Implementation of an optical diagnosis strategy saves costs and does not impair clinical outcomes of a fecal immunochemical test-based colorectal cancer screening program

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ABSTRACT

Background and study aims In an optical diagnosis strategy, diminutive polyps that are endoscopically characterized with high confidence are removed without histopathological analysis and distal hyperplastic polyps are left in situ. We evaluated the effectiveness and costs of optical diagnosis.

Methods Using the Adenoma and Serrated pathway to Colorectal CAncer (ASCCA) model, we simulated biennial fecal immunochemical test (FIT) screening in individuals aged 55 – 75 years. In this program, we compared an optical diagnosis strategy with current histopathology assessment of all diminutive polyps. Base-case assumptions included 76 % high-confidence predictions and sensitivities of 88 %, 91 %, and 88 % for endoscopically characterizing adenomas, sessile serrated polyps, and hyperplastic polyps, respectively. Outcomes were colorectal cancer burden, number of colonoscopies, life-years, and costs.

Results Both the histopathology strategy and the optical diagnosis strategy resulted in 21 life-days gained per simulated individual compared with no screening. For optical diagnosis, €6 per individual was saved compared with the current histopathology strategy. These cost savings were related to a 31 % reduction in colonoscopies in which histopathology was needed for diminutive polyps. Projecting these results onto the Netherlands (17 million inhabitants), assuming a fully implemented FIT-based screening program, resulted in an annual undiscounted cost saving of €1.7 – 2.2 million for optical diagnosis.

Conclusion Implementation of optical diagnosis in a FIT-based screening program saves costs without decreasing program effectiveness when compared with current histopathology analysis of all diminutive polyps. Further work is required to evaluate how endoscopists participating in a screening program should be trained, audited, and monitored to achieve adequate competence in optical diagnosis.

Introduction

Colorectal cancer (CRC) is among the most prevalent forms of cancer in Europe [1]. CRC originates from precancerous adenomatous and serrated lesions [2]. Progression of both types of polyps into cancer is presumed to take 10 – 15 years, offering a window of opportunity for intervention [3, 4]. Colonoscopy with polypectomy halts the process towards CRC, and decreases the incidence and mortality of CRC [5]. The vast majority of polyps detected during colonoscopy, however, are diminutive in size (1 – 5 mm), and these polyps rarely contain advanced histological features or CRC [6]. The observation that almost all diminutive polyps are benign has been one of the main reasons for considering alternatives to the current practice of submitting these polyps for histopathological analysis [7].

Several advanced endoscopic imaging techniques have been developed over the past decade and allow endoscopists to accurately differentiate between serrated polyps and adeno-

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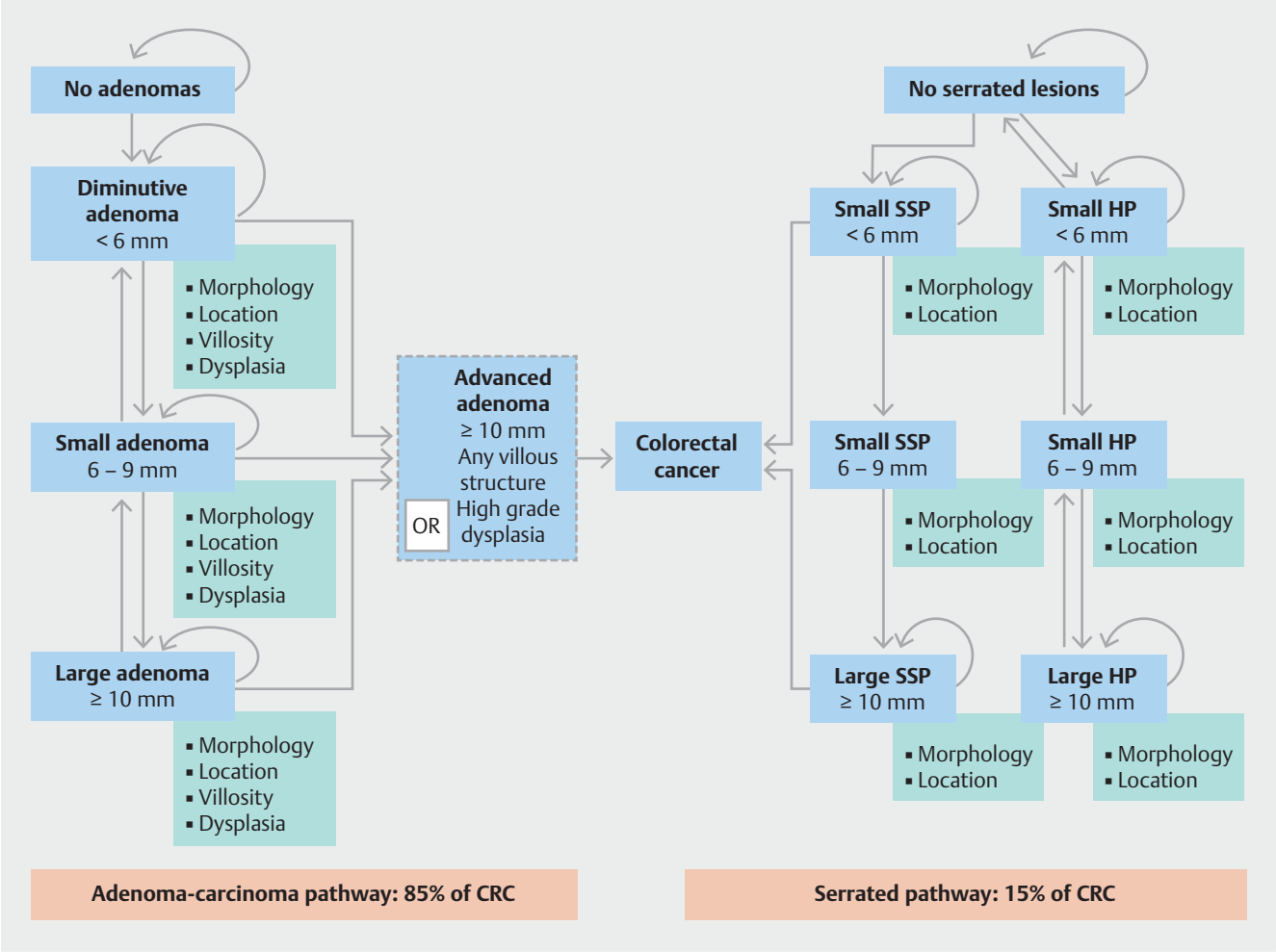


