ORIGINAL ARTICLE

Cost-effectiveness of colonoscopy in an organized screening program

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KEY WORDS

colonoscopy economic evaluation, colonoscopy screening, colorectal cancer screening, cost-effectiveness colonoscopy, cost-effectiveness colorectal cancer

ABSTRACT

INTRODUCTION Colorectal cancer (CRC) is a serious health problem, and various screening programs to reduce CRC have been introduced worldwide. However, the cost-effectiveness of a program based on once-in-a-lifetime colonoscopy in Poland is unknown.

OBJECTIVES The main aim of this study was to assess the cost-effectiveness of Polish Colonoscopy Screening Platform (PCSP), the colonoscopy screening program in Poland.

PATIENTS AND METHODS A Markov model was constructed to compare the strategy of colonoscopy screening as compared with no screening in 100 000 subjects. The model was based on data collected from the nationwide Polish CRC screening program whenever possible. The incremental cost-effectiveness ratio (ICER) was calculated and compared with the willingness-to-pay thresholds. A sensitivity analysis was also performed using the Monte Carlo simulation.

RESULTS Colonoscopy screening within PCSP resulted in a 18.9% reduction in CRC incidence and 19.8% reduction in CRC mortality. The strategy allowed a gain of 2317 life-years saved (1959 after discounting). The cost of colonoscopy screening per participant examined was estimated at 267.70 USD (95% CI, 263.08–272.32 USD). The ICER was less than 6500 USD, which was much lower than the accepted willingness-to-pay thresholds, indicating that the screening was cost-effective.

CONCLUSIONS Colonoscopy screening within the PCSP is cost-effective and may have a substantial impact on the Polish society due to life-years saved. The results have good informative value not only for health policy makers and medical practitioners, but also for health technology assessment.

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INTRODUCTION Colorectal cancer (CRC) is the second leading cause of cancer death in Poland and Europe.[1,2] Treating symptomatic cancer may be expensive for healthcare systems, mainly due to the costs of chemotherapy, which in the case of CRC varies between 1028 USD and 35 971 USD for 6 cycles depending on the regimen.[3] However, CRC develops slowly. Usually, it starts with adenomas, which are nonmalignant precursor lesions. Thus, screening tests have become an important tool to reduce CRC incidence and mortality. In many European countries, different screening policies have been introduced for CRC, including colonoscopy, sigmoidoscopy, and immunochemical fecal occult blood test (FIT).

In Poland, colonoscopy has been chosen as a primary tool for detecting CRC due to its high accuracy.[4] Colonoscopy as a screening test has the greatest potential for preventing cancer because of its high accuracy and the possibility to remove adenomas.[5] Notably, in the United States, this is the most common screening test for CRC.[6] Colonoscopy is portrayed as the most effective screening test because it allows detection of CRC

WHAT'S NEW?

Many studies concerning the cost-effectiveness of colonoscopy screening for colorectal cancer (CRC) have not been based on real-life data. Our study fills this gap using real-life data whenever possible. We found that the cost of colonoscopy screening in Poland per examined participant is approximately 267.70 USD, and the CRC screening strategy is cost-effective bearing in mind the accepted willingness-to-pay thresholds of 46 000 to 200 000 USD. Given the high efficiency of colonoscopy, we conclude that this CRC screening strategy is needed and useful for the Polish society.

and removal of polyps at the early stages of cancer development. However, colonoscopy is also a very costly procedure, as it requires well-trained staff and appropriate equipment to perform it safely and at a high-quality level.[7]

The main aim of the present study was to assess the cost-effectiveness of the Polish Colonoscopy Screening Platform (PCSP), the Polish CRC screening program. This study will also allow differences in CRC incidence and mortality to be addressed, as well as differences in life-years lost between colonoscopy screening and no screening, and to estimate life-years saved and discounted life-years saved due to colonoscopy screening. Such a comparative economic evaluation, which will provide a clear overview of the costs and effects of the screening and potentially demonstrate cost-effectiveness of the organized program, may have significant meaning for health policymakers, medical practitioners, and health technology assessment processes. The analysis was performed based on the Markov model comparing the strategy of colonoscopy screening with no screening in 100 000 subjects.

