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Summary

Background Artificial intelligence (AI) tools increase detection of precancerous polyps during colonoscopy and might contribute to long-term colorectal cancer prevention. The aim of the study was to investigate the incremental effect of the implementation of AI detection tools in screening colonoscopy on colorectal cancer incidence and mortality, and the cost-effectiveness of such tools.

Methods We conducted Markov model microsimulation of using colonoscopy with and without AI for colorectal cancer screening for individuals at average risk (no personal or family history of colorectal cancer, adenomas, inflammatory bowel disease, or hereditary colorectal cancer syndrome). We ran the microsimulation in a hypothetical cohort of 100 000 individuals in the USA aged 50–100 years. The primary analysis investigated screening colonoscopy with versus without AI every 10 years starting at age 50 years and finishing at age 80 years, with follow-up until age 100 years, assuming 60% screening population uptake. In secondary analyses, we modelled once-in-life screening colonoscopy at age 65 years in adults aged 50–79 years at average risk for colorectal cancer. Post-polypectomy surveillance followed the simplified current guideline. Costs of AI tools and cost for downstream treatment of screening detected disease were estimated with 3% annual discount rates. The main outcome measures included the incremental effect of AI-assisted colonoscopy versus standard (no-AI) colonoscopy on colorectal cancer incidence and mortality, and cost-effectiveness of screening projected for the average risk screening US population.

Findings In the primary analyses, compared with no screening, the relative reduction of colorectal cancer incidence with screening colonoscopy without AI tools was 44·2% and with screening colonoscopy with AI tools was 48·9% (4·8% incremental gain). Compared with no screening, the relative reduction in colorectal cancer mortality with screening colonoscopy with no AI was 48·7% and with screening colonoscopy with AI was 52·3% (3·6% incremental gain). AI detection tools decreased the discounted costs per screened individual from $3400 to $3343 (a saving of $57 per individual). Results were similar in the secondary analyses modelling once-in-life colonoscopy. At the US population level, the implementation of AI detection during screening colonoscopy resulted in yearly additional prevention of 7194 colorectal cancer cases and 2089 related deaths, and a yearly saving of US$290 million.

Interpretation Our findings suggest that implementation of AI detection tools in screening colonoscopy is a cost-saving strategy to further prevent colorectal cancer incidence and mortality.

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Introduction

In the USA, colorectal cancer has the second highest incidence of all cancers, is the third leading cause of cancer-related death,[1,2] and contributes to substantial economic and patient burden for therapy and palliative care.[3]

Screening colonoscopy with removal of colorectal polyps every 10 years from age 50 years reduces colorectal cancer incidence and mortality.[4] Approximately 60% of eligible people in the USA are currently up to date with colorectal cancer screening.[5–9] Screening colonoscopy is costly and resource-demanding, but has been deemed cost-effective due to savings related to cancer treatment.[5–8,10,11]

The effect of screening colonoscopy on colorectal cancer prevention is strongly related to the detection of cancer and premalignant polyps and adenomas.[12–14] Adenoma detection rates (ADRs) of individual endoscopists are a strong predictor of cancer prevention.[15] Intensive endoscopist training might increase polyp detection and thus contribute to benefit of screening colonoscopy, but such training is time and resource demanding, and costly.[16]

Recently developed artificial intelligence (AI) software tools aim at guiding endoscopists to identify polyps during colonoscopy by real-time pattern recognition, similar to face-recognition applications (figure 1A).[17] Use of AI primarily increases identification of colorectal polyps, including adenomas. This increase will lead to an additional cost for polypectomies and post-polypectomy surveillance. On the other hand, the increment of the

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See Online for appendix

Research in context

Evidence before this study

We searched PubMed for peer-reviewed original articles in English published between Jan 1, 1966, and May 31, 2020, with keywords "artificial intelligence", "cost-effectiveness", and "colonoscopy". We found a meta-analysis of five randomised controlled trials, which showed that the adoption of artificial intelligence (AI) for detecting polyps during colonoscopy was associated with a 1·44 times relative increase in the adenoma detection rate. We did not find any cost-effectiveness analyses of AI polyp detection.

Added value of this study

To our knowledge, this is the first cost-effectiveness analysis of polyp detection by AI in a colorectal cancer screening scenario, evaluating the costs of this new technology and its health benefits regarding cancer prevention. Our microsimulation model indicates that polyp detection aids during screening colonoscopy might be cost-effective to reduce incidence and mortality of colorectal cancer.