▶ **Fig. 1** Structure of the Adenoma and Serrated pathway to Colorectal CAncer (ASCCA) model. Please note that advanced adenoma is a definition and not a state in the model. CRC, colorectal cancer; SSP, sessile serrated polyp; HP, hyperplastic polyp.

mas [8]. With an optical diagnosis strategy, diminutive polyps (1–5 mm) throughout the colon are documented with a high resolution photograph, and then resected and discarded without histopathological analysis (resect-and-discard). The endoscopic diagnosis is then used to recommend the interval for the surveillance colonoscopy. Furthermore, diminutive rectosigmoid hyperplastic polyps can be left in situ, as these are considered harmless (resect-or-leave-in). If a polyp lacks morphological features leading to a confident optical diagnosis by the endoscopist (i.e. classification as adenoma, sessile serrated polyp [SSP] or hyperplasia), it is resected and submitted for pathological assessment. Only those diminutive polyps that are endoscopically characterized with high confidence can be discarded without histology analysis or left unresected in the rectosigmoid [9].

Implementation of an optical diagnosis strategy may result in reduced polypectomy-related complications, direct surveillance interval assignment, and cost savings. Two previously published cost-effectiveness studies have provided evidence that the implementation of such a strategy would not impair the effectiveness of colonoscopy and would lead to economic benefits [10, 11]. However, these modeling studies were based on primary screening colonoscopies only, did not include the serrated neoplasia pathway, and assumed a rather high percentage of confidently characterized diminutive polyps. The aim of the current modeling study was to determine the potential benefits and risks of implementing an optical diagnosis strategy in a CRC screening program consisting of biennial fecal immunochemical test (FIT) screening.

Methods

Model

For this study, we used the Adenoma and Serrated pathway to Colorectal CAncer (ASCCA) model. The structure and calibration of the model have been described extensively in a previous study [12]. In short, individual life cycles are simulated from the age of 20 until the age of 90 or death, whichever comes first. During this lifetime, an individual can develop up to 10 adenomas and 10 serrated polyps, which are both CRC precursor lesions (▶ **Fig. 1**). The former develop via the adenoma–carcinoma pathway, in which the progression of adenomas to ad-

vanced adenomas to CRC is simulated. Serrated polyps (i.e. hyperplastic polyps and SSPs), develop via the serrated pathway to CRC. This pathway is assumed to contribute to 15% of CRC cases [13].