PATIENTS AND METHODS

Source data The cost-effectiveness has been analyzed in CRC previously, including in the evaluation of CT colonography, colonoscopy, virtual colonoscopy, flexible sigmoidoscopy, or FIT tests in preventing and screening for CRC.[8-13] However, studies using real-life data, and those examining the costs of screening and healthcare in Poland and many other countries are lacking.

To assess cost-effectiveness in Poland, it was necessary to gather data from several different institutions. National data on cancer treatment costs are gathered by the National Health Fund, whereas data concerning effectiveness outcomes are gathered mainly by the National Cancer Registry.[14] In addition to the data obtained from these institutions, we also used data collected from the Polish Ministry of Health, the Central Statistical Office of Poland, the Organization for Economic Co-operation and Development (OECD), the World Bank, and the Polish CRC Screening Program database.

Overview of the Polish Colonoscopy Screening Platform The national CRC screening program based on colonoscopy was launched in Poland in October 2000.[15] However, it was initially run as an opportunistic screening program in which participants were recruited by direct contact with their general practitioners or families. The evolution into an organized population-based program in which the eligible target population was identified through the Population Registry (PESEL registry) and individually invited for screening started from the beginning of 2012. Participants are divided into screening and control groups, as the population-based program is run as an experimental public health platform. The division is stratified by age and sex cohorts. All costs generated by screening procedures and program coordination are financed by the Polish Ministry of Health. A 10-year time horizon is defined in terms of a window of efficacy of the CRC screening. According to the organized program policy for CRC screening in Poland, people aged 55 to 64 years are offered screening with colonoscopy once in their lifetime, including individuals without clinical symptoms suggesting CRC, as well as people with symptoms of the disease if they received the invitation for the screening.[16,17] Each individual can get the invitation only once, though the invitation is valid until participants reach the age limit of the program. Invitation reminders are made via telephone contact.

Structure of the model **Natural history** For the simulation, we used a Markov process model with equal time cycles of 1 year (FIGURE 1). During these increment cycles, patients may move from one state to the other. The model included following states: CRC-, non–CRC-, and CRC-related death. The use of decision-analytical models allows the management of uncertainty due to threshold and sensitivity analyses and is relatively effective.[18] The model was constructed in such a way as to not be overloaded with too many unnecessary data affecting general observations. Such a simplified model was designed to give a clear overview of the situation regarding the basics of CRC treatment in Poland.

Age- and sex-specific mortality and incidence rates for CRC as well as CRC stages distribution were extracted directly from the National Cancer Registry and adjusted appropriately for the PCSP. The age range for screening used in the simulation was 55 to 64 years, which is consistent with the program policy for screening CRC in Poland. Regarding natural history, the only associated costs are simply the cost of CRC treatment and cost of necessary medicines. These were based on data collected from the National Health Fund with association of CRC stage distribution. Because gathered cost data were expressed in PLN, we used the rates of currency conversion taking into account purchasing power parities (PPP) supplied by the OECD[19] to express them in USD for comparability with other studies.

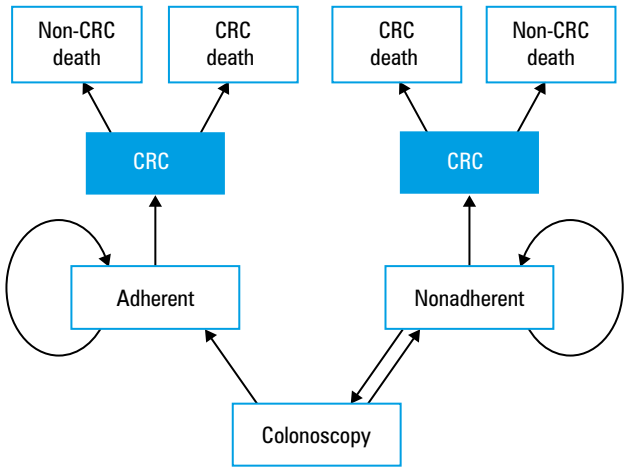

FIGURE 1 Markov states in colonoscopy screening for colorectal cancer (CRC) in the Polish Colonoscopy Screening Platform

