ORIGINAL RESEARCH

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Screening for Colorectal Cancer With Fecal Immunochemical Testing With and Without Postpolypectomy Surveillance Colonoscopy

A Cost-Effectiveness Analysis

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Background: Population-based screening to prevent colorectal cancer (CRC) death is effective, but the effectiveness of postpolypectomy surveillance is unclear.

Objective: To evaluate the additional benefit in terms of cost-effectiveness of colonoscopy surveillance in a screening setting.

Design: Microsimulation using the ASCCA (Adenoma and Serrated pathway to Colorectal CAncer) model.

Data Sources: Dutch CRC screening program and published literature.

Target Population: Asymptomatic persons aged 55 to 75 years without a prior CRC diagnosis.

Time Horizon: Lifetime.

Perspective: Health care payer.

Intervention: Fecal immunochemical test (FIT) screening with colonoscopy surveillance performed according to the Dutch guideline was simulated. The comparator was no screening or surveillance. FIT screening without colonoscopy surveillance and the effect of extending surveillance intervals were also evaluated.

Outcome Measures: CRC burden, colonoscopy demand, life-years, and costs.

Results of Base-Case Analysis: FIT screening without surveillance reduced CRC mortality by 50.4% compared with no screening or surveillance. Adding surveillance to FIT screening reduced mortality by an additional 1.7% to 52.1% but increased lifetime colonoscopy demand by 62% (from 335 to 543 colonoscopies per 1000 persons) at an additional cost of €68 000, for an increase of 0.9 life-year. Extending the surveillance intervals to 5 years reduced CRC mortality by 51.8% and increased colonoscopy demand by 42.7% compared with FIT screening without surveillance. In an incremental analysis, incremental cost-effectiveness ratios (ICERs) for screening plus surveillance exceeded the Dutch willingness-to-pay threshold of €36 602 per life-year gained.

Results of Sensitivity Analysis: When using a parameter set representing low colorectal lesion prevalence or when colonoscopy costs were halved or colorectal lesion incidence was doubled, screening plus surveillance became cost-effective compared with screening without surveillance.

Limitation: Limited data on FIT performance and background CRC risk in the surveillance population.

Conclusion: Adding surveillance to FIT screening is not cost-effective based on the Dutch ICER threshold and substantially increases colonoscopy demand. Extending surveillance intervals to 5 years would decrease colonoscopy demand without substantial loss of effectiveness.

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Several countries have implemented a colorectal cancer (CRC) screening program, often in addition to an existing colonoscopy surveillance program. Although robust evidence shows that screening considerably reduces CRC mortality (1–3), the effect of surveillance is less clear.

Observational studies have shown that persons who undergo polypectomy have an increased risk for CRC compared with the general population (4, 5). Standardized incidence ratios of 1.26 and 1.40 have been reported (6, 7), suggesting that surveillance is justified in this subgroup. Surveillance for persons with lesions at colonoscopy is recommended, but the benefit of surveillance in a screening setting has thus far not been assessed.

Optimizing surveillance intervals in persons at different levels of CRC risk is challenging, as reflected by the variation in surveillance guidelines (8–12). The NPS (National Polyp Study), the only published trial to date that compared 2 different surveillance intervals, concluded that the interval can be at least 3 years (13). Ideally, the interval would be as long as possible while still being considered safe. The recently begun EPoS (European Polyp Surveillance) trial aims to determine the optimal surveillance strategy by randomly assigning participants to different surveillance intervals based on colonoscopy findings (14). Although the results are likely to increase our understanding of optimal surveillance strategies, data collection is scheduled to end no earlier than 2028.

Given that prospective data on surveillance are limited and will remain so for some time, we used the ASCCA (Adenoma and Serrated pathway to Colorectal

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CAncer) model to address the following questions. First, what is the additional benefit of colonoscopy surveillance in a screening setting? Second, what is the colonoscopy demand associated with screening plus surveillance, and how does this relate to that of screening without surveillance? Finally, how do changes in surveillance intervals affect the benefit and colonoscopy demand associated with surveillance?

METHODS

ASCCA Model

The ASCCA model has been described extensively elsewhere (15). In brief, the model simulates Dutch persons from age 20 years to age 90 years or death, whichever comes first. During their lives, persons are at risk for up to 10 adenomas and 10 serrated lesions.