Implications of all the available evidence

Integration of AI detection tools in screening colonoscopy might be considered an attractive option to further increase screening efficacy and reduce costs, but confirmation with long-term data is needed.

ADR will result in more effective cancer prevention with less financial burden for cancer treatment. Preliminary evidence has shown that the use of AI increases ADR by 1·44 times. Furthermore, using AI was shown to increase the number of adenomas per colonoscopy (APC), irrespective of adenoma size; APC increased with a relative risk (RR) of 1·69 (95% CI 1·48–1·84) for diminutive polyps 5 mm or smaller, RR 1·44 (1·19–1·75) for small 6–9 mm polyps, and RR 1·46 (1·04–2·06) for large polyps 10 mm or larger.[17] However, the effect of polyp detection and removal on colorectal cancer incidence and mortality is unknown.

Implementation of AI detection tools for screening colonoscopy requires substantial costs and might lead to an eventual excess of polypectomies and surveillance colonoscopies due to the improved adenoma detection, which might not be balanced by improved cancer prevention (figure 1B).[18] Thus, it is important to investigate the incremental benefits and the incremental burden and costs of AI-assisted detection in screening colonoscopy. To this end, we constructed a microsimulation model to assess the incremental effect of AI implementation on long-term colorectal cancer incidence and mortality, and the related incremental costs of such implementation in the USA.

Methods

Model structure and cohort

We constructed a Markov model with 1-year cycles and simulated on a hypothetical cohort of 100 000 US individuals at average risk for colorectal cancer (no personal or family history of colorectal cancer, adenomas, inflammatory bowel disease, or hereditary colorectal cancer syndrome) aged 50–100 years. We applied current life expectancy at birth in the USA[19,20] and simulated the natural history of colorectal cancer with no screening through both adenoma–carcinoma sequence and de-novo pathways, including progression from no adenoma to low-risk and high-risk adenomas, early to late stages of colorectal cancer, and colorectal cancer-related death (appendix p 23). Sessile serrated lesions were not modelled separately but included in the de-novo pathway.

The variables used in the decision analytic model are shown in the appendix (p 6). Transitional probabilities among different health states and mortality rates were derived from a systematic literature search.[21,22] Inputs on polyp prevalence were derived from endoscopic data,[23–25] and data on colorectal cancer incidence and stage distribution were from Surveillance, Epidemiology, and End Results (SEER).[26] Large-scale clinical studies were used to extract rates of adverse events and survival outcomes after colorectal cancer treatment.[15,27,28] For survival of patients with colorectal cancer, a 5-year time horizon was simulated as a clinically relevant outcome based on US-based estimates. Natural history models were calibrated against SEER data of colorectal cancer incidence and death from 1994 (before the widespread use of screening colonoscopy),[26] as well as against previous validated models. Further details on the model calibration and validation are shown in the appendix (pp 1, 9, 24).

We compared colonoscopy with and without use of AI for polyp detection against the natural history (no screening) model. In the primary analysis, screening uptake was set at 60%, as currently observed in the USA.[9]

In the primary analyses, the following assumptions were applied for screening colonoscopy. As currently recommended by the American Cancer Society, colorectal cancer screening and surveillance after screening was simulated between 50 and 80 years of age.[4] We assumed the screening begins at 50 years of age because it was a strong recommendation (whereas starting at age 45 was a qualified recommendation).[4] At each screening test, if no cancer or adenoma was detected, the next screening colonoscopy was to be performed after 10 years. If polyps were detected, they were removed by polypectomy. Patients with adenomas were scheduled for surveillance colonoscopy according to current guidelines, which we

simplified for use in this study:[29] those with low-risk adenomas (1–2 non-advanced adenomas) were returned to screening colonoscopy in 10 years' time and those with high-risk adenomas (≥3 non-advanced adenomas or ≥1 advanced adenomas) were scheduled to every-3-year colonoscopy until they had negative results in surveillance colonoscopy. No follow-up was simulated for hyperplastic or sessile serrated lesions. Patients with colorectal cancer were assumed to be treated according to stage at diagnosis. We also performed two kinds of subanalysis: one in which we assumed 100% uptake for screening colonoscopy and one in which we assumed screening in the Medicare population only (ie, screening started at the age of 65 years instead of 50 years). The external validation of our model against previous randomised trials and similar estimates of already published colorectal cancer screening models is shown in the appendix (pp 4, 16–21).