TABLE 1 Mean value of colonoscopy examination (per examined participant) at different centers within the Polish organized screening program

Cost category	Value in USD	Percentage value in total cost, %	SD	95% CI
Personnel (physician, nurse, anesthesiologist)	109.09	41	32.57	(103.12–115,06)
Histopathology	19.61	7	11.2	(17.55–21.66)
Administrative (secretary)	9.82	4	9.31	(8.11–11.53)
Invitation (invitations, phone calls)	7.4	3	8.06	(5.92–8.88)
Equipment	35.17	13	27.06	(30.21–40.13)
Bowel preparation	18.34	7	7.66	(16.93–19.74)
Other (accounting and payments, IT specialists, stationery, mail)	18.19	7	21.43	(14.27–22.12)
Depreciation data, unit cost approach[a]	33.39	12	22.28	(29.31–37.47)
Anesthesia in every 5th colonoscopy examination	16.69	6	16.74	(13.63–19.76)
Total costs	267.7	100	25.21	(263.08–272.32)

a Assuming 1500–2000 of colonoscopy examinations performed during estimated useful life of a colonoscope

Abbreviations: IT, information technology

Colonoscopy Attendance rate The adherence rate within the PCSP was approximately 17.25% in the years 2012 and 2013.[20,21] However, later data presented by the coordinator of the PCSP indicated that the expected adherence rate in the program is higher (30%).[22] The literature indicates even higher rates for colonoscopy attendance. Areia et al[23] conducted a cost-utility analysis and presented that colonoscopy adherence can differ from 38% as reported by Aronsson et al[24] or Kingsley et al[25] to 40% as reported by Hassan et al,[26] 50% by Dan et al,[27] 63% by Heitman et al,[28] and even 100% as presented by Ladabaum and Mannalithara,[29] Coldman et al,[30] Knudsen et al,[31] or Telford et al.[32] However, Areia et al[23] emphasized that the real-life rate of colonoscopy adherence ranges between 18% and 38%, assuming that the 100% rate in some studies is completely unrealistic. Therefore, in the base case scenario, we used an adherence rate of 30%, and in the sensitivity analysis, we used the range of 17% to 68%.

Efficacy Screening efficacy is measured in terms of life-years saved. In the calculation of the number of life-years saved, we included attrition data in population coming from life-expectancy tables for Poland supplied by the Central Statistical Office of Poland[33] as well as incidence and mortality rate reductions obtained by means of colonoscopy. Many studies suggest a positive influence of colonoscopy on CRC incidence and mortality reduction.[5,7,11,32,34-42] Thus, incidence and mortality rate reductions were extracted as average values from studies supplying rates of incidence and mortality reduction. To estimate the final ranges for the sensitivity analysis, we used the results of the National Polyp Study,[36] as it was the first study to estimate rates of CRC incidence reduction and is probably the most important study in the literature. The study suggested that the reduction in CRC incidence gained through colonoscopy screening is between 76% and 90%. We also incorporated the meta-analysis conducted by Pignone et al,[37] which is also an important study, in the final range estimates for the rates of CRC incidence and mortality reduction. CRC mortality reduction gained through colonoscopy screening is suggested to be 64% to 90% and CRC incidence reduction, 58% to 86%. This meta-analysis was based, as far as colonoscopy was concerned, on the studies conducted by Fraizer et al,[39] Khandker et al,[40] Sonnenberg et al,[11] and Vijan et al.[41] Another study that we took into account while estimating the final ranges was the one conducted by Prakash et al[42] suggesting that a single colonoscopy screening might reduce incidence approximately on average by 36% and mortality by 41%.