When a colorectal lesion arises, it is assigned such characteristics as location, morphology, dysplasia, and histology. The development of each lesion in terms of growth and malignant characteristics is modeled independently. When a lesion progresses to advanced adenoma or arises as a sessile serrated adenoma, it can progress to CRC. We assumed that 15% of CRC cases develop from serrated lesions (serrated pathway) (16–22).

Each year, a tumor may be detected or may progress to a more advanced stage. Four stages for both asymptomatic and symptomatic CRC are included. An overview of natural history parameters is provided in Appendix Table 1 (available at Annals.org), and a flow chart of the model is shown in Appendix Figure 1 (available at Annals.org). The natural history model satisfactorily reproduces Dutch colorectal lesion prevalence rates (23) as well as Dutch CRC incidence and mortality rates in the absence of screening (Appendix Figures 2 and 3, available at Annals.org) (24). Of note, the lifetime CRC risk without screening in the U.S. population is similar to that in the Dutch population (23). The model is supplemented with a flexible screening-and-surveillance component that can evaluate a range of strategies. Parameters of the screening-and-surveillance component are updated regularly using the results of the national monitor of the Dutch CRC screening program.

Strategies

In the reference strategy, persons do not have screening or surveillance. Those who develop CRC may initiate treatment after becoming symptomatic. Five additional strategies were simulated: fecal immunochemical test (FIT) screening without colonoscopy surveillance; FIT screening plus colonoscopy surveillance performed according to the Dutch guideline; or FIT screening plus colonoscopy surveillance, with surveillance intervals extended to 5 years for all persons at increased risk, 5 years for those at high risk and 10 years for those at intermediate risk, or 10 years for all persons at increased risk.

Table 1. Dutch Surveillance Guideline*

Variable	Points	Recommended Surveillance Interval†
Number of adenomas		
0–1	0	–
2–4	1	–
≥5	2	–
Presence of ≥1 large adenoma		
No	0	–
Yes	1	–
Presence of ≥1 large serrated lesion		
No	0	–
Yes	1	–
Presence of ≥1 adenoma with villous architecture		
No	0	–
Yes	1	–
Presence of ≥1 proximal adenoma		
No	0	–
Yes	1	–
Risk group	**Total**	
Low	0	Return to screening after 10 y
Intermediate	1–2	5 y
High	≥3	3 y

* From reference 8.
† Surveillance is discontinued when a patient has 2 negative surveillance colonoscopy results and has never scored ≥3 points or has reached age 75 y unless his or her clinical condition justifies further surveillance.

Screening

Screening was modeled according to the Dutch CRC screening program. Model evaluations have shown that FIT screening is the strategy of choice in the Netherlands (25, 26). The Dutch screening program consists of biennial FIT screening in asymptomatic persons aged 55 to 75 years without a prior CRC diagnosis. We assumed a screening participation rate of 72.6% (27) (national monitor of the Dutch CRC screening program. Unpublished data).

Persons with a positive FIT result are referred to screening colonoscopy ("FIT-positive colonoscopy"). Both the FIT and the FIT-positive colonoscopy are considered part of screening. During colonoscopy, all detected lesions are removed by polypectomy, except for small hyperplastic polyps located in the rectosigmoid (8, 28). We assumed that 92% of persons with a positive FIT result have this procedure (7) (national monitor of the Dutch CRC screening program. Unpublished data).

No Surveillance

In the strategy of FIT screening without colonoscopy surveillance, all persons considered to be at low risk for metachronous lesions after FIT-positive

Table 2. Participation Rates, Test Characteristics, and Costs

Variable	Value		Reference
Overall FIT participation rate*	0.726		29–31
Low	0.05		–
Intermediate	0.70		–
High	0.95		–
	Men	**Women**	
FIT positivity rate per adenoma†			32
Diminutive	0.004	0.0003	–
Small	0.12	0.10	–
Large	0.30	0.28	–
FIT positivity rate per serrated lesion†			32
Small	0.004	0.003	–
Large	0.004	0.003	–
FIT positivity rate per CRC case†			32
Early-stage	0.50	0.50	–
Late-stage	0.85	0.85	–
FIT negativity rate per healthy person	0.96	0.97	32
Colonoscopy participation rate			
FIT-positive colonoscopy	0.92		27; national monitor of the Dutch CRC screening program (unpublished data)
Surveillance colonoscopy	0.92		–
Colonoscopy detection rate			33
Diminutive adenoma	0.74		–
Small adenoma	0.87		–
Large adenoma	0.98		–
Small serrated lesion	0.70		–
Large serrated lesion	0.12		–
Early- and late-stage CRC	1.00		–
	Costs		
	2016 Euros	**2015 U.S. Dollars**	
FIT			34
Test kit‡	1.38	1.56	–
Organization‡	15.10	17.06	–
Analysis§	4.84	5.47	–
Colonoscopy			35–38; Bergman Clinics (unpublished data)
Without polypectomy	729.26	824.06	–
With polypectomy	943.24	1065.97	–
Complications after colonoscopy‖	1386.51	1566.76	–
CRC treatment			39
Stage I	26 585	30 041	–
Stage II	41 735	47 161	–
Stage III	54 815	61 941	–
Stage IV	40 980	46 307	–