The model-predicted adenoma and serrated lesion prevalence are in accordance with the findings of the Dutch COCOS trial [14], whereas CRC incidence and mortality rates correspond to figures reported by the Dutch Cancer Registry in 2009 (i.e. before the implementation of the screening program) [15]. CRC consists of four stages, based on the TNM classification. Each year, an asymptomatic tumor can progress to a subsequent cancer stage or may become symptom- or screen-detected. To fully evaluate the potential risk of an optical diagnosis strategy, we included the possibility that adenomas can harbor CRC [7]. These adenomas that harbor CRC can progress in size, whereas the tumor inside the adenoma can progress to a more advanced stage or become detected. If a tumor progresses to stage 2, we assumed that the tumor is no longer inside the adenoma. We also incorporated the possibility of incomplete polypectomy into the model to allow for the small possibility in optical diagnosis that a diminutive adenoma harboring CRC is not completely removed and not sent to pathology, thereby treating the cancer insufficiently. ▶ **Table 1** provides an overview of model parameters, together with the source of each item.

FIT and colonoscopy screening program

In the Dutch FIT-based screening program, individuals aged 55–75 years are biennially invited for screening. Individuals with a positive test outcome are referred for a diagnostic colonoscopy during which all detected lesions are removed. There is a small risk of complications and mortality due to the procedure (▶ **Table 1**) [16–19]. Participation rates for FIT and subsequent diagnostic colonoscopy were based on reports of the national monitor of the Dutch CRC screening program, and set at 73% and 92%, respectively [20].

Based on the findings during diagnostic colonoscopy, individuals may enter the surveillance program. Participation rate for surveillance colonoscopy was assumed to be 75% [21, 22]. Post-polypectomy surveillance intervals were guided by the Dutch surveillance guideline [23]. This surveillance guideline uses the number, size, location, and histology of colorectal polyps encountered to calculate a risk score (see ▶ **Appendix 1**). When this risk score equals zero, the individual returns to the screening program after 10 years. A risk score of 1–2 leads to a recommended surveillance interval of 5 years. A score of 3 or more leads to a recommended surveillance interval of 3 years. Individuals aged over 75 years will exit both the screening and surveillance programs.

Strategies

We first simulated a treatment-only strategy in which individuals are not subjected to screening. For FIT screening, we considered a histopathological diagnosis strategy, in which all detected lesions are removed and sent for histopathological analysis, as well as an optical diagnosis strategy. In the latter strategy, diminutive hyperplastic polyps characterized by the endoscopist with high confidence and located in the rectosigmoid are left in situ, whereas diminutive lesions throughout the colon endoscopically characterized with high confidence are removed but not sent for histopathological analysis. Based on recent literature, we assumed that 76% of optical diagnoses would be made with high confidence. This rate reflects the percentage of diminutive polyps for which histopathological analysis could be avoided because the histology (adenoma, hyperplastic polyp or SSP) of these polyps was characterized endoscopically [24]. The polyps characterized with low confidence are all removed and sent for histopathological analysis. The diagnostic sensitivity of the endoscopist to classify diminutive adenomas, SSPs, and hyperplastic polyps was assumed to be 88%, 91%, and 88%, respectively [24].

Test characteristics and costs

Following a previously reported calibration procedure [12], we derived lesion-specific FIT test characteristics (cutoff 75 ng/mL) from a Dutch FIT screening trial [25] (▶ **Table 1**). Adenoma detection rates for colonoscopy were based on a systematic review on adenoma miss rates [26]. As the pale color, proximal location, and flat appearance hamper the visual detection of serrated polyps [27], we assumed a 10% lower detection rate for serrated polyps than for adenomas.

No additional costs for colonoscopies performed in the optical diagnosis strategy were included, as advanced endoscopic imaging techniques are incorporated as standard in the current generation of endoscopy systems. Using the consumer price index, all costs were converted to 2016 euros (€) [28]. Total costs were determined using a healthcare perspective.

Analyses

We simulated a cohort consisting of 30 000 000 individuals. Outcomes of each strategy included CRC cases, CRC deaths, deaths due to colonoscopy, the number of colonoscopies with and without polypectomy, and with or without pathology, life-years lived, and total lifetime costs. Costs and effects were discounted using a discount rate of 3% [29].

The outcomes of each FIT screening strategy were compared with the treatment-only strategy without screening. Furthermore, we compared the optical diagnosis strategy with the histopathological strategy. For each comparison, we calculated the incremental cost-effectiveness ratio (ICERs), which is the difference in costs divided by the difference in life-years. A strategy was considered cost-effective when the ICER was below the Dutch GDP per capita in 2013, that is €35 916/life-year gained (LYG) [28, 30].