To project the outcomes of our primary simulation on the US population, we assumed a steady state for population size and age distribution, represented by the year 2008 US census data (ie, pre-screening population).[27,30] We then multiplied each age-specific model output by the number of people of that age in the US population and corrected these to represent a 60% participation rate in screening. Adding the results for all ages under each strategy yielded national estimates. Health outcomes (ie, number of colorectal cancer cases and colorectal cancer-related deaths) were obtained from the model for each screening cohort (ie, colonoscopy with and without AI) and a Poisson regression model was applied to obtain an estimate of the hazard ratio. No discounting was used in these national projections because the model estimates are for a single year across a cross-sectional population (ie, all individuals aged 50–100 years in 2008) rather than several years with the same cohort.

We also adapted the model to the Medicare population (ie, aged 65–100 years).[9] External validation of our national projections against previous analysis with similar methodology is shown in the appendix (pp 4, 16–21).

This study is reported in accordance with Consolidated Health Economic Evaluation Reporting Standards (appendix p 22).[31] Ethics approval was not required as there were no human participants.

Health outcomes

Interval colorectal cancer was defined as colorectal cancer diagnosed as symptomatic colorectal cancer after screening colonoscopy. We calibrated the overall effect of colonoscopy screening on the subsequent risk of post-colonoscopy interval colorectal cancer to match the 0·022% (95% CI 0·016–0·029) annual rate of interval colorectal cancer that was shown in the only available large series of screening colonoscopy (42 interval cancers were detected during a post-colonoscopy follow-up period of 188 788 person-years[14]). Additional details on the calibration of our model against such series is provided in the appendix (p 1). To estimate the additional effectiveness of AI, we applied a gradient in ADR between the two strategies based on a recent meta-analysis of six randomised trials (4354 patients) comparing colonoscopy with and without AI that showed a 44% relative increase in ADR between AI and no AI.[15,17] In detail, the model was calibrated to match an average 28–40% ADR gradient when only one screening colonoscopy was performed among patients aged 50–80 years (mean age 60; proportion of male patients 50%) based on a previous study.[15] Of note, ADR for colonoscopy with AI virtually corresponds with endoscopists with the highest ADR quintile as estimated by the published studies.[15] For further information, see also the appendix (p 3).

The main effectiveness outcomes were long-term colorectal cancer incidence and mortality with and without AI.[17,32,33–37] Estimates of utilities were obtained from clinical studies, providing utility valuation by colorectal cancer stage at diagnosis from stage I to IV.[38,39]

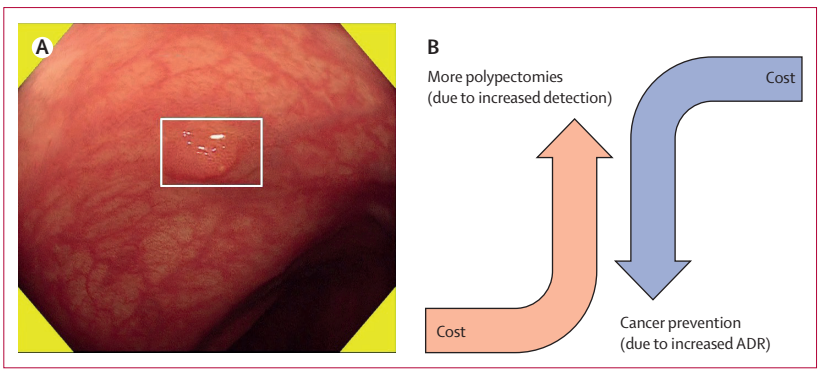

Figure 1: **(A) An AI tool for polyp detection indicating the area suspicious of a polyp; (B) the effect of the use of AI for polyp detection on the overall cost**
ADR=adenoma detection rate. AI=artificial intelligence.

Cost outcomes

We applied a societal perspective analysis, accounting for direct and indirect costs, including for patients, families, health-care systems, and employers.[31] Costs and resources were obtained from recent published literature (appendix p 6). Health-care costs for colorectal cancer treatment (according to disease stage and available treatment) and costs for treatment of adverse events (for colonoscopy and colorectal cancer treatment) were included. Medical costs including colorectal cancer care were derived from the 2018 Centers for Medicare & Medicaid Services reimbursement rates.[19,40] The costs of the AI systems per procedure was calculated to be US$19 on the basis of the average prices of available AI tools on the market in October, 2020. We asked all the endoscopy manufacturers to provide the prices of the AI tools for colonoscopy and obtained the data shown in the appendix (p 8); we assumed that each AI tool would be

