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Efficacy and cost-effectiveness of screening colonoscopy according to the adenoma detection rate

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Abstract

Background: The adenoma detection rate of the endoscopist has been related to the post-colonoscopy interval risk of colorectal cancer.

Objective: The objective of this article is to estimate the impact of adenoma detection rate on the long-term colorectal cancer prevention rate.

Methods: A Markov model was constructed to simulate the efficacy and cost of colonoscopy screening according to the adenoma detection rate of the endoscopist in 100,000 individuals. Post-colonoscopy interval colorectal cancer risk and the relative risk of interval cancer among endoscopists with different adenoma detection rates were extracted from the literature. A 1.5 relative risk was assumed between endoscopists with low and average adenoma detection rates, and a relative risk of 11 between those with average and high adenoma detection rates. Both efficacy and costs were projected over a steady-state American population.

Results: Screening colonoscopy performed by endoscopists with low adenoma detection rates resulted in a 7% absolute reduction in the long-term colorectal cancer incidence prevention rate as compared to the same procedure performed by those with an average adenoma detection rate (70% vs. 77%). This difference increased to 21% when comparing endoscopists with an average with those with a high adenoma detection rate. When projected on the US population, this reduced efficacy resulted in an additional 1728 and 16,123 colorectal cancer cases and the loss of $117 million and $906 million per year in the two scenarios, respectively. These estimates were sensitive to the risk of post-colonoscopy interval colorectal cancer.

Conclusions: A substantial reduction in long-term colorectal cancer prevention rate may be expected when screening colonoscopy is performed by endoscopists with a suboptimal adenoma detection rate. A substantial saving may be expected when implementing policies to improve endoscopist adenoma detection rate.

Keywords

Colorectal cancer screening, endoscopist, adenoma detection rate, interval cancer, colonoscopy, cost-effectiveness

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Abbreviations

CRC: colorectal cancer; LOC: localized; REG: regional; DIS: distant; ICER: incremental cost-effectiveness ratio; ADR: adenoma detection rate; PDR: polyp detection rate

Introduction

The long-term efficacy of colonoscopy in preventing colorectal cancer (CRC) incidence and/or mortality has been addressed in cohort and case-control studies.[1–4] Although the majority of these studies showed a very high CRC prevention rate, some studies showed a suboptimal CRC protection rate.[2,3] This appeared to be related to an unexpectedly high risk of

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post-colonoscopy CRC in the early years after colonoscopy. In a large administrative cohort of largely symptomatic patients with negative colonoscopy, CRC prevention rate appeared to be markedly higher when assessed 10 years after colonoscopy rather than after five years—i.e. 72% vs. 41%—because of the unexpected occurrence of interval cancer in the early years following colonoscopy.[3]

Quality of endoscopy has been strictly related to the risk of post-colonoscopy CRC.[5] In large administrative cohort or case-control studies, the risk of early post-colonoscopy cancer appeared to be independently predicted by a relatively low adenoma/polyp detection rate (ADR/PDR).[6–8] In detail, such risk was higher when comparing the lowest quartile of endoscopists with those with a higher ADR/PDR. It was similarly lower when the ADR/PDR of the selected endoscopist was ranked as high ($\geq$20%) as compared with those with a lower ADR.[9] This has been recently confirmed in a randomized clinical trial (RCT) on sigmoidoscopy screening, in which the risk of distal interval cancer was significantly increased for patients of examiners with a low distal ADR.[10]

No study assessed the role of ADR in determining the long-term colonoscopy-related CRC prevention rate, causing uncertainty as to the potential benefit of any interventional policy on this issue. Additionally, it is unclear whether the main aim of such a policy would be either to simply focus on the (few) endoscopists with low ADR or to also include those with a medium ADR in order to achieve a uniformly high ADR.

The aim of this micro-modelling simulation was to calculate the potential impact of endoscopist ADR and related policies on the efficacy and costs of screening colonoscopy.

Methods

End-points of this analysis address the following:

1. What is the difference in long-term efficacy of colonoscopy between endoscopists with low ADR and those with average ADR, and between those with average and those with high ADR?
2. What is the projected impact on the United States (US) population of different degrees of long-term colonoscopy efficacy according to the ADR of the endoscopists?
3. What is the projected improvement in the efficacy of colonoscopy when implementing policies to increase the ADR of endoscopists with an initially low or average ADR?