Sensitivity analysis

To allow for comparability of model results with other studies on the cost-effectiveness of optical diagnosis, we repeated all base-case analyses assuming a colonoscopy screening program. In this program, individuals aged 55–75 years are invited every 10 years to undergo screening colonoscopy and, dependent on the findings, may enter colonoscopy surveillance. Participation rates for screening and surveillance colonoscopy were set at 22% and 75%, respectively [14, 21, 22].

▶ **Table 1** Overview of important model parameters.

Variable	Value			Reference
	Base-case analysis		Sensitivity analyses	
FIT-screening				National monitor of the Dutch CRC screening program [20]
▪ Participation FIT	0.73			[21, 22]
▪ Participation diagnostic colonoscopy	0.92			
▪ Participation surveillance colonoscopy	0.75			
Colonoscopy screening				
▪ Participation rate screening colonoscopy	0.22			[14]
▪ Participation rate surveillance colonoscopy	0.75			[21, 22]
FIT positivity rate per lesion	Men	Women		[25]
▪ Healthy	0.96[1]	0.97[1]		
▪ Diminutive adenoma	0.004	0.003		
▪ Small adenoma	0.12	0.10		
▪ Large adenoma	0.30	0.28		
▪ Small serrated polyp	0.004	0.003		
▪ Large serrated polyp	0.004	0.003		
▪ Early-stage CRC	0.50	0.50		
▪ Late-stage CRC	0.85	0.85		
Colonoscopy detection rates				[26]
▪ Diminutive adenoma	0.74			
▪ Small adenoma	0.87			
▪ Large adenoma	0.98			
▪ Small serrated polyp	0.70			
▪ Large serrated polyp	0.88			
Incomplete polypectomy				[16]
▪ 1 – 5 mm polyps	0.03			
▪ 6 – 9 mm polyps	0.07			
▪ ≥ 10 mm polyps	0.14			
CRC in adenoma				[7]
▪ Diminutive adenoma	0.0004		0.0002 – 0.001	
▪ Small adenoma	0.0007			
Optical diagnosis (1 – 5 mm polyps)				[24]
▪ High-confidence diagnosis	0.76		0.50 – 1.00	
▪ Accuracy adenomas	0.88		0.75 – 1.00	
▪ Accuracy hyperplastic polyps	0.88		0.75 – 1.00	
▪ Accuracy sessile serrated polyps	0.91		0.75 – 1.00	
Optical diagnosis (6 – 9 mm polyps)				[24]
▪ High-confidence diagnosis			0.79	
▪ Accuracy adenomas			0.93	

▶ **Table 1** (Continuation)

Variable	Value		Reference
	Base-case analysis	Sensitivity analyses	
▪ Accuracy hyperplastic polyps		0.90	
▪ Accuracy sessile serrated polyps		0.91	
FIT costs			[38]
▪ Testkit[2]	€1.38		
▪ Organization[2]	€15.10		
▪ Analysis[2]	€4.84		
Colonoscopy costs			[17, 19,39,40]
▪ Without polypectomy	€729.96		
▪ With polypectomy	€871.45		
▪ Pathology	€71.79	€50–€150	
▪ Complications after colonoscopy (2.8 per 1000)[3]	€1386.51		
CRC treatment costs			[41]
▪ Stage I	€26585		
▪ Stage II	€41735		
▪ Stage III	€54815		
▪ Stage IV	€40980		

CRC, colorectal cancer; FIT, fecal immunochemical test.
All costs are presented in 2016 Euros.
[1] Specificity per individual.
[2] Costs per invitee.
[3] Fatal complications occur in 0.09 per 10 0000 colonoscopies without polypectomy, and in 0.9 per 10 000 colonoscopies with polypectomy [18,19,39].

To explore the impact of uncertainty regarding several key assumptions on model predictions, we varied the following parameters in one-way sensitivity analyses. First, we increased and decreased the rate of high-confidence predictions to 100% and 50%. Second, the proportion of accurately diagnosed polyps was adjusted to 100% and 75%. Third, pathology costs per set of polyps were increased to €150 and decreased to €50. Fourth, we set the prevalence of CRC within diminutive polyps at 0.02% and 0.10%. Furthermore, we assessed an optical diagnosis strategy in which small polyps (6–9 mm) are also not submitted for histopathological analysis. Finally, we modified the model-predicted surveillance recommendations in accordance with the European Society of Gastrointestinal Endoscopy (ESGE) post-polypectomy surveillance guideline [31].