	No screening	Colonoscopy without AI	Colonoscopy with AI
Colorectal cancer cases per 100 000 people	5965 (6·0%)	3327 (3·3%)	3049 (3·0%)
Incidence reduction	..	44·2%	48·9%
Colorectal cancer stage, number of cases per 100 000 people (% of all cases)			
Localised	2339 (39·2%)	1469 (44·2%)	1320 (43·3%)
Regional	2211 (37·1%)	1188 (35·7%)	1096 (36·0%)
Distant	1415 (23·7%)	669 (18·1%)	633 (20·9%)
Interval colorectal cancer, number of cases per 100 000 person-years	..	88·0	83·0
Screen-detected adenoma per 100 000 people			
Low-risk adenoma	..	17 000	22 400
High-risk adenoma	..	5337	4323
Colorectal cancer deaths per 100 000 people	2393 (2·4%)	1227 (1·2%)	1142 (1·1%)
Mortality reduction	..	48·7%	52·3%
Lifetime colonoscopies per 100 000 people			
Screening procedure	..	202 200	200 577
Surveillance colonoscopy, total	..	13 402	12 406
Breakdown of surveillance colonoscopies			
3–10 years after the first screening	..	4123	4706
11–20 years after the first screening	..	3445	2901
21–30 years after the first screening	..	3415	2883
31–50 years after the first screening	..	2419	1916
Discounted cost per person, $	..	$3400	$3343
Discounted colorectal cancer care cost per person, $	$2921	$1636	$1502
Discounted cost of screening testing per person including surveillance colonoscopies and testing complications, $	..	$1764	$1841
Incremental cost per person, $	..	$479	$422

All costs are in US$. A 60% uptake with screening was assumed. AI=artificial intelligence.

Table 1: **Effectiveness and cost estimates under the three different screening strategies superimposed on a simulated cohort of 100 000 people**

used for 1000 colonoscopies per year with a lifespan of 5 years. We discounted rates at 3% annually for future costs as recommended.[41] All statistical analyses were conducted with R (version 4.0.3), using the dampack functions.[42]

Secondary analyses

In addition to the primary effectiveness and cost analyses, we applied secondary analyses to simulate once-in-life screening colonoscopy, as applied in some European countries.[42–45] For this analysis, we simulated a cohort of individuals aged 50–79 years who had a once-in-a-lifetime screening colonoscopy at the age of 65 years. Effectiveness and cost estimates under the three different screening strategies were superimposed on a simulated cohort of 100 000 individuals. A 100% uptake with screening was assumed. We also did a secondary analysis in which we restricted follow-up after screening to 15 years, which might contribute to less uncertainty of simulated data. We did a sensitivity analysis assuming equal detection rates of high-risk adenomas for AI-assisted colonoscopy and standard colonoscopy (appendix pp 2, 14).

Consideration of life years

Most previous modelling studies have based calculated life-time gained by cancer screening on extrapolations of cancer-specific effects on all-cause death.[10,19] However, a recent systematic review of population-based trials showed the cancer-specific mortality reduction had limited or no effect on all-cause mortality.[46] Although this assumption might be due to the lack of statistical power, we considered quality-adjusted life years or incremental cost-effectiveness ratios were difficult to apply for assessment of cancer screening programmes. Therefore, our primary analyses do not include simulations of life-years gained (including quality-adjusted life years or incremental cost-effectiveness ratios), instead, we included such simulations in sensitivity analyses (appendix p 2).

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

In the no-screening simulation, 5965 (6·0%) colorectal cancer cases and 2393 (2·4%) colorectal cancer-related deaths per 100 000 people were estimated in the 50–100 years' time horizon of the simulation. Costs in the no-screening simulation were related to expenditure for colorectal cancer care and were estimated as $2921 per screened individual (table 1).

Assuming 60% screening uptake, screening colonoscopy reduced colorectal cancer incidence from 5965 (6·0%) cases per 100 000 individuals to 3327 (3·3%) cases per 100 000, corresponding to an absolute reduction of 2638 cases per 100 000 people, or 44·2% relative reduction compared with no screening (table 1).

Screening colonoscopy reduced colorectal cancer mortality from 2393 (2·4%) deaths per 100 000 people to 1227 (1·2%) deaths per 100 000 due to both colorectal cancer prevention owing to increased adenoma detection and removal, and diagnosis of colorectal cancer at earlier stages with consequent improved survival (table 1), corresponding to a 48·7% relative reduction compared with no screening.