Costs The cost of colonoscopy was estimated on the basis of the analytical process conducted within the organized screening program in Poland. To obtain a detailed cost estimation of colonoscopy screening, the data from the Polish Ministry of Health concerning general costs for colonoscopy were collected including personnel costs, administrative costs, histopathology costs, medical material costs, medical equipment costs, depreciation data, and costs of inviting to screening per examined participant for various centers taking part in the organized program. Then, to reflect the PCSP conditions in the best way and not to omit any of the centers taking part in the program, we calculated the mean value of colonoscopy examination for further analysis (TABLE 1). In the case of patients who did not have colonoscopy examination in the colonoscopy screening scenario, we assumed that the only associated costs are simply the cost of CRC treatment and cost of necessary medicines. These were based on data collected from the National Health Fund with association of CRC stage distribution. As costs concerning

TABLE 2 Model characteristics and parameters used for the baseline case and ranges tested in probabilistic sensitivity analyses

Characteristic or variable		Description or value
Model characteristics		
Model type		State transition model (Markov)
Hypothetical population		100 000 Polish citizens aged 55–64 years
Perspective		Third-payer (societal)
Time horizon		A window of the efficacy of CRC screening (10 years)
Intervention		Single colonoscopy during lifetime
Annual CRC treatment costs according to stage		
I		7293.2 USD
II		8510.71 USD
III		11 761.22 USD
IV		17 700.59 USD
Natural history – No screening CRC stage distribution, %		
I		13
II		25
III		41
IV		21
Colonoscopy efficacy, %		
Adherence,[20-32] predicted value[a] (range)		30 (17–63)
CRC incidence reduction,[5,7,32,36–38] mean (range)		63 (36–90)
CRC mortality reduction,[7,32,37] mean (range)		66 (41–90)
CRC stage	I	23
	II	24
	III	43
	IV	9
Colonoscopy costs		
Colonoscopy cost, USD, mean (95% CI)		267.70 (263.08–272.32)
Other colonoscopy cost assumptions		
Discount, %,[33]		3.7
CEA thresholds, USD,[43,44]		50 000
		100 000
		200 000
		46 000–70 000 (GDP estimation)

Point estimates and ranges for the parameter distributions are reported.

a As described in the Methods section.

Abbreviations: CEA, cost-effectiveness analysis; CRC, colorectal cancer

colonoscopy screening were expressed in PLN, we used the rates of currency conversion taking into account purchasing power parities (PPPs) supplied by the OECD[19] to express them in USD.

All of the input data and relative ranges for the sensitivity analysis concerning colonoscopy screening and the no-screening scenario are presented in TABLE 2.

Cost-effectiveness analysis The cost-effectiveness analysis (CEA) is a technique designed to measure costs and health benefits attributable to 2 or more medical interventions or no intervention. It allows choosing the best scenario from competing healthcare scenarios. The CEA is one of the methods used for the evaluation of costs and outcomes of medical interventions. Usually, the CEA results in calculating the series of incremental cost-effectiveness ratios (ICERs) that represent the cost of achieving one unit of a health outcome.[43]

In our study, the health outcomes of the PCSP, representing effectiveness, were measured in terms of life-years saved by screening for CRC. Cost data came from the National Health Fund and the Polish Ministry of Health. In our analysis, we compared colonoscopy screening with no screening. To measure the performance of colonoscopy screening, we used the ICER, defined as the additional cost of a strategy based on colonoscopy screening, divided by its additional clinical benefit (life-years saved) compared with the no-screening scenario.

We decided to use a series of cost-effectiveness thresholds acceptable from the societal and taxpayer's perspectives, indicating willingness to pay for health improvements, to assess the obtained results, as there is no clear information regarding the threshold in such analyses. The most popular thresholds in the CEA are 50 000 USD and 100 000 USD. However, there have been suggestions to incorporate higher thresholds into the analysis, such as 200 000 USD, or the thresholds that are strictly connected to the economic situation of the analyzed country, which is estimated to be 2- to 3-fold the gross domestic product (GDP) per capita.[44]

To determine whether the colonoscopy screening strategy was effective, we used ICERs of 50 000 USD, 100 000 USD, and 200 000 USD, as well as ICERs based on the economic situation in Poland, which were calculated as twice to triple the Polish GDP per capita taking into account purchasing power parity. Using data from the World Bank,[45] we established a range of values for the willingness-to-pay threshold based on GDP (46 000–70 000 USD; the first value is 2-fold and the latter 3-fold the GDP per capita).

We conducted our analysis from a third-payer perspective. Poland has a single-payer system and, as far as public funds are concerned, such an analysis can also be portrayed as being conducted from a societal perspective.[5] In Poland, a single institution can be distinguished as the third payer, that is, the National Health Fund.