Results

Impact on CRC burden and colonoscopy demand

▶ **Table 2** shows the CRC burden and colonoscopy demand for each strategy. Without screening, the ASCCA model predicted 68.9 CRC cases and 28.2 CRC-related deaths in the lifetime of 1000 individuals. FIT screening with histopathological diagnosis (current practice) decreased the CRC burden to 46.6 cases and 14.1 deaths, corresponding to a 32% and 50% reduction in CRC incidence and mortality, respectively. Implementation of an optical diagnosis strategy in a FIT-based screening program led to a 0.1 increase in CRC incidence (46.7 cases) and a 0.1 increase in CRC mortality (14.2 deaths).

Both the histopathological diagnosis strategy and the optical diagnosis strategy required 305 diagnostic colonoscopies, of which 101 were negative in a cohort of 1000 individuals. A colonoscopy is considered negative when no polyps or tumors are detected. In both strategies, 14 individuals were diagnosed with CRC. In the optical diagnosis strategy, the number of colonoscopies in which histopathological assessment was required was reduced by 31% compared with the histopathological diagnosis strategy (132 vs. 190). Optical diagnosis led to 10 procedures in which suspected hyperplastic polyps in the rectosigmoid were left in situ, and to 48 procedures with polypectomy in which diminutive polyps were the most advanced polyps and were discarded without histology analysis. In addition, the number of deaths due to colonoscopy per 1000 individuals was 0.001 lower in the optical diagnosis strategy (0.030 vs. 0.031) because fewer polypectomies were performed in the rectosigmoid.

For surveillance colonoscopies, optical diagnosis resulted in a 53% reduction in the number of colonoscopies in which pa-

▶ **Table 2** Colorectal cancer burden and colonoscopy demand in the lifetime of a cohort of 1000 individuals.

Strategy	CRC cases	CRC deaths	Deaths due to colonoscopy	Diagnostic colonoscopies							Surveillance colonoscopies						
							Diagnostic colonoscopies categorized by findings						Surveillance colonoscopies categorized by findings				
				Total	No polyps	CRC	Polyps: no POL, no PA	Polyps: with POL, no PA	Polyps: with POL, with PA	No. of adenomas to PA	Total	No polyps	CRC	Polyps: no POL, no PA	Polyps: with POL, no PA	Polyps: with POL, with PA	No. of adenomas to PA
No screening	68.9	28.2	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
FIT-based screening																	
▪ Histopathological diagnosis	46.6	14.1	0.031	305	101	14	0	0	190	326	192	83	1	0	0	107	161
▪ Optical diagnosis	46.7	14.2	0.030	305	101	14	10	48	132	213	190	75	1	8	56	50	75
Colonoscopy-based screening																	
▪ Histopathological diagnosis	53.4	20.5	0.035	542	294	5	0	0	243	282	143	66	1	0	0	77	113
▪ Optical diagnosis	53.5	20.5	0.032	542	291	5	27	118	101	151	142	59	1	6	39	37	52

CRC, colorectal cancer; FIT, fecal immunochemical test; NA, not applicable; POL, polypectomy; PA, pathology.

thology was required compared with the histopathological diagnosis strategy (50 vs. 107). Avoiding histopathological analysis for diminutive polyps resulted in a 1.1 % decrease in 3-year surveillance intervals and a 1.5 % increase in 5-year surveillance intervals. As a result, there were fewer surveillance colonoscopies (190 vs. 192) in the optical diagnosis strategy. Furthermore, fewer colonoscopies were negative in the optical diagnosis strategy.

Cost-effectiveness analysis

The results of the cost-effectiveness analysis are shown in ▶ **Table 3**. Implementation of optical diagnosis in FIT-based screening led to a 0.1 increase in CRC mortality on the one hand and to 0.001 fewer deaths due to colonoscopy on the other hand in the lifetime of 1000 individuals. As a result, there was no difference in health gain between the two FIT-based screening strategies (0.058 LYG – equivalent to 21 life-days – per simulated individual compared with no screening). The optical diagnosis strategy was predicted to cost € 6 per simulated individual less than the histopathological diagnosis strategy. This difference was mainly driven by lower pathology costs of the optical diagnosis strategy.

When taking no screening as the reference, both FIT-based screening strategies were cost-effective (▶ **Table 3**). Each strategy led to more life-years at lower costs than no screening. We also compared the optical diagnosis strategy with the histopathological strategy. As optical diagnosis led to an equal health gain at lower costs, it was considered the dominant strategy compared with histopathological diagnosis.

Sensitivity analyses

We repeated all base-case analyses assuming a primary colonoscopy screening program and similar observations were seen. Optical diagnosis in a colonoscopy screening program reduced the number of pathological evaluations in screening and surveillance colonoscopies with polypectomy by 58 % and 52 %, respectively. The optical diagnosis strategy led to equal health gains as histopathological diagnosis but at lower costs (€ 10 difference). As in FIT-based screening, this cost difference was mainly due to lower pathology costs.