Screening colonoscopy resulted in additional cost of $1764 per person (including surveillance colonoscopies and treatment of adverse events). This cost increment was partly offset by 56·0% due to reduction of colorectal cancer treatment-related costs, resulting in a saving of $1285 per individual. The total cost per individual with screening with no AI was estimated to be $3400. This represents a 16·4% increase compared with no screening.

Compared with colonoscopy without AI, the implementation of AI further reduced colorectal cancer incidence from 3327 (3·3%) to 3049 (3·0%) cases per 100 000 people, and colorectal cancer mortality from 1227 (1·2%) to 1142 (1·1%) per 100 000 people. This

corresponds to an additional 0·3% absolute reduction (8·4% relative reduction) in colorectal cancer incidence and 0·1% absolute reduction (6·9% relative reduction) of colorectal cancer mortality, compared with colonoscopy without AI (table 1). Compared with no screening, colonoscopy with AI conferred a 48·7% relative reduction in colorectal cancer incidence and 52·3% relative reduction in colorectal cancer mortality. These findings correspond to a 3·0% absolute reduction in colorectal cancer incidence and 1·3% absolute reduction in colorectal cancer mortality (table 1).

AI further decreased colorectal cancer treatment-related costs by 8·2%, from $1636 to $1502 per individual. This was partly offset by the cost of AI implementation that increased screening costs from $1764 to $1841 per person (also including surveillance colonoscopies and adverse events treatment). The total cost per person of screening colonoscopy with AI was estimated as $3343, corresponding to a saving of $57 per individual compared with screening colonoscopy without AI (table 1; figure 2).

Subanalyses assuming 100% screening uptake showed similar results to the primary analyses. When compared with colonoscopy without AI, the implementation of AI further reduced colorectal cancer incidence from 1565 (1·6%) cases per 100 000 individuals to 1106 (1·1%) cases per 100 000 individuals, and colorectal cancer mortality from 449 (0·5%) deaths per 100 000 individuals to 307 (0·3%) per 100 000 individuals. These findings correspond to an additional 0·5% absolute reduction and 29·1% relative reduction in colorectal cancer incidence and 0·2% absolute reduction and 31·6% relative reduction in colorectal cancer mortality, compared with colonoscopy without AI, and a 4·9% absolute reduction and 81·4% relative reduction in incidence and 2·1% absolute reduction and 87·2% relative reduction in mortality compared with no screening. The use of AI resulted in a saving of $94 per individual (appendix p 10). Similar data were shown in the Medicare population scenario in which screening started at age 65 years instead of age 50 years (appendix p 11). Results of deterministic sensitivity and probabilistic analyses are provided in the appendix (pp 2, 12–15, 25–27).

When assuming 60% uptake for screening colonoscopy and projecting the outcome of the model on the steady-state US population, the absolute number of colorectal cancer cases without colorectal cancer screening was estimated to be 148 204 per year, resulting in an undiscounted cost for colorectal cancer treatment of $10·90 billion; the number of colorectal cancer-related deaths was 56 278 per year (table 2). The strategy of screening colonoscopy without AI resulted in 84 463 colorectal cancer cases and 29 342 colorectal cancer-related deaths per year, corresponding to a reduction of 63 741 cases and 26 936 deaths per year compared with the no-screening scenario. Compared with the no-screening scenario, there was a decrease in the undiscounted cost for colorectal cancer treatment to $6·33 billion in the screening without AI scenario that was offset by the $5·13 billion cost of colorectal cancer screening and surveillance, resulting in a total cost of $11·46 billion (table 2). When assuming the implementation of AI in screening colonoscopy, the number of colorectal cancer cases further decreased by 7194 to 77 268 and deaths further decreased by 2089 to 27 253. The addition of AI also contributed to a yearly saving of $290 million (from $11·46 billion to $11·17 billion).

The secondary analysis based on once-in-life colonoscopy at the age of 65 years showed similar effects of the introduction of AI in screening colonoscopy as in the main analysis (table 3). When assuming a 100% screening uptake, introduction of screening colonoscopy without AI showed a 36·0% reduction in colorectal cancer incidence and a 41·0% reduction in colorectal cancer mortality. The addition of AI increased these effects to a 42·2% reduction in incidence and a 46·0% reduction in mortality. Total cost per person was estimated to be $2203 for no screening, $3877 for colonoscopy without AI, and $3702 for colonoscopy with AI.