Based on the inflation data from the Central Statistical Office of Poland,[33] we used a 3.7% annual rate to discount costs and effects in the analysis. However, due to suggestions supplied in the regulation issued by the Polish Ministry of Health[46] to use different discount rates for the costs and effects, we conducted an extra analysis to include suggested measures of 5% for costs and 3.5% for health outcomes (Supplementary material, Appendix).

Sensitivity analysis In the sensitivity analysis, we assumed the same cost conditions for necessary

TABLE 3 Costs and effects of colonoscopy screening compared with no screening in the base case scenario

Variable	No screening	Colonoscopy
CRC cases, n	1126	914
CRC deaths, n	566	454
CRC prevented, %	–	18.9
CRC deaths prevented, %	–	19.8
Life-years lost, n	11 704	9387
Life-years saved, n	–	2317
Life-years saved discounted, n	–	1959
Cost CRC care, USD	13 076 409	10 290 580
Cost screening, USD	–	14 803 168
Total cost, USD	13 076 409	25 093 748
Total cost discounted, USD	10 971 854	23 437 552
ICER vs. no screening, USD per life-year saved (discounted)	–	6364

Abbreviations: ICER, incremental cost-effectiveness ratio; others, see TABLE 2

medicines and treatment of CRC using real data from the National Health Fund. Therefore, we did not need to make any additional cost simulations. The variables considered in the sensitivity analysis were those that seemed to be the most uncertain in the whole study: screening costs, adherence, and the rates of CRC incidence and mortality reduction.

Screening costs differentiated between the medical centers taking part in the PCSP. Exact costs of colonoscopy screening are given in TABLE 1. The main determinants of the cost associated with colonoscopy screening were personnel costs (41%), equipment costs (13%), and costs of depreciation (12%). These cost categories also had the highest differences between oncology centers taking part in the program. The proportions attributed to the rest of the cost components (ie, costs of histopathology, administration, invitations, bowel preparation, and anesthesia in every 5th colonoscopy examination) were lower than 10% in each case.

Approximately 17.25% of adherence was reported in Poland at the beginning of the screening program,[20-21] but a higher adherence of 30% was expected in subsequent years.[22] Much higher adherence is furthermore presented in the literature.[23-32]

The rates of CRC incidence and mortality reduction were extracted strictly from the subject literature. The results presented in the literature differ significantly. Such differences probably occur due to many factors that may affect the efficacy of colonoscopy screening. For example, the rate of CRC incidence reduction may be affected by the type of endoscopist conducting the examination. Higher incidence reduction rates were reported with gastroenterologists, but lower in rates with other types of endoscopists.[47]

Statistical analysis To make our cost estimation concerning colonoscopy as accurate as possible, we used the Monte Carlo method relying on repeated random sampling, which supplied final ranges for the colonoscopy costs in the sensitivity analysis. To determine how changes in the uncertain variables influence the results of our baseline case, we conducted a probabilistic analysis using the Monte Carlo simulation with 100 000 iterations.

Ethics Written informed consent was obtained from all individuals undergoing screening colonoscopy. As the manuscript is based on retrospective analysis of medical and financial data, the research proposal was deemed exempt from oversight by an institutional ethics committee.

RESULTS

Baseline analysis

No screening

The no-screening scenario resulted in 1126 cases of CRC and 566 deaths because of CRC within the simulated cohort of 100 000 subjects. It resulted in the loss of 11 704 undiscounted life-years. The cost of CRC care and medicines for the patients was 10 971 854 USD for 100 000 subjects after discounting, which was approximately 110 USD per person (TABLE 3).

The results obtained in the extra analysis taking into account different discount rates for the costs and the effects (Supplementary material, Appendix 1) were very similar. The only difference in this case was associated with the cost of CRC care and medicines for the patients, which was 11 071 613 USD for 100 000 subjects after discounting (Supplementary material, *Table S1*).