CRC = colorectal cancer; FIT = fecal immunochemical test.
* Because some persons are more willing to participate than others (29, 30), we allocated persons in the model to a low-, intermediate-, or high-participation group. Following a previously described calibration procedure, we determined the percentage of persons in each group and assigned a screening participation rate (31). Calibration targets were derived from a Dutch trial evaluating participation over 3 FIT screening rounds (29).
† Sensitivity per lesion/tumor.
‡ Cost per invitee.
§ Cost per participant.
‖ Complications occur in 2.8 per 1000 colonoscopies. Fatal complications occur in 1 per 10 000 colonoscopies (35, 37).

colonoscopy return for screening in 10 years. Those at intermediate or high risk for metachronous lesions return for screening immediately after polypectomy and are reinvited for FIT 2 years later.

Surveillance

The Dutch surveillance guideline recommends calculation of a risk score based on the number of colorectal lesions as well as the presence of large lesions,

adenomas with villous components, and proximal adenomas detected during colonoscopy (Table 1) (8). Persons with a score of 0 at FIT-positive colonoscopy (low-risk persons) are referred back to screening after 10 years, and those at intermediate or high risk enter the surveillance program. The surveillance interval is 5 years for persons considered to be at intermediate risk (score of 1 to 2) and 3 years for those at high risk (score ≥3).

In addition to screening plus surveillance performed according to the Dutch guideline, we simulated 3 strategies that differed from the guideline with respect to surveillance intervals. First, we set the interval for the intermediate- and high-risk groups at 5 years. Second, we used intervals of 10 years for the intermediate-risk group and 5 years for the high-risk group. Finally, we set the interval for both groups at 10 years.

For all surveillance colonoscopies, we assumed a 92% participation rate, identical to that for FIT-positive screening colonoscopy. We also assumed that surveillance ended when the patient had 2 negative results on surveillance colonoscopy in combination with risk scores less than 3 points or when the patient reached age 75 years.

CRC Risk in the Surveillance Population

The benefit of surveillance in addition to screening depends on the increase in adenoma and CRC risk in the surveillance population compared with the screening population. To allow appropriate judgment of the results of our study, we first obtained adenoma prevalence and CRC incidence curves for both the general population and the surveillance population by tracking the characteristics of persons considered to be at intermediate or high risk after FIT-positive colonoscopy. We then set up the model to simulate a cohort of 20 000 000 persons with these characteristics who did not undergo screening or surveillance. Outcomes were age-specific adenoma prevalence and CRC incidence.

Test Characteristics

Table 2 provides an overview of test characteristics related to screening, surveillance, and treatment. Lesion-specific test characteristics for FIT (cutoff of 75 ng/mL) were obtained from a Dutch FIT screening trial (32) following a previously reported calibration procedure (15). Colonoscopy detection rates were derived from a systematic review on adenoma miss rates (33). Because detection rates for serrated lesions are not reported but are likely to be lower than for adenomas (40, 41), we assigned a 10% lower detection rate to serrated lesions than for adenomas. We also assumed that colonoscopy was associated with a small risk for complications (38).

Costs

Costs were determined from a health care payer perspective (Appendix Figure 4, available at Annals.org) (42) and were converted to 2016 euros using the consumer price index for that year (43). To facilitate comparison of our results, costs are also reported in the tables in 2015 U.S. dollars using the purchasing power parity for that year (1 euro = 1.13 U.S. dollars) (44).

Outcomes

We simulated a cohort of 20 000 000 persons. Results for each strategy included the number of CRC cases and deaths, the number of colonoscopies, life-years, and total lifetime costs. Costs and effects were discounted at 3% annually (45).