To address these issues, we simulated primary prevention with colonoscopy in a theoretical cohort of 100,000 male and female American citizens generated by a Markov model. Briefly, endoscopic screening was simulated to be repeated every 10 years between 50 and 80 years, with post-polypectomy surveillance according to polyp size and histology. Age- and site-related CRC incidence and mortality were assumed from the Surveillance, Epidemiology, and End Results (SEER) database for the natural history cohort, in order to exclude any model-related uncertainty, due to the incomplete knowledge of the inter-polyp transition rates, as previously reported.[11–13]

Efficacy of colonoscopy screening

Long-term reduction of CRC incidence and mortality by colonoscopy screening was calculated in order to match with the risk of post-colonoscopy interval CRC available in the literature. In detail, we calibrated the overall efficacy of colonoscopy screening on the subsequent risk of post-colonoscopy interval CRC in order to match the 0.02% annual rate of interval CRC showed in the only available large series of screening colonoscopy, including 188,788 person-years of post-colonoscopy follow-up with a mean age of 55 years.[9]

Efficacy of colonoscopy screening according to ADR/PDR

In order to include the role of endoscopist ADR/PDR, we further calibrated the long-term efficacy of colonoscopy screening based on the available data on the association between the endoscopist ADR and the post-colonoscopy risk of interval cancer. In detail, we calibrated the long-term efficacy of colonoscopy screening for each ADR category in order to match with the relative risk (RR) of post-colonoscopy interval CRC among the different ADR categories shown in recent studies.[6,8–10] The available series may be divided into two different scenarios (Table 1):

1. Those comparing the few (i.e. lowest quartile) endoscopists with low ADR with those with average (i.e. medium or high) ADR. For this scenario, we adopted a 1.5 RR of post-colonoscopy interval CRC between the endoscopists with low ADR and those with average ADR, as median of the RRs estimated by the available series (Table 1).[6,8,10]
2. Those comparing the few (i.e. 22%) endoscopists with high ADR with those with average (i.e. low or medium) ADR. For this scenario, we adopted a RR of 11 of post-colonoscopy interval CRC between the endoscopists with average ADR and those with high ADR.[9]

Table 1. Relative risk (RR) for the incidence of post-colonoscopy interval colorectal cancer between the endoscopists below and above the ADR/PDR threshold adopted in the available studies

Author	ADR/PDR	Threshold	Percentage of endoscopists above threshold	RR
Kaminski et al.[9]	ADR	20%	22%	11–12.5
Rogal et al.[10]	ADR	8%	75%	1.4
Cooper et al.[6]	PDR	25%	75%	1.2–1.4
Baxter et al.[8]	PDR	14%	–	1.3–1.9

ADR: adenoma detection rate; PDR: polyp detection rate.

Because of the lack of direct comparisons between the low and the high ADR endoscopists, we performed two different simulations (low vs. average ADR and high vs. average ADR) in order to base our model on the precise estimates of the original studies. Of note, the low- and the high-risk groups virtually correspond with the lowest and highest quartiles of the corresponding series, so that the first simulation actually compares the lowest quartile with the remaining three higher quartiles, while the second compares the highest with the remaining three lower quartiles.

Endoscopic training

In order to estimate the eventual cost of training for endoscopists in order to increase ADR, we assumed the 2010 estimate by the American Board of Internal Medicine of 12,907 board-certified gastroenterologists.[14] Despite the fact that no recommendation on an eventual policy for improving the endoscopists ADR has been officially proposed, a two-session training course (one day) has actually been tested in two RCTs aiming at improving the ADR.[15]

Costs

Age-/size-/site-specific prevalence of non-advanced and advanced adenomas were matched with estimates from autopsy and endoscopic data in order to compute the costs related to polypectomy and follow-up (Supplementary material). Reimbursement data for direct costs of endoscopy and related complications, as well as for stage-specific CRC treatment, were based on Medicare data.[16] According to a 2010 estimate by the Bureau of Labor Statistics, the mean annual wage for an American endoscopist was $200,000.[17] In order to include in the simulation the potential higher costs of polypectomy and post-polypectomy surveillance, we assumed different sensitivities for adenomatous polyps, in order to match with the different prevalence of ADR available in the different series.[9]