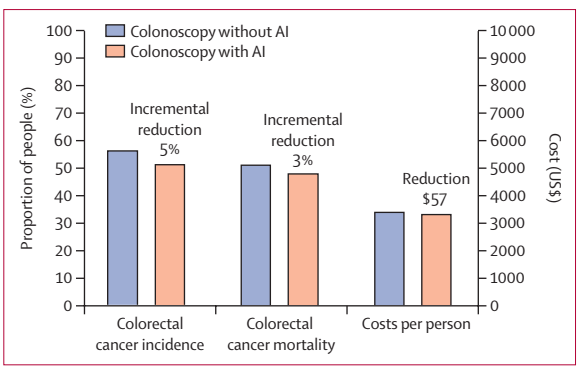

Figure 2: **Results of the primary health and cost analyses**
Expected risk of colorectal cancer incidence and mortality of colonoscopy screening with and without AI compared with non-screening. Estimated costs per person are also presented. AI=artificial intelligence.

	No screening	Colonoscopy without AI	Colonoscopy with AI
Colorectal cancer cases per year	148 204	84 463	77 268
Deaths from colorectal cancer per year	56 278	29 342	27 253
Colorectal cancer care cost per year, billion $	$10·90	$6·33	$5·79
Screening costs per year,* billion $	..	$5·13	$5·38
Total cost per year, billion $	$10·90	$11·46	$11·17

All costs are in US$. AI=artificial intelligence. *Including polypectomies, follow-up colonoscopies, and complications.

Table 2: **Projection on the US population of the superimposed screening strategies, assuming a 60% adherence to screening colonoscopy among individuals aged 50–100 years**

Discussion

To the best of our knowledge, this is the first study showing that adoption of AI can possibly contribute to a

	No screening	Colonoscopy without AI	Colonoscopy with AI
Colorectal cancer cases per 100 000 people	4277	2738	2470
Incidence reduction	..	36·0%	42·2%
Colorectal cancer stage, number of cases per 100 000 people (% of all cases)			
Localised	2339 (39·2%)	1301 (47·5%)	1191 (48·2%)
Regional	2211 (37·1%)	961 (35·0%)	863 (34·9%)
Distant	1415 (23·7%)	476 (17·4%)	417 (16·9%)
Screen-detected colorectal cancer cases per 100 000 people (% of all cases)			
Localised	..	464 (35·7%)	480 (40·3%)
Regional	..	245 (25·6%)	256 (29·5%)
Distant	..	64 (13·4%)	66 (15·8%)
Symptomatic colorectal cancer, cases per 100 000 person-years*	..	60	35
Screen-detected adenoma per 100 0000 people			
Low-risk adenoma	..	10 794	16 514
High-risk adenoma	..	5768	6280
Colorectal cancer deaths per 100 000 people (% of all cases)	1542 (1·5%)	912 (0·9%)	838 (0·5%)
Mortality reduction	..	41·0%	46·0%
Lifetime colonoscopies per 100 000 people*			
Screening procedure	..	89 275	89 275
Surveillance colonoscopy	..	13 370	15 645
Mean discounted cost per person, $	$2203	$3877	$3702
Discounted colorectal cancer care cost per person, $	$2203	$1580	$1487
Discounted cost of screening testing per person including surveillance colonoscopies and testing complications, $	..	$2297	$2215
Incremental cost per person, $	..	$1674	$1499

All costs are in US$. AI=artificial intelligence. *Symptomatic colorectal cancer included colorectal cancer diagnosed younger than 65 years and colorectal cancer diagnosed as interval colorectal cancer after screening colonoscopy.

Table 3: **A scenario analysis of once-in-life colonoscopy at the age of 65 years**

reduction of colorectal cancer incidence and mortality with a sustainable cost-saving profile. Our simulation model showed that the use of AI during screening colonoscopy resulted in an additional 8·4% relative reduction in colorectal cancer incidence and 6·9% relative reduction in colorectal cancer mortality compared with the simulation of the screening colonoscopy without AI, when assuming a 60% uptake of colorectal cancer screening. The implementation of AI also contributed to cost reduction, resulting in a saving of $57 per person. When restricting the analysis to individuals compliant with screening (ie, the subanalysis assuming 100% screening uptake), there was a 29·1% reduction in colorectal cancer incidence and 31·6% reduction in colorectal cancer mortality in the colonoscopy with AI scenario compared with colonoscopy without AI, resulting in a saving of $94 per person.