We compared the outcomes of screening without surveillance and screening plus surveillance versus no screening or surveillance by calculating CRC incidence and mortality reductions and incremental cost-effectiveness ratios (ICERs) (the difference in costs divided by the difference in life-years). Strategies were compared in an incremental analysis. First, they were ordered on the basis of increasing costs, and dominated strategies (those that led to fewer life-years at higher or equal costs) were excluded. Then, ICERs between subsequent nondominated strategies were calculated.

Sensitivity Analyses

We repeated all analyses assuming an alternative strategy of FIT screening without surveillance, in which all persons returned to the screening program after 2 years, both after a negative result on FIT-positive colonoscopy and after removal of colorectal lesions. We also repeated the base-case analysis using costs per quality-adjusted life-year as the outcome. Utilities for cancer stages were derived from Ness and colleagues (46).

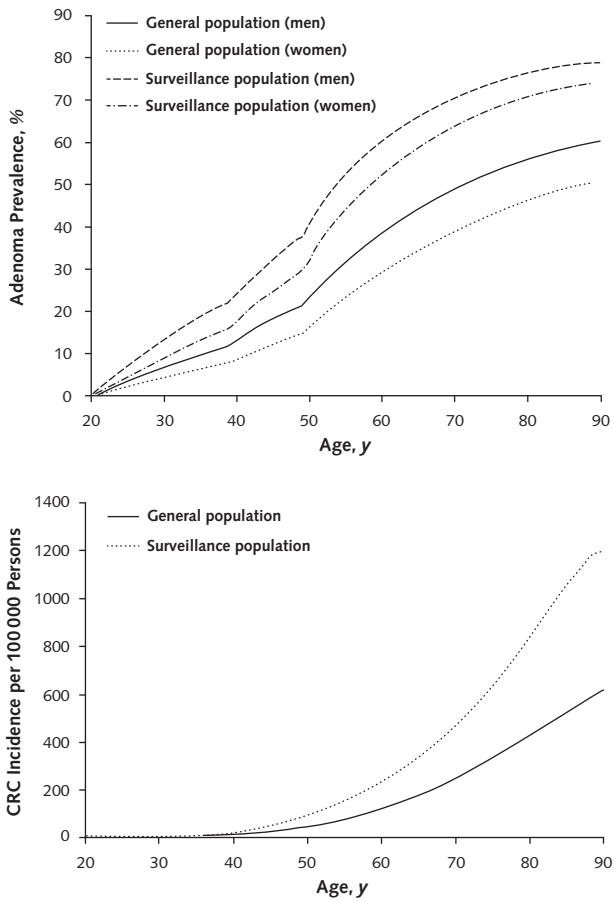
To improve international comparability of our findings, we also evaluated surveillance based on the Eu-

Table 3. ESGE and AGA Surveillance Guidelines

Guideline	Low-Risk Group	High-Risk Group	Stopping Age for Surveillance
ESGE (12)	1–2 tubular adenomas <10 mm with LGD or serrated polyp <10 mm without dysplasia Surveillance interval: 10 y/no surveillance*	Villous histology, HGD, ≥10 mm or ≥3 adenomas or serrated polyp ≥10 mm, with dysplasia Surveillance interval: 3 y	80 y
AGA (10)	1–2 tubular adenomas <10 mm with LGD or serrated polyp <10 mm without dysplasia Surveillance interval: 5†–10* y	Villous histology, HGD, ≥10 mm or ≥3 adenomas or serrated polyp ≥10 mm, with dysplasia Surveillance interval: 3 y	85 y

AGA = American Gastroenterological Association; ESGE = European Society of Gastrointestinal Endoscopy; HGD = high-grade dysplasia; LGD = low-grade dysplasia.
* In the model, we assumed a surveillance interval of 10 y.
† In case of inadequate bowel preparation or poor-quality examination.

Figure 1. Age-specific adenoma prevalence (*top*) and CRC incidence (*bottom*) in the general population and the surveillance population, assuming no screening or surveillance.



CRC = colorectal cancer.

ropean Society of Gastrointestinal Endoscopy (ESGE) and American Gastroenterological Association (AGA) guidelines (Table 3) (10, 12). Furthermore, to assess the effect of natural history assumptions, we repeated all base-case analyses using a set of natural history parameters representing low and high prevalence of colorectal lesions. We also assessed the effect of the following changes on model predictions in 1-way sensitivity analyses: 1) increasing and decreasing the surveillance participation rate by 5% (absolute change), 2) increasing and decreasing the detection rate of colonoscopy by 5% and 10% (absolute change) for all lesions, 3) halving and doubling colonoscopy costs, and 4) setting the contribution of the serrated pathway to CRC incidence to 0% and 30%.