Cost-effectiveness analysis

Future costs and life-years saved were discounted using an annual rate of 3%. The relative performance of the strategies was measured using the incremental cost-effectiveness ratio (ICER), defined as the additional cost of a specific strategy, divided by its additional clinical benefit, compared with the next least expensive strategy. An ICER of $50,000 per life-year gained was used as the willingness-to-pay threshold to differentiate between efficient and inefficient procedures.[18]

Simulation output. In the reference case scenario, we assumed a complete adherence, in order to simulate the efficacy and cost of colonoscopy screening in those actually screened (i.e. per protocol analysis), analogously to similar analysis.[11,19] To obtain the national projection of the CRC prevention rate of a primary colonoscopy screening according to the ADR of the endoscopist, we corrected the initial simulation for the actual adherence rate (intention-to-treat analysis).[11,19] In detail, adherence of the American population to CRC screening was estimated to be 65%.[20] In order to project the outcomes of our simulation on the US population, we assumed a steady state for population size and age distribution, represented by the year 2009 US census data. No discounting was used in these national projections.[19] The model was simulated by using Excel spreadsheets (Microsoft Corp., Redmond, WA).

Sensitivity analysis. A systematic sensitivity analysis was performed for all the variables of the model, with the most relevant results being reported.

Results

As shown in Table 2, in the no screening simulation, 5903 CRC cases and 2482 CRC-related deaths occurred in the simulated cohort of 100,000 Americans, resulting in the loss of 31,839 undiscounted life-years. Costs in the no screening simulation were purely related with the expenditure for CRC care, with an estimate of $2227 per person (Table 2).

Reference case scenario

According to the model, the value of long-term CRC incidence prevention rate by screening colonoscopy corresponding to an age-adjusted 0.02% annual risk of post-colonoscopy interval CRC—as estimated in a

Table 2. Costs and efficacies for all the simulated strategies for a cohort of 100,000 individuals. The strategy indicated as ''overall colonoscopy screening'' represents the reference case scenario

	No screening	Overall colonoscopy screening	Low-ADR	Average ADR[a]	High ADR
CRC cases, *n*	5903	1460	1771	1353–1726	459
CRC prevented, *n*	–	4442	4132	4177–4549	5443
CRC prevention rate, %	–	75	70	71–77	92
CRC deaths, *n*	2482	681	808	637–790	273
CRC death prevention rate, %	–	73	67	68–74	89
Life-years gained, *n*	–	14,960	13,881	14,036–15,333	18,443
Screening cost, $/person	–	2387	2259	2387	2486
Care for CRC, $/person	2227	503	624	461–606	112
Total, $/person	2227	2890	2883	2848–2993	2598
ICER vs no screening, $ per life-year gained	–	4424	4781	3980–5451	2014

CRC: colorectal cancer; ICER: Incremental cost-effectiveness ratio. [a]The upper and lower limits of each variable in this scenario represent the estimates for the average-risk endoscopists in the two different simulations. In detail, in the low- adenoma detection rate (ADR) scenarios, the average risk endoscopists were supposed to represent those in the upper 75% of the endoscopist population, whilst in the high-ADR scenario those in the lower 78%.

previous study[9]—in the patients attending screening was equal to 75%. Colonoscopy screening also resulted in a substantial decrease in CRC treatment costs when compared with no screening ($503/person vs. $2227/person). This was offset by the cost of screening and follow-up testing ($2387/person), resulting in an overall discounted cost/person of $2890 (Table 2). Colonoscopy screening appeared to be a cost-effective alternative to no screening with an ICER of $4424 per life-year saved (Table 2).

Efficacy according to ADR-endoscopists

Low vs. average ADR. When assuming a 1.5 RR of interval CRC between endoscopists with low and average ADR and a 25%/75% distribution of the screening colonoscopies between the two groups, the corresponding values of long-term CRC incidence prevention rate by screening colonoscopy were 70% and 77%, respectively. Endoscopists with low ADR were associated with substantially higher CRC-related costs ($624/person vs. $461/person) that were only partially offset by the lower cost in polypectomy and post-polypectomy surveillance ($2259/person vs. $2387/person).