▶ **Fig. 2** shows the results of the sensitivity analyses concerning the rate of high-confidence predictions, the proportion of accurately diagnosed polyps, costs of pathology, the probability of cancer in diminutive adenomas, extending the optical diagnosis strategy to small polyps, and the use of the ESGE surveillance guideline. In all analyses, the optical diagnosis strategy remained less costly than histopathology for all diminutive polyps (cost savings of € 2 – 11 per individual). Varying these key parameters led to similar model predictions of CRC burden and health gains as in the base-case analysis.

Discussion

Over the past few years, the development of advanced endoscopic imaging techniques has allowed endoscopists to differentiate between the histological subtypes of diminutive polyps. An accurate endoscopic diagnosis can avoid the need for histo-

▶ **Table 3** Results of cost-effectiveness analysis. The incremental cost-effectiveness ratio (ICER) of each screening strategy compared with the no screening strategy is indicated by ICER 1, whereas ICER 2 is calculated using the histopathological strategy as the reference.

Strategy	Undiscounted, per individual		Discounted, per individual						Difference in costs	LYG	ICER 1	Difference in costs	LYG	ICER 2
			Costs of colonoscopy											
	Costs	LY	Procedure	Polypectomy	Pathology	Complications	Total costs	LY						
No screening	2743	30.081	NA	NA	NA	NA	1437	19.412	Ref	Ref	Ref	NA	NA	NA
FIT-based screening														
▪ Histopathological diagnosis	2275	30.218	231	27	14	2	1361	19.470	−76	0.058	Dominant	Ref	Ref	Ref
▪ Optical diagnosis	2268	30.217	231	26	8	2	1355	19.470	−82	0.058	Dominant	−6	0	Dominant
Colonoscopy-based screening														
▪ Histopathological diagnosis	2627	30.148	332	29	15	2	1513	19.440	76	0.028	2714	Ref	Ref	Ref
▪ Optical diagnosis	2614	30.148	332	27	6	2	1503	19.440	66	0.028	2357	−10	0	Dominant

ICER, incremental cost-effectiveness ratio; LY, life-year; LYG, life-years gained; NA, not applicable; Ref, reference; FIT, fecal immunochemical test.

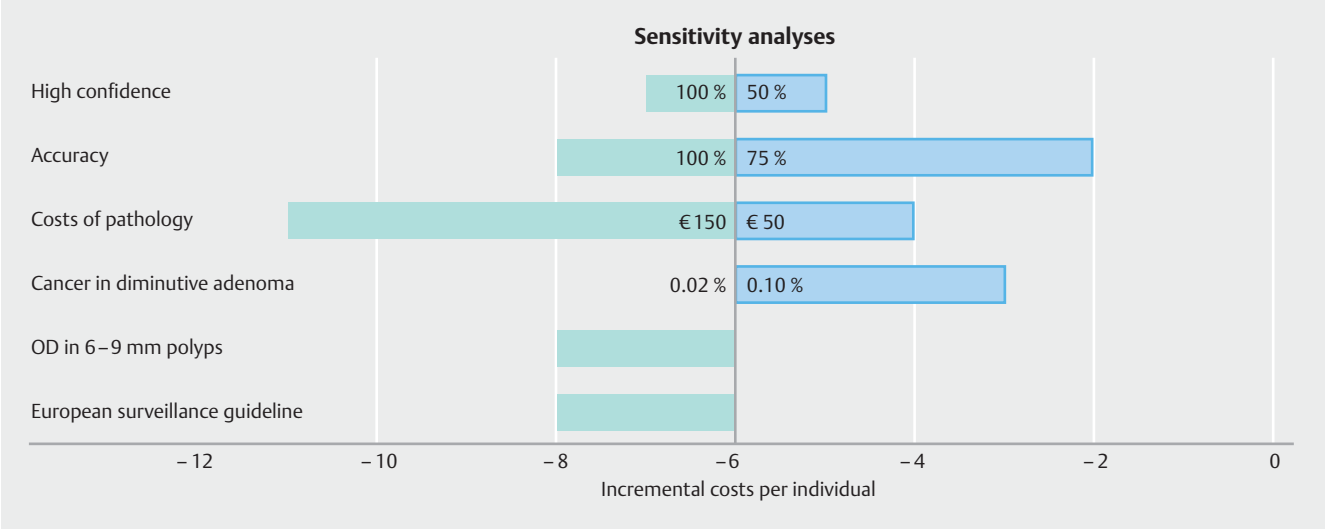
pathological analysis of diminutive polyps and instead their endoscopic appearance can be used to guide the post-polypectomy surveillance recommendations. Furthermore, diminutive hyperplastic polyps located in the rectosigmoid can be left without resection. In this study, the ASCCA model showed that a FIT-based screening strategy with histopathology for all diminutive polyps (current regular care) results in 21 life-days gained per simulated individual compared with no screening. The optical diagnosis strategy within the FIT-based screening program, however, led to similar health gains but saved €6 per simulated individual compared with the histopathology strategy. When projecting these results onto a fully implemented FIT-based screening program in the Netherlands with 17 million inhabitants, the optical diagnosis strategy results in an annual undiscounted benefit of €1.7 – 2.2 million.