In addition, we doubled and halved the colorectal lesion incidence rate, resulting in a roughly 10% increase and decrease, respectively, in colorectal lesion prevalence rates in the general population. This also altered the probability of developing new colorectal lesions after polypectomy in the surveillance population.

Role of the Funding Source

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RESULTS

CRC Risk in the Surveillance Population

Figure 1 shows the age-specific adenoma prevalence and CRC incidence in the general population and the surveillance population. These curves depict background risks with no screening or surveillance. Model-predicted CRC risk was markedly higher in the surveillance population than in the general population; at age 55 to 75 years, the risk was almost 2-fold.

Effectiveness

The model predicted that no screening or surveillance would result in 68.8 CRC cases and 28.2 deaths per 1000 average-risk persons (Table 4), with a 33.3% reduction in CRC cases and a 50.4% reduction in deaths with FIT screening without surveillance and reductions of 36.2% and 52.1%, respectively, with FIT screening with surveillance based on the Dutch guideline. Extending the surveillance intervals decreased the effectiveness of surveillance, but all screening-plus-surveillance strategies were still more effective than screening without surveillance.

Colonoscopy Use

Screening without surveillance resulted in 335 lifetime colonoscopies per 1000 average-risk persons. The number increased to 543 for FIT screening with surveillance based on the Dutch guideline but then decreased to 376 when all surveillance intervals were increased to 10 years. In screening without surveillance, all procedures are FIT-positive colonoscopies, whereas in screening plus surveillance, a distinction can be made between FIT-positive and surveillance colonoscopies. In a cohort of average-risk persons, 20% are diagnosed with colorectal lesions during FIT-positive colonoscopy in their lifetime. At the first screening round at age 55 years, 48% of persons who have FIT-positive colonoscopy are referred for surveillance. Of these, 29% are considered to be at high risk and 71% are considered to be at intermediate risk. Screening plus surveillance required fewer FIT-positive colonoscopies (305 per 1000 persons) than screening without surveillance because persons remained under surveillance instead of returning for screening.

The number of surveillance colonoscopies varied considerably. The Dutch guideline strategy required 238 surveillance colonoscopies per 1000 persons, and the number decreased when the surveillance interval

Table 4. Effectiveness and Burden of Biennial FIT Screening and Alternative Colonoscopy Surveillance Strategies

Strategy	CRC Cases, *n*	CRC Deaths, *n*	In Lifetime of Cohort of 1000 Average-Risk Persons			
			Deaths Due to Colonoscopy, *n*	Total Colonoscopies, *n*	Surveillance Colonoscopies, *n*	Negative Surveillance Colonoscopy Results, %
No screening or surveillance	68.8	28.2	NA	NA	NA	NA
Screening without surveillance	45.9	14.0	0.03	335	NA	NA
Screening plus surveillance						
Dutch guideline strategy	43.9	13.5	0.05	543	238	43
All intervals set at 5 y	44.2	13.6	0.05	478	173	39
Intervals set at 5 or 10 y*	44.7	13.7	0.04	422	117	32
All intervals set at 10 y	45.2	13.9	0.04	376	71	28

CRC = colorectal cancer; FIT = fecal immunochemical test; NA = not applicable.
* 5 y for high-risk persons and 10 y for intermediate-risk persons.

was extended. The demand was lowest when all intervals were 10 years (71 per 1000 persons).

We also assessed the proportion of colonoscopies with negative results (that is, those in which no colorectal lesions are found). The proportion of negative colonoscopy results after a positive FIT result with screening plus surveillance was similar to that for screening without surveillance (33%). However, the proportion of surveillance colonoscopies with negative results differed considerably. In the Dutch guideline strategy, 43% of surveillance colonoscopies had negative results; this decreased when the surveillance intervals were extended and was 28% when all intervals were 10 years.