When assuming all the endoscopists with low ADR become average ADR endoscopists owing to the simulated training, the overall CRC incidence prevention rate increased from 75% (reference case scenario) to 77%. This training-related improvement was also associated with a further reduction of the CRC-related costs as compared with the reference case scenario ($461/person vs. $503/person) (Table 2). Being more effective and less costly, the reference case scenario appeared to be dominated by the post-training scenario with a discounted savings of $42 per person.

Average vs. high ADR. When assuming an RR of 11 of interval CRC between endoscopists with average and high ADR, as well as a 78%/22% distribution of the screening colonoscopies between the two groups, the corresponding values of long-term CRC incidence prevention rate were 71% and 92%, respectively. Endoscopists with high ADR were also associated with a substantial reduction of the CRC-related costs ($112/person vs. $606/person), while the additional cost for polypectomy and post-polypectomy surveillance was marginal ($2486/person vs. $2387/person), as shown in Table 2.

When assuming all the endoscopists with average ADR become high ADR endoscopists owing to the simulated training, the overall CRC incidence prevention rate increased from 75% (reference case scenario) to 92%. This training-related improvement resulted in a further reduction of the CRC-related costs as compared with the reference case scenario ($112/person vs. $503 person) (Table 2). Being more effective and less costly, the reference case scenarios appeared to be dominated by the high ADR endoscopist strategy, resulting in a discounted savings of $292 per person.

Projection on the US population

In the no screening scenario, the actual number of CRC cases and CRC deaths simulated for the entire US population were 144,424 and 58,311 per year, respectively, resulting in an annual undiscounted cost of

Table 3. Projection of the model outputs on the American population. No discounting was applied because the model outputs reflected all persons aged 50–100 years of age at a given point in time in the steady state. The post-training estimates represent the potential improvement when applying endoscopist-training in the two scenarios of low- and high-ADR endoscopists (see text)

	No screening	Overall colonoscopy screening	Post-training low ADR scenario	Post-training high ADR scenario
CRC cases, *n*	144,424	72,491	70,763	56,368
CRC prevented, *n*	–	66,417	73,661	88,057
CRC deaths, *n*	58,311	30,132	29,449	23,754
CRC deaths prevented, *n*	–	28,179	28,862	34,557
Total cost, $ billion	9.7	10.9	10.8	10

ADR: adenoma detection rate; CRC: colorectal cancer.

$9.7 billion for CRC care (Table 3). When assuming a 65% adherence rate and the 75% CRC prevention rate shown in the reference case scenario, the absolute number of CRC and CRC deaths prevented per year by screening colonoscopy in the US population were 71,933 and 28,179, respectively (Table 3). The undiscounted annual cost of this strategy was equal to $10.9 billion. Of these, only $5.9 billion were due to CRC treatment cost, the remaining $5 billion being related to the costs of the screening program.

When simulating the training-related improvement in the low and high ADR scenarios (see above), the additional reductions in CRC cases and CRC-related deaths (vs. the reference case scenario) were 1728 and 684 per year, and 16,123 and 6378, respectively (Table 3). Because of the additional reduction of CRC-related costs, the cost of the two post-training scenarios were $10.8 and $10 billion, respectively, corresponding to an annual difference of $117 million and $906 million. This gain appeared to be only marginally affected by the initial investment in endoscopist training ($770 for each endoscopist), resulting in a total of $2.4 and $8 million in the low- and high-ADR endoscopist scenarios, respectively.

Sensitivity analysis

Low vs. average ADR. The difference in the CRC prevention rate according to the ADR of endoscopists was sensitive to the RR of post-colonoscopy interval cancer. When assuming a RR of 2 (as compared with the baseline 1.4), the values of long-term CRC incidence prevention rate for low and average ADR endoscopists appeared to be 64% and 79%, respectively, the absolute difference passing from 7% in the reference case scenario to 15% (Figure 1). In this scenario, the post-training-related improvement in the CRC prevention rate increased from the baseline 2% to 4%.