When projected on the US population with a 60% compliance to screening colonoscopy, these data potentially indicate that screening with AI could additionally prevent 7194 colorectal cancer cases and 2089 colorectal cancer deaths per year, as well as save $290 million per year. Colonoscopy with AI appeared to be more cost-effective than colonoscopy without AI. Such a favourable profile for screening with AI was confirmed in the once-in-life colonoscopy scenario as well.

The main result of our analysis comes from the assumption that the AI-driven ADR increase contributes to reduction of colorectal cancer incidence and mortality. In the simulated model, an absolute 12% increase of ADR driven by AI resulted in the additional 29·1% reduction of the colorectal cancer incidence (subanalysis assuming 100% screening uptake). Current evidence shows that AI increases the ADR by 1·44 times, enhancing the detection of diminutive 1–5 mm lesions by 1·69 times, small 6–9 mm polyps by 1·44 times, and large polyps that are 10 mm or more by 1·46 times.[17] The improved detection rates are observed regardless of the polyp sizes, thus we did not conduct any additional size-specific analyses.

Our results are in line with the estimate of a large-scale observational study in which a 1% increase in ADR was associated with a 3% decrease in colorectal cancer incidence.[15] This relationship between the ADR and colorectal cancer prevention was also shown in the high-tier ADR subgroups in previous large-scale, registry-based trials,[14,15] which corresponds to the simulated cohort of the present study.

Our analysis also showed the impact of using AI with screening colonoscopy on costs. First, the direct cost of AI—estimated to be at $19 per colonoscopy—only slightly affected the cost of screening colonoscopy. The main drivers of the cost increase in this strategy were the additional numbers of surveillance colonoscopies and related polypectomies and pathologies. Regarding the increase in surveillance colonoscopies, we assumed a 10-year surveillance policy for low-risk adenomas that is in line with the recent relaxation of the recommended surveillance interval from 5–10 years to 7–10 years.[47] On the other hand, we assumed an intensive strategy for the subgroup of patients with high-risk adenomas.[48] However, the reduction in the cost of colorectal cancer treatment offset such an increase in screening costs, resulting in an overall saving.

There is no reason to conclude that our findings on effectiveness data cannot be generalised to other populations outside the USA because the natural history of colorectal cancer and clinical outcomes of screening colonoscopy with or without AI tools are expected to be quite similar worldwide. On the other hand, health-care costs and insurance systems greatly differ between countries, thus further investigation in accordance with each country's situation is needed to translate our data to countries outside the USA. Strengths of our analysis include the transparent conversion of an ADR gradient into a long-term colorectal cancer incidence prevention gradient. In addition, the equally simple conversion of costs of colorectal cancer treatment and screening or surveillance colonoscopies to the overall cost of the

strategies were conducted. Furthermore, the costs of AI systems were based on a survey of devices already on the market in many countries.

In the present study, we did not simulate the role of computer-aided diagnosis (CADx).[49] Different from the AI-detection system (computer-aided detection [CADe]), CADx is aimed at real-time identification of histology of polyps to determine which polyps need to be removed or are exempt from pathological assessment. These new CADx tools might have a future role in mitigating increased colonoscopy costs due to the increased polyp detection by CADe. However, we did not incorporate CADx in our simulation because this strategy is rarely adopted in practice due to legal, social, and psychological reasons and there are no clinical trials that investigate how CADx mitigates the CADe-driven cost increase.[50] Future studies should focus on the possible benefits and harms of the combined use of CADe and CADx.