Cost-Effectiveness

Screening without surveillance led to 58.1 life-years gained (LYGs) and cost savings of €260 000 per 1000 persons compared with no screening or surveillance (Table 5). Surveillance strategies were cost-saving and prolonged life compared with no screening or surveillance; for example, the Dutch guideline strategy increased life expectancy by 59.0 life-years and reduced costs by €193 000 per 1000 persons. Extending the surveillance interval led to fewer LYGs (58.0 to 58.7) but higher cost savings (€218 000 to €253 000 per 1000 persons). Thus, screening without surveillance and all screening-plus-surveillance strategies were more effective and less costly than no screening or surveillance. In the incremental analysis, screening without surveillance dominated no screening or surveillance as well as screening plus surveillance in which all intervals were 10 years. Two more effective, nondominated strategies were screening plus surveillance with intervals of 5 and 10 years (ICER, €55 000 per LYG) and screening plus surveillance performed according to the Dutch guideline (ICER, €90 000 per LYG). In the Netherlands, a strategy is considered cost-effective when the ICER is below the Dutch gross domestic product per capita (€36 602 per LYG) (43, 47). Based on this cutoff, screening plus surveillance was not cost-effective compared with screening without surveillance, mainly due to high surveillance costs.

Sensitivity Analyses

In a sensitivity analysis, we evaluated an alternative strategy of FIT screening without surveillance in which all persons who had FIT-positive colonoscopy returned to screening after 2 years. This strategy dominated all screening-plus-surveillance strategies (Figure 2) and had the lowest colonoscopy demand (358 per 1000 persons). Appendix Tables 2 and 3 (available at Annals.org) show the results of the other sensitivity analyses on cost per quality-adjusted life-year, surveillance guideline, parameter set, surveillance participation rate, colonoscopy detection rate, colonoscopy cost, contribution of the serrated pathway to CRC incidence, and colorectal lesion incidence. Model predictions were robust to changes in these parameters; based on the Dutch ICER threshold, adding surveillance to FIT screening was cost-effective in a minority of sensitivity analyses. Specifically, screening plus surveillance was cost-effective when a parameter set representing low colorectal lesion prevalence was used, when colonoscopy costs were halved, or when the incidence of colorectal lesions was doubled.

DISCUSSION

This study evaluated the additional benefit and colonoscopy demand associated with surveillance in a screening setting. Our model predicted that FIT screening without colonoscopy surveillance reduced CRC mortality by 50% compared with no screening or surveillance. When surveillance performed according to the Dutch guideline was added to FIT screening, the mortality reduction increased to 52%. Colonoscopy demand and the proportion of procedures with negative results were markedly higher when surveillance was added to screening. Extending surveillance intervals decreased program effectiveness slightly but reduced colonoscopy demand and the proportion of colonoscopies with negative results. Incremental cost-effectiveness ratios for screening plus surveillance exceeded the Dutch willingness-to-pay threshold of €36 602 per LYG (43, 47). Thus, adding surveillance to FIT screening was not cost-effective, mainly due to high surveillance costs. In sensitivity analyses, we found that when using a parameter set representing low colorectal lesion prevalence or when colonoscopy costs were halved or colorectal lesion incidence was doubled, screening plus surveillance became cost-effective compared with screening without surveillance.

Table 5. Results of the Cost-Effectiveness Analysis*

Strategy	Undiscounted LYs per 1000 Average-Risk Persons	Discounted per 1000 Average-Risk Persons				
		Surveillance Costs		Total Costs		LYs
		2016 Euros	2015 U.S. Dollars	2016 Euros	2015 U.S. Dollars	
Screening without surveillance	30 219.7	NA	NA	1 176 000	1 329 000	19 470.5
Screening plus surveillance						
All intervals set at 10 y	30 219.5	34 000	38 000	1 183 000	1 337 000	19 470.4
Intervals set at 5 or 10 y‡	30 220.9	58 000	66 000	1 198 000	1 354 000	19 470.9
All intervals set at 5 y	30 221.5	87 000	98 000	1 218 000	1 376 000	19 471.1
Dutch guideline strategy	30 222.1	118 000	133 000	1 243 000	1 405 000	19 471.4
No screening or surveillance	30 082.1	NA	NA	1 436 000	1 623 000	19 412.4

ICER = incremental cost-effectiveness ratio; LY = life-year; LYG = life-year gained; NA = not applicable.
* Strategies are ordered according to increasing discounted total costs. When strategies have equal total costs, they are ordered according to decreasing LYs. The reference strategy is the comparator strategy consisting of screening without surveillance. Dominated strategies led to fewer LYs at higher or equal costs than the comparator strategy.
† Calculated using the nearest cheaper strategy that is not dominated as the reference.
‡ 5 y for high-risk persons and 10 y for intermediate-risk persons.
§ Subject to extended dominance.