Our modeling study has several strengths. The ASCCA model used in the study includes both the adenoma–carcinoma pathway and the serrated neoplasia pathway, and provides a realistic description of the development of precursor lesions to CRC. In addition, we included both clinical consequences of optical diagnosis (i. e. resect-and-discard), and the consequences of resect-or-leave-in. Furthermore, we included the small possibility that diminutive adenomas harbor CRC in the ASCCA model. Therefore, we can fully evaluate the potential risk of an optical diagnosis strategy. Finally, to compare the results of our study with previously published studies that were based on screening colonoscopies, we included an analysis of the optical diagnosis strategy in a colonoscopy screening program.

Our study confirms that optical diagnosis is cost-saving without impairing the effectiveness of a screening program, a finding that is compatible with earlier published modeling studies on the cost-effectiveness of optical diagnosis [10, 11]. However, these studies reported substantially higher economic benefits, as US$ 25 [10] and US$ 77 [11] per screened individual were saved. This difference is mainly related to a higher prevalence of synchronous polyps sized ≥5 mm in a FIT-based program. Furthermore, pathology costs were calculated per individual polyp instead of per set of polyps. The latter is routine practice in the Netherlands. The study from the USA also assumed a higher rate of high-confidence diagnoses (84 % vs. 76 %) [10]. In our study, the reduction in number of diagnostic colonoscopies with pathology in the primary colonoscopy screening setting is larger compared with the FIT-based screening setting (58 % vs. 31 %). As a result, the cost savings per individual are higher in the primary colonoscopy setting (€10 vs. €6 gained per individual).

The higher prevalence of synchronous larger polyps might also prove advantageous for the implementation of an optical diagnosis strategy in a FIT-based screening setting, as the assignment of surveillance intervals is less dependent on the histology of diminutive polyps. In our study, the variation in 3-year, 5-year, and total number of surveillance colonoscopies ranged between −1.2 % and +1.4 %. In the study of Kessler et al., a higher variability of up to 11.8 % was seen [11].

In the sensitivity analyses, we confirmed the robustness of our model predictions. In the study from the USA, the rate of high-confidence predictions was the most influential variable



▶ **Fig. 2** Incremental costs of several optical diagnosis strategies compared with the histopathological diagnosis strategy. The dark grey vertical line indicates the base-case optical diagnosis (OD) strategy.

[10]. In our study, changing the accuracy to 75 % and 100 % had more impact on the predicted costs than the rate of high-confidence predictions because costs were calculated per set of polyps. Owing to the structure of the model, we were not able to perform an additional analysis to calculate costs per individual polyp. In the sensitivity analysis in which surveillance was guided by the ESGE guideline, an additional € 2 per individual was saved. This mainly related to a larger reduction of surveillance colonoscopies in which histopathology was needed when compared with the base-case scenario using the Dutch post-polypectomy surveillance guideline (▶ **Appendix 1**). Finally, we included 6 – 9 mm polyps in the optical diagnosis strategy. This saved additional costs. Although optical diagnosis for these lesions probably results in higher accuracies [24], future studies should determine whether optical diagnosis of 6 – 9 mm polyps can be safely implemented.

Our study has several limitations. The outcomes of modeling studies rely largely on the underlying assumptions. The accuracy of endoscopic polyp differentiation used in our model is based on an image-based optical diagnosis study [24], and these numbers might not reflect accuracies achieved in daily practice. We chose the results of this study for our assumption, as it is the only study in which participating endoscopists were trained and audited in optical differentiation of adenomas, hyperplastic polyps, and SSPs. On the one hand, the rate of high-confidence predictions of 76 % reflects the rates that were also achieved in two recently published large optical diagnosis studies performed by nonexperts [32, 33]. Furthermore, the chosen sensitivity for adenomas is conservative when compared with results from meta-analyses in which pooled sensitivities for adenomas between 91.0 % and 93.8 % were calculated [8, 34]. On the other hand, we used a sensitivity of 88 % for hyperplastic polyps, which is higher than the values reported in these meta-analyses, which ranged between 82.6 % and 85.6 % [8, 34]. The accuracy of 91 % for the optical differentiation of SSPs can be regarded as high. A recent published meta-analysis showed pooled sensitivities for differentiation between SSPs and non-neoplastic polyps of between 47 % and 80 % in real-time studies using different advanced imaging techniques [35]. However, additional analyses assuming a sensitivity for SSPs of 47 % did not change our outcomes [12].