The result of the analysis also varied according to the baseline risk of post-colonoscopy interval cancer. By increasing this risk from the baseline 0.02% to 0.06%—corresponding to a decrease of colonoscopy efficacy from 75% to 48%—the corresponding CRC prevention rates for low and average ADR endoscopists were 35% and 52%, respectively, the difference between the two groups increasing from the baseline 7% to 17% (Figure 1). By further increasing the risk of interval CRC to 0.1%—corresponding to a 30% CRC prevention rate—, the difference in long-term CRC prevention rate between the two groups would further increase to 23% (12% vs. 35%).

At two-way sensitivity analysis, when assuming a 0.06% risk of interval CRC and a RR of 2 between low and average ADR endoscopists, the difference in the CRC prevention rate between the two groups increased to 38% (19% vs. 57%) (Figure 1). In this case, the training-related improvement appeared to be associated with an absolute 7% increase in the CRC prevention rate (i.e. from 48% to 55%). The higher impact of the training in this scenario—in which a reduced overall efficacy of colonoscopy in preventing CRC was simulated—was related with the higher burden of CRC on which the improvement of quality could be applied.

Average vs. high ADR. When assuming a 5 and 2 RR (as compared with the baseline 11) for interval CRC between the average and high ADR endoscopists, the absolute difference in CRC prevention rate between the two groups was reduced from 21% to 19% and 11%, respectively (Figure 2). In these cases, the post-training-related improvement in the CRC prevention rate was reduced from the baseline 17% to 15% and 9%, respectively.

By increasing the baseline risk of post-colonoscopy interval cancer in the reference case scenario to 0.06%, the corresponding CRC prevention rates for average and high ADR endoscopists were 36% and 89% (Figure 2). At two-way sensitivity analysis, when assuming a 0.06% risk of interval CRC and a RR of

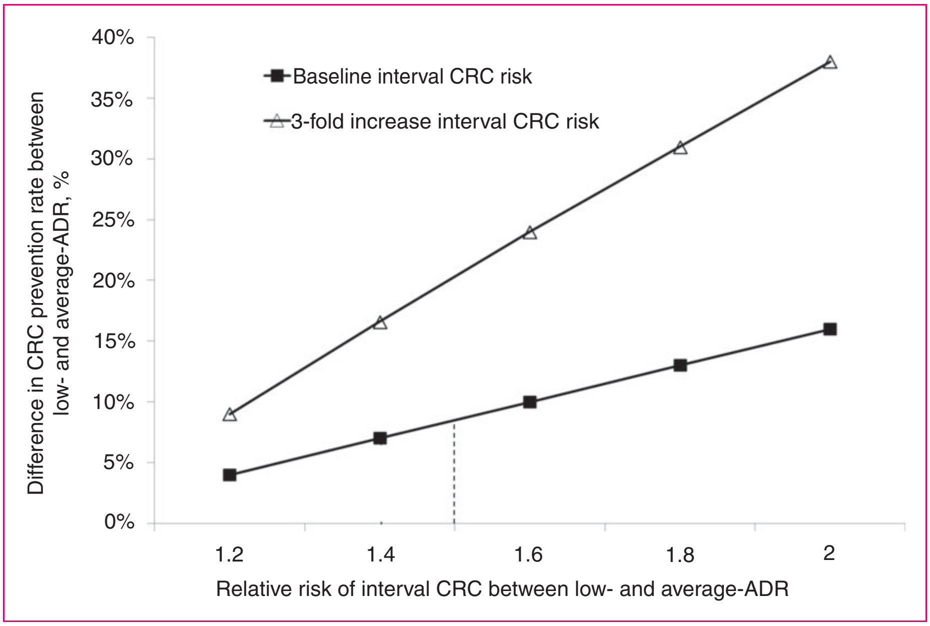

Figure 1. Absolute difference in long-term CRC prevention rate between low and average ADR endoscopists according to the relative risk of post-colonoscopy interval CRC and the absolute risk of post-colonoscopy interval CRC (see text). CRC: colorectal cancer; ADR: adenoma detection rate.

