastic	98	6	1
Non-neoplastic	5	138	1
Non-analyzable	1	0	0

Note. Values are numbers. AI, artificial intelligence

Table 2. Estimated average cost per colonoscopy and gross annual reimbursement for colonoscopies based on the diagnose-and-leave strategy supported by the AI prediction and the resect-all-polyps strategy in Japan, England, Norway, and the United States.

	Japan [dollars (yen)]		England [dollars (pounds)]		Norway [dollars (Norwegian krone)]		United States [dollars]	
	Average cost per colonoscopy	Gross annual reimbursement for colonoscopies	Average cost per colonoscopy	Gross annual reimbursement for colonoscopies	Average cost per colonoscopy	Gross annual reimbursement for colonoscopies	Average cost per colonoscopy	Gross annual reimbursement for colonoscopies
Resect-all-polyps strategy	634 (69,688)	791,027,887 (86,926,141,383)	753 (579)	178,916,037 (128,119,761)	448 (4076)	14,609,811 (132,816,460)	1,146	775,316,481
Diagnose-and-leave strategy supported by the AI prediction	*515 (56,542)	641,807,754 (70,528,324,619)	701 (539)	166,555,689 (137,627,721)	414 (3765)	13,495,078 (122,682,525)	1,020	690,072,261
Cost reduction by adopting the diagnose-and-leave strategy supported by the AI prediction	119 (13,146)	149,220,133 (16,397,816,764)	52 (40)	12,360,348 (9,507,960)	34 (311)	1,114,733 (10,133,935)	125	85,244,220

Note: Values are expressed in dollars (local currency). Gross annual reimbursement for colonoscopies in the whole national population was predicted assuming that: 1) the annual number of colonoscopies under public insurance systems was 3,636,623 in Japan in 2014 [21], 693,000 in England in 2017[22], 95,000 in Norway in 2018, and 1,972,424 in the United States in 2015[24], 2) diminutive rectosigmoid polyps would be found in 34.3% (271/791) of colonoscopies [8], and 3) artificial intelligence was implemented in 100% of colonoscopy procedures. * The cost calculation in consideration of the fees required to implement the AI tool was conducted only for the Japanese simulation because EndoBRAIN is currently available only in Japan and has a fixed price. AI, artificial intelligence

Supplementary Table 1: Reimbursement rates of procedures related to colonoscopy under the Japanese public insurance system.[34]

Procedures related to colonoscopy	Reimbursement rates (yen)
Colonoscopy without polyp removal	15,500
Additional fee for the use of magnifying narrow-spectrum imaging	2,000
Colonoscopy with removal of polyps < 20mm	50,000 (regardless of the number of removed lesions)
Colonoscopy with removal of polyps ≥ 20mm	70,000 (regardless of the number of removed lesions)
Preparation of pathological specimens	8,600 (*per anatomical section)
Pathological diagnosis	4,500 (regardless of number of specimens)

Note: *Colorectum is divided into four anatomical sections: 1. Cecum, 2. Ascending colon, transverse colon, and descending colon, 3. Sigmoid colon, and 4. Rectum. Cost for preparation of pathological specimens are multiplied according to the number of anatomical sections where removed polyps are found.

Supplementary Table 2: Reimbursement rates of procedures related to colonoscopy under the National Health Service insurance system in England.[35]

Procedures related to colonoscopy	Reimbursement rates (pounds)
Colonoscopy without polypectomy	451
Colonoscopy with polypectomy	*579

Note: *The total cost for polypectomy including the cost for pathological diagnosis is included in the colonoscopy procedure fee.

Supplementary Table 3: Reimbursement rates of procedures related to colonoscopy under the Medicare insurance system in Norway

Procedures related to colonoscopy	Reimbursement rates (Norwegian krone)
Colonoscopy without polypectomy	3,069
Colonoscopy with polypectomy	*4,076

Note: *Cost for pathological diagnosis is included in the colonoscopy procedure fee.

Supplementary Table 4: Reimbursement rates of procedures related to colonoscopy under the Medicare insurance system in the United States.[36]

Procedures related to colonoscopy	Reimbursement rates (dollars)
Colonoscopy without polypectomy	*748.84
Colonoscopy with polypectomy	*996.98
Cost for pathological diagnosis per specimen	70.28

Note: *Cost per colonoscopy was calculated assuming 47.3% of colonoscopies are done in ambulatory surgery centers, 49.4% of colonoscopies are done in outpatient hospitals, and 3.3% of colonoscopies are done in physician offices. [25, 36]

Figure 1 (A, B): A diminutive hyperplastic polyp (A) was predicted as having a 73% probability of being non-neoplastic by the artificial intelligence system (B) (EndoBRAIN, Cybernet Corp. Tokyo). EndoBRAIN works in conjunction with endocytoscopy (520-fold contact endomicroscopy; CF-H290ECI, Olympus Corp. Tokyo) combined with narrow-band imaging.