We found interesting results in a sensitivity analysis where we evaluated FIT screening without surveillance, with all persons returning to screening after 2 years. This differs from the base-case strategy of screening without surveillance, where low-risk persons returned to screening after 10 years and intermediate- and high-risk persons returned after 2 years. The former strategy dominated all screening-plus-surveillance strategies and was also more effective and less costly than the base-case screening-without-surveillance strategy. Although these results warrant further investigation, we considered this analysis exploratory given that the risk for CRC after a negative colonoscopy result is generally believed to be low (48). Nevertheless, ensuring high-quality colonoscopy is important because most CRC cases that develop in these 10 years may result from lesions that are missed at colonoscopy or incomplete polypectomy (49, 50).

It is important to note that our study was based on the Dutch screening program (which consists of biennial FIT screening) and that we evaluated the Dutch surveillance guideline. However, we believe that our conclusions with regard to surveillance likely apply to other primary screening strategies because of the marginal benefit of surveillance after detection. Furthermore, although we did not aim to compare surveillance guidelines, we conducted sensitivity analyses using the ESGE and AGA guidelines (10, 12). Surveillance based on these guidelines was more effective than with the Dutch guideline strategy, but ICERs for such surveillance versus screening without surveillance were higher, possibly due to the higher stopping age for surveillance. Adding ESGE- or AGA-based surveillance to screening was not cost-effective, based on the Dutch ICER threshold, but thresholds for determining cost-effectiveness differ among countries. Converting the Dutch threshold to U.S. dollars using the purchasing power parity results in a threshold of about $42 000 per LYG (44), but much higher thresholds are applied in the United States. Thus, additional analyses are required to make country-specific recommendations for surveillance.

To our knowledge, no other studies have compared screening plus surveillance versus screening without surveillance. To date, only 1 trial conducted more than 20 years ago has compared 2 surveillance intervals, and it concluded that the interval can be at least 3 years (13). Our results suggest that the interval may be 5 years for all persons at increased risk because this strategy is only slightly less effective than the Dutch guideline strategy (with intervals of 3 and 5 years for high- and intermediate-risk persons, respectively) and requires substantially fewer invasive colonoscopies. If we assume a fully implemented FIT screening program in the Netherlands (31), extending all intervals to 5 years would lead to about 13 000 fewer colonoscopies per year.

A recently published study on CRC incidence in a surveillance population (51) showed that persons considered to be at intermediate risk at baseline colonoscopy have CRC incidence similar to that in the general population. When persons with intermediate-risk adenomas at baseline colonoscopy were divided into low- and high-risk subgroups, CRC incidence in the low-risk subgroup was lower than that in the general population, prompting the authors to question whether colonoscopy surveillance is required in this subgroup. In contrast, the high-risk subgroup had a 30% increased risk for CRC compared with the general population. Although colonoscopy surveillance reduced CRC incidence in this subgroup, the authors speculated that 1 surveillance colonoscopy may suffice. These results support our main finding that the current Dutch surveillance program is probably too intensive.

We evaluated a limited number of surveillance strategies because we did not aim to find the optimal one. In line with the results of Atkin and colleagues (51), cost-effective colonoscopy surveillance strategies may exist with intervals based on improved selection of persons at high risk for CRC. However, additional evidence is required to optimize the surveillance interval. Such evidence is currently being collected in the EPoS trial (14), in which persons are randomly assigned to different surveillance intervals on the basis of findings during

Table 5–Continued

LYGs	Difference in Costs		ICER†	
	2016 Euros	2015 U.S. Dollars	2016 Euros	2015 U.S. Dollars
58.1	–260 000	–294 000	Reference	Reference
58.0	–253 000	–286 000	Dominated	Dominated
58.5	–238 000	–269 000	55 000	62 500
58.7	–218 000	–246 000	Dominated§	Dominated§
59.0	–193 000	–218 000	90 000	102 000
Reference	Reference	Reference	Dominated	Dominated

colonoscopy. The trial is limited in the number of colonoscopy surveillance strategies it can evaluate. However, in the future, EPoS study data may be used to update and provide further detail in existing CRC models, which will enable extrapolation of trial results to alternative surveillance strategies and facilitate optimization efforts.