Colonoscopy screening The colonoscopy screening scenario with adherence of 30% resulted in 914 cases of CRC and 454 CRC-related deaths. This translates into a 19.8% reduction in mortality and 18.9% reduction in incidence. Colonoscopy screening resulted in 1959 discounted life-years saved, which is 7.2 days gained per person. As a screening technique, colonoscopy resulted in a 21.3% reduction in costs for CRC care, which is 27.86 USD undiscounted savings per person. However, total discounted costs were 12 465 698 USD higher for colonoscopy screening than no screening due to the costs associated with the screening (TABLE 3).

The results obtained in the extra analysis taking into account different discount rates for the costs and the effects (Supplementary material, Appendix) were also very similar in this case. The only differences were in the number of discounted life-years saved, which was 1976, and in total discounted costs which were in this case 11 882 073 USD higher for colonoscopy screening (Supplementary material, *Table S1*).

Cost-effectiveness Colonoscopy screening turned out to be a cost-effective scenario with an ICER of 6364 USD per discounted life-year saved (TABLE 3). Although it was not a cost-saving strategy due to

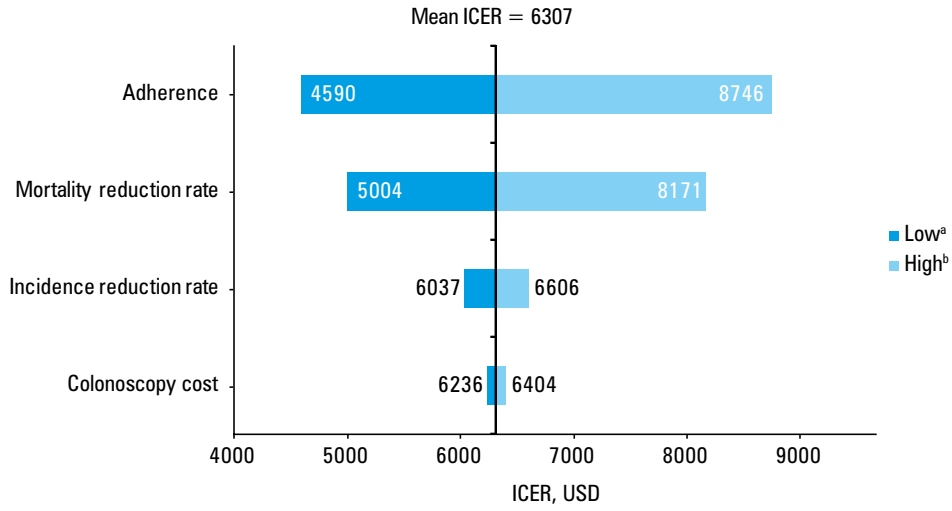

FIGURE 2 A tornado diagram of differences in incremental cost-effectiveness ratio (ICER) according to the variables used in the sensitivity analysis.
a Low indicates lower values of ICER than the mean value obtained in the probabilistic analysis
b High indicates higher values of ICER than the mean value obtained in the probabilistic analysis.

the costs associated with the screening, the estimated ICER was still far below all of the analyzed cost-effectiveness thresholds (50 000 USD, 100 000 USD, 200 000 USD, 46 000–70 000 USD). Therefore, compared with the no-screening scenario, colonoscopy allows for a high number of life-years saved at a relatively low and reasonable price.

The overall results obtained in the extra analysis taking into account different discount rates for the costs and the effects (Supplementary material, Appendix) remained unchanged with the slightly lower ICER of 6013 USD (Supplementary material, *Table S1*).

Sensitivity analysis Variables that may have had a significant impact on our analysis were the level of adherence, CRC incidence and mortality reduction rates, and cost of colonoscopy examination. Conducting probabilistic analysis using Monte Carlo simulation with 100 000 iterations (FIGURE 2), we achieved a mean ICER of 6307 USD per discounted life-year saved (95% CI, 3941–9950 USD).

The results obtained in the extra analysis taking into account different discount rates for the costs and the effects (Supplementary material, Appendix) seemed very similar with the lower mean ICER of 5966 USD (Supplementary material, *Figure S1*).

These results confirmed the use of colonoscopy as a cost-effective strategy, as the obtained values for the ICER were still far below the accepted willingness-to-pay thresholds (50 000 USD, 100 000 USD, 200 000 USD, 46 000–70 000 USD).