Another limitation is that the manner in which the optical differentiation is implemented in our model reflects the assumption that all endoscopists participating in a FIT-based screening program are equally high performers in optical diagnosis. Although multiple studies have demonstrated that with short videos and image-based training sessions, inexperienced endoscopists can become high performers [36, 37], studies in daily colonoscopy practice with nonexpert endoscopists have shown conflicting results [32, 33]. Future studies should determine whether endoscopists working in nonacademic hospitals could be trained to meet current optical diagnosis accuracy standards and how this should be organized.

In line with earlier published modeling studies, we did not include any costs associated with the implementation of an optical diagnosis strategy. As advanced imaging techniques are now incorporated as standard in new-generation endoscopy systems, we also did not include additional costs for colonoscopies with optical diagnosis. Training, monitoring, and auditing endoscopists to ensure that current optical diagnosis benchmarks are met might be costly and there is currently no financial incentive to implement the optical diagnosis strategy. On the other hand, the time, costs, and efforts associated with collecting diminutive polyps (different snare, polyp trap) and the pathology outcome, including outpatient clinic visits and/or telephone calls, have not been taken into account in our model either, leading to an underestimation of the cost savings of an optical diagnosis strategy. To overcome these issues, real-life studies in daily colonoscopy practices are needed in which resource use including all these aspects is measured accurately to further define the cost-effectiveness of an optical diagnosis strategy.

Very recently, the National Institute for Health and Care Excellence has facilitated the implementation of optical diagnosis in clinical practice in the UK, through the publication of an extensive report [38]. In this report, the advisory committee recommends to use advanced endoscopic imaging techniques, such as narrow-band imaging (NBI), flexible spectral imaging color enhancement (FICE) or I-SCAN, to assess diminutive polyps instead of histopathology to determine whether these polyps are adenomatous or hyperplastic if the following conditions are met. First, optical diagnosis needs to be performed with high definition equipment and can only replace histopathology if optical diagnosis is made with high confidence. The second condition includes training and accrediting of endoscopists in the use of these advanced imaging techniques under a national accreditation service. Furthermore, this service is able to audit and provide ongoing performance feedback. The report also includes a cost-effectiveness analysis. In this analysis, the differences in costs per person undergoing colonoscopy ranged from −£ 87.70 when FICE was compared with histopathology, to −£ 73.10 when NBI was compared with histopathology. The recommendations in this document help to ensure that international health societies are able to adopt optical diagnosis in clinical practice rapidly and consistently by providing evidence-based guidance.

In conclusion, the implementation of an optical diagnosis strategy in a FIT-based screening program is predicted to save costs without decreasing the effectiveness of the screening program when compared with current histopathology analysis of all diminutive polyps. Further work is required to evaluate how endoscopists participating in a screening program should be trained, audited, and monitored to achieve adequate competence in optical diagnosis.

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Competing interests

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▶ **Appendix 1** Dutch post-polypectomy surveillance guideline [23].

Polyp characteristics	Value	Score
Total number of adenomas	0 – 1	0
	2 – 4	1
	≥ 5	2
Presence of at least one adenoma sized ≥ 10 mm and/or serrated polyp[1] ≥ 10 mm	No	0
	Yes	1
Presence of at least one villous[2] adenoma	No	0
	Yes	1
Presence of at least one proximal[3] adenoma	No	0
	Yes	1
Total score		

[1] Serrated polyps comprise hyperplastic polyps, sessile serrated polyps, and traditional serrated polyps.
[2] Villous is defined as ≥ 75 % villosity.
[3] Proximal is defined as proximal of colon descendens including splenicflexure.

Score in index colonoscopy	Interval after index colonoscopy	Score in surveillance colonoscopy	Interval after surveillance colonoscopy
0	No surveillance	0	5 years[1]
1 – 2	5 years	1 – 2	5 years
3 – 5	3 years	3 – 5	3 years

[1] For patients without high risk (score ≥ 3), colonoscopy surveillance can be stopped after two negative surveillance colonoscopies.