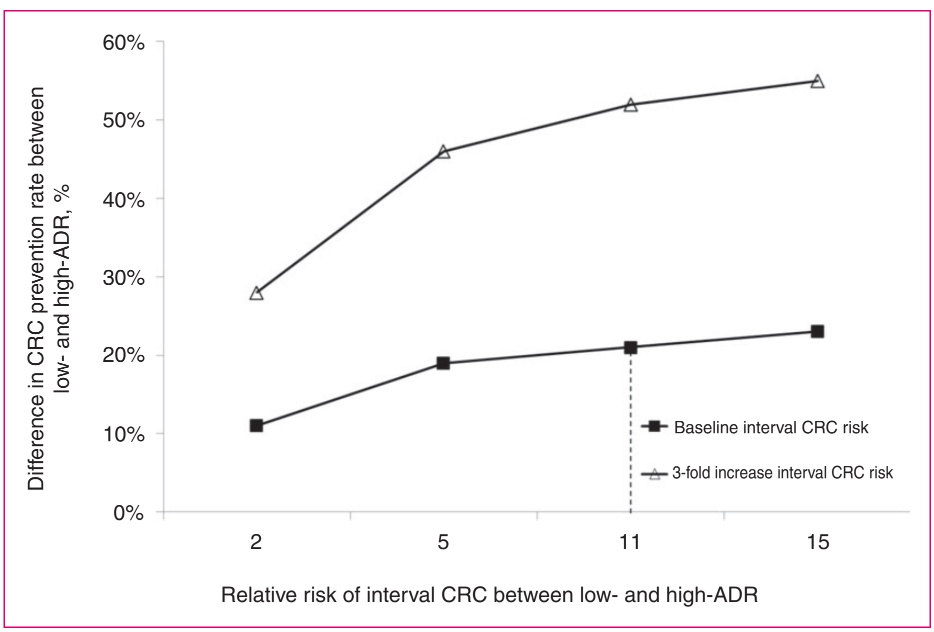

Figure 2. Absolute difference in long-term CRC prevention rate between average and high ADR endoscopists according to the relative risk of post-colonoscopy interval CRC and the absolute risk of post-colonoscopy interval CRC (see text). CRC: colorectal cancer; ADR: adenoma detection rate.

5 between the endoscopists with average and high ADR, the post-training improvement in the CRC prevention rate further decreased to 8%.

The main results of our analysis were robust to changes in overall adherence to colonoscopy screening.

Discussion

According to our simulation, there is a 7%–21% absolute difference in the long-term CRC prevention rate when subgrouping endoscopists with different ADR, accounting for a substantial loss of life-years due to unprevented CRC deaths and related costs in the US population. We also showed that there is a substantial difference when comparing two possible training policies for improving endoscopist ADR. In detail, the training-related improvement in long-term CRC prevention appeared to be three times higher when passing from an average to high ADR than when passing from low to average ADR. We also showed that the eventual cost of training for endoscopists only marginally affected the potential economic impact of any policy aiming at improving the endoscopist ADR.

According to our sensitivity analysis, the gradient between endoscopists with lower and higher ADR increased when assuming a suboptimal efficacy of colonoscopy in preventing CRC. When assuming a reduced protection by screening colonoscopy, the difference in CRC prevention rate between the endoscopists with lower and higher ADR substantially increased. When assuming the same 0.1% risk of interval CRC recently estimated in Canada,[2] the difference in CRC prevention rate between the endoscopists with different ADR ranged from 23% to 52% according to the adopted classification.

The main limitation of our analysis is represented by the lack of studies showing a higher long-term CRC prevention rate when screening colonoscopy is performed by endoscopists with high or average ADR. We compensated for such a deficiency by exploiting a simulation model in order to convert the RRs of post-colonoscopy interval CRC to the long-term CRC prevention rate.

When subgrouping endoscopists with different ADR, a 7%–21% reduction in long-term CRC prevention rate may be estimated, resulting in a substantial loss of life-years and economic resources.

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Conflicts of interest

DR has received research support from Olympus. The other authors have nothing to declare.

Guarantor of the article

CH, DR, CH, MK, GC: study concept and design; acquisition of data; drafting of the manuscript. CH: analysis and interpretation of data; statistical analysis; all authors approved the final version of the manuscript.

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