The most important uncertain variables, that is, with the most serious impact on the results of the model, were the rate of adherence, mortality reduction rate, incidence reduction rate, and cost of colonoscopy (FIGURE 2; Supplementary material, *Figure S1*).

DISCUSSION

Some studies analyzed the cost-effectiveness of colonoscopy screening,[11,39-42] but several did not use real-life data for the costs of screening and healthcare. To the best of our knowledge, this study is not only the first to assess the cost-effectiveness of colonoscopy screening in Poland, where it is the only method of screening for CRC, but is the first to apply real-life data whenever possible.

Our analysis suggests that colonoscopy screening is a cost-effective strategy for Poland. The conclusions obtained in the baseline analysis were confirmed in the sensitivity analysis. ICERs were much lower than the accepted willingness-to-pay thresholds. In addition, the cost of CRC care was lower in the case of colonoscopy compared with no screening. The results demonstrate that colonoscopy has a relatively low cost in Poland, and its cost-effectiveness is further augmented by high efficacy. The efficacy of colonoscopy screening was also observed in the analysis of the CRC stage distribution in the no-screening and colonoscopy screening groups. The first group had more CRC cases in the later stages of the disease, whereas in the screening scenario, almost 50% of CRC cases were stage I and II (TABLE 2).

The results indicate that colonoscopy screening may have a positive impact on the Polish society due to life-years saved by screening.

This study has some limitations. Some preliminary results have suggested that colonoscopy screening may have a positive impact on reducing CRC incidence and mortality in the general population, but full and reliable results of large population-based CRC screening trials will not be available until 2024[48]; therefore, we had to adopt several assumptions to conduct our analysis. Yet, according to our model, once-in-a-lifetime colonoscopy screening for CRC is effective and cost-effective compared with no screening.

We conducted our study bearing in mind screening conditions that were applied in Poland. Hence, we did not include any other comparators to colonoscopy concerning CRC screening modalities (eg, FIT, flexible sigmoidoscopy) due to the fact that in Poland colonoscopy is the only screening method used. Though, we are aware that they might be also considered as reasonable screening policy options, especially fecal markers which are less invasive, easily accessible, and also cost-effective, and thus very

often recommend by the current guidelines as screening tools. Nevertheless, colonoscopy examination makes it possible to combine screening population against CRC with diagnosing other enteric diseases[49] and also removing adenomas and polyps.[5,7] Colonoscopy is also among the tools used for surveillance in patients after surgery for colorectal cancer.[50]

The obtained results are substantial mainly due to the fact that we tried to use as much real-life data as possible. A lot of data came directly from the PCSP. Obtaining some data required a great deal of cooperation with many Polish institutions such as the Polish Ministry of Health and The National Health Fund. Thus, many of the input data and detailed cost estimates presented in our study can be portrayed as novel. Such data enable reliable evaluations. We tried to design our study in a way that would be comparable with other studies assessing the cost-effectiveness of colonoscopy screening in other countries, and the results of our study were consistent with those of other important studies regarding the cost-effectiveness of colonoscopy screening.[11,39-42] The uncertainty of our model was minimized by the sensitivity analysis, as colonoscopy screening remained cost-effective in all conducted scenarios, even in the case of high variation in crucial variables.

The present study demonstrated the cost--effectiveness of colonoscopy screening, which may have significant meaning and good informative value for medical practitioners, health policymakers, and health technology assessments not only in Poland, but also for international comparisons.

SUPPLEMENTARY MATERIAL

Supplementary material is available at www.mp.pl/paim.

ARTICLE INFORMATION

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CONTRIBUTION STATEMENT MFK, JR, AC-C, CH, and BK conceived the concept of the study. BK, CH, OK, MFK, and JR contributed to the study design. AS, MFK, JR, RP, and BK were involved in data collection. BK, OK, PW, and MFK analyzed the data. BK, CH, OK, PW, MP, AC-C, MR, JR, and MFK were involved in critical analysis of the methodology applied, interpretation of the study results, and drafting the manuscript for publication purposes. All authors approved the final version of the manuscript.

CONFLICT OF INTEREST None declared.

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