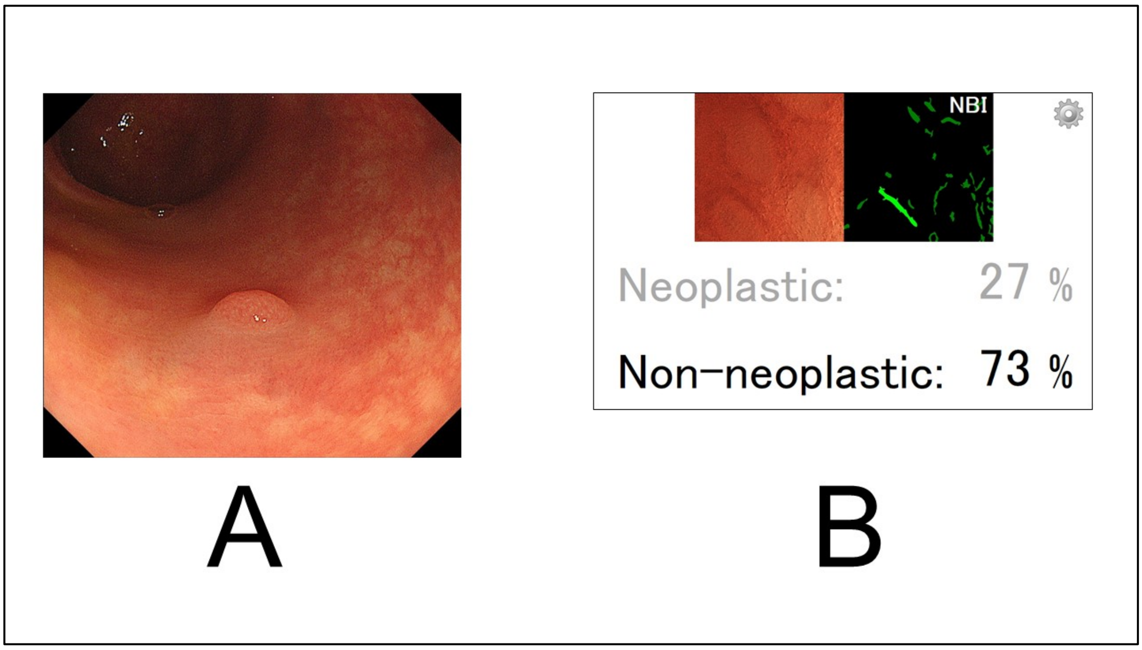

Figure 2: Overview of the study design. The average cost per colonoscopy was calculated under two scenarios; A) A diagnose-and-leave strategy supported by the artificial intelligence (AI) prediction; 2) a resect-all-polyps strategy.

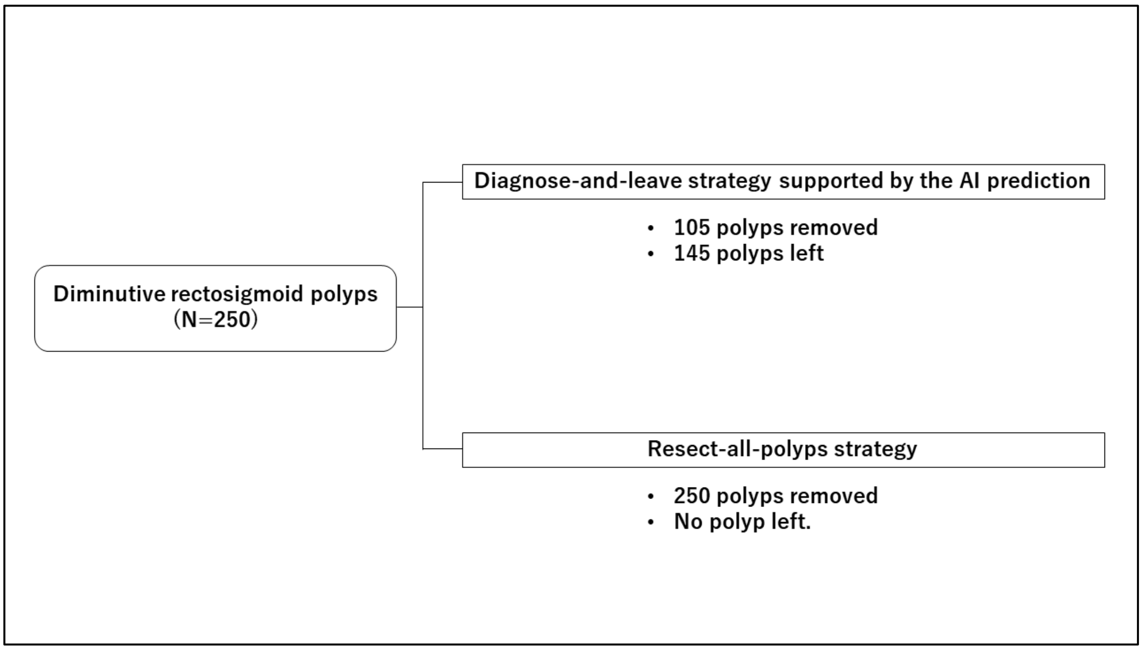

Figure 3: Estimated gross annual reimbursement for colonoscopies under the diagnose-and-leave strategy supported by the artificial intelligence (AI) prediction and the resect-all-polyps strategy in Japan, England, Norway, and the United States. A percentage of the cost reduction by the use of AI in each country is also shown.