Our study has several limitations. First, microsimulation inherently includes considerable uncertainties due to many assumptions used for calculation. To minimise these uncertainties, we conducted the scenario analysis on the basis of once-in-life screening colonoscopy with a relatively short follow-up period (ie, 15 years after colonoscopy). Second, although we assumed a linear relationship between the cancer prevention effect and increased ADR, there is an ongoing discussion about whether there is a threshold effect of ADR in cancer prevention (eg, 20% ADR[51]). Currently, gastrointestinal endoscopy societies recommend minimum acceptable thresholds for detection in screening patients aged 50 years and older.[13] Although the utility of a minimum threshold signalling the need for remedial work if not reached has been demonstrated,[52] other data indicate that protection from colorectal cancer continues to increase as the ADR increases above the minimum thresholds, with one study indicating progressively improving protection up to an ADR of 50%.[15] According to these findings, the minimum threshold ADRs should not be considered a static target. Thus, the search for greater ADRs should be encouraged, respecting the peculiarities of each population and region. Third, we assumed the same increase of the detection rate of high-risk adenomas as low-risk adenomas under the use of AI for polyp detection, although the detection rate of advanced adenomas was not shown in the previous meta-analysis.[17] Nevertheless, we could justify this approximation of the increased detection of advanced adenomas because the average number of advanced adenomas per colonoscopy has been reported to increase with the aid of AI for polyp detection.[17] Furthermore, we did a sensitivity analysis assuming equal detection rates of high-risk adenomas for AI-assisted colonoscopy and standard colonoscopy (appendix pp 2, 14), which still showed a cost-saving of $22 per person with AI-assisted colonoscopy and increased reduction of colorectal cancer incidence. We also did not consider the effect of different morphological types of adenomas on ADR. Fourth, the overall estimated number of colorectal cancer deaths with standard screening colonoscopy in the model for the USA with 60% screening uptake was lower than the actual number of colorectal cancer deaths (approximately 50 000 per year). However, this difference could be due to demographic differences between the pre-screening population in 2008 and the more recent population. This is because current deaths from colorectal cancer are likely to reflect the screening uptake of 10 or more years ago, which was less than 60%, and a lower quality of endoscopy including ADR at that time. In addition, the actual number of deaths includes people who were uninsured, and thus had little chance of receiving cancer screening. As well as the actual uptake rate, we assumed a high compliance with subsequent repetition of the test (every 10 years) and follow-up that has not yet been captured by current surveys. These assumptions might contribute to the difference between the mortality estimate for colonoscopy without AI shown in table 2 and actual colorectal cancer deaths in the USA. However, our results are similar to those of other models constructed independently and using different methods and various software packages.[23,53] Other limitations include uncertainty as to whether the AI technology will produce the same gains in clinical practice that have been seen in clinical trials, and it is uncertain if the need for AI will be sustained.

In conclusion, our results suggest that implementation of AI detection tools in screening colonoscopy is a cost-saving strategy to further prevent colorectal cancer incidence and mortality.

Contributors

MA, YM, FT, GA, JA, IB, and CH did the literature search and data collection. MA, YM, FT, GA, JA, MD-R, and CH did the study design and data analysis. MA, YM, AR, MB, MS, AE, SK, JA, PS, MFK, DKR, HM, MD-R, and CH interpreted the data. MA, YM, MB, and CH drafted the manuscript. MA, YM, MD-R, CH, and LC verified the underlying data. All authors approved the final version of the manuscript. All authors had access to all of the data in the study and had final responsibility for the decision to submit for publication.

Declaration of interests

YM declares consultancy work for and having equipment on loan from Olympus, and ownership interest in Cybernet System. AR has done consultancy work for and received research grants from Fujifilm, has been on advisory boards for and received speaker fees from Medtronic, has received speaker fees and research grants from Boston Scientific, and has done consultancy work for Cosmo Pharmaceuticals. MB has done consultancy work for Cybernet System. PS has done consultancy work for Medtronic, Olympus, Boston Scientific, Fujifilm, Salix Pharmaceuticals, and Lumendi; and has received research grants from Ironwood, Erbe, Docbot, Cosmo Pharmaceuticals, and CDx Labs. MFK has done consultancy and teaching work for Olympus, has equipment on loan from Fujifilm, and has done teaching work for Boston Scientific. HM has done consultancy work for and has equipment on loan from Olympus and Medtronic; and has done consultancy work for Boston Scientific. DKR has ownership interest in Satisfai Health and has done consultancy work for Olympus. MD-R has received a teaching grant from Olympus, a research grant from Fujifilm, and has done consultancy work for Medtronic. CH has done consultancy work for and has equipment on loan from Medtronic and Fujifilm, and has done consultancy work for Pentax. All other authors declare no competing interests.

Data sharing

The structure of the model, its calibration, the cost-utility analysis, sensitivity analysis and results, all variables' values and ranges used in the model, health, and cost estimates under the three different screening strategies are all available in the appendix (pp 1–30). Any additional data is available upon request from the corresponding author. The codes for the simulation model that underlie the results reported in this article will be available beginning 1 year and ending 5 years following article publication to researchers who provide a methodologically sound proposal. The use of the data should be approved by an independent review committee. Proposals should be directed to Yuichi Mori (ibusiginjp@gmail.com)—to gain access, data requestors will need to sign a data access agreement.

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