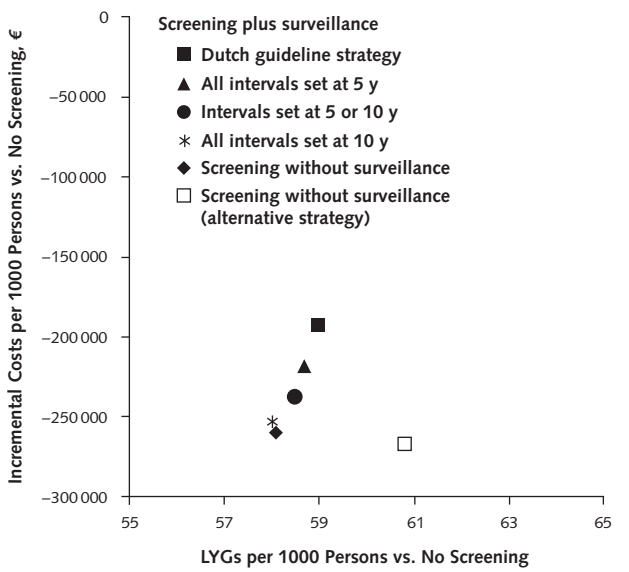
When important decisions, such as implementation of screening or surveillance, are based on model predictions, validity of the model is essential. A crucial factor in gaining confidence in model predictions is adequate reporting of model structure, assumptions, and data on which model parameters are based. The ASCCA model and its calibration have been described in detail by Greuter and colleagues (15). Various intermediate end points were used during calibration to increase model validity. Furthermore, the model was able to replicate the results of 2 Dutch screening trials (32, 52). With respect to surveillance, insight into model-predicted CRC risk is important because the rationale of surveillance is that CRC risk is higher in persons who undergo polypectomy than in the general population (4, 5). Risk ratios of 1.26 and 1.40 have been reported (6, 7); this risk may be decreased to a level close to that in the general population by endoscopic follow-up (6). In our model, the surveillance population of persons aged 55 to 75 years had a background risk for CRC that was almost 2-fold higher than in the general population. Our projected background risk was higher than reported estimates (6, 7) because we assumed no screening or surveillance, whereas persons in the aforementioned studies had colonoscopy with polypectomy, which decreased CRC risk (6, 7). Although the model is based primarily on Dutch data, model predictions will be similar for countries with similar prevalence of colorectal lesions. In countries with prevalence that differs considerably from that in the Netherlands, adding surveillance to FIT screening may be cost-effective, as shown in our sensitivity analyses.

In addition to background risk and surveillance interval, the effectiveness and colonoscopy demand associated with surveillance are determined by the age at which surveillance ends. We assumed that surveillance ends at age 75 years for all persons. However, the risk for adenomas and interval carcinoma increases with age (4, 5, 53, 54). Therefore, the Dutch surveillance guideline recommends individualization of the stopping age based on the patient's clinical condition. Because surveillance may be continued after age 75 years in clinical practice, we could have underestimated the effectiveness and colonoscopy demand associated with surveillance.

A key assumption of this study was that FIT positivity rates in the surveillance population were similar to those in the general population. Evidence on the performance of FIT in a surveillance population is limited. Terhaar sive Droste and colleagues (55) reported similar miss rates for advanced adenomas and CRC in the respective populations (56–59). However, the cutoff and the type of FIT differed between studies, hampering direct comparison. More research on FIT performance in a surveillance population is needed.

A false-positive FIT result may have an underlying cause, such as antiplatelet drug use, hemorrhoids, or angiodysplasia (60, 61). In persons with a known underlying cause of fecal bleeding, FIT participation after a negative colonoscopy result may be lower. However, data on such participation patterns are lacking. We assumed equal participation after a false-positive result, as in the general population; however, participation in breast cancer screening is lower in women with a false-

Figure 2. Cost-effectiveness plane depicting incremental LYGs (*x*-axis) against incremental costs (*y*-axis) for FIT screening without colonoscopy surveillance and FIT screening plus colonoscopy surveillance versus no screening.



In the alternative strategy of FIT screening without surveillance, all persons who undergo FIT-positive colonoscopy return for screening after 2 y. This strategy was cost-saving and life-prolonging relative to all other strategies. FIT = fecal immunochemical test; LYG = life-year gained.

positive result (62). Thus, we may have overestimated screening participation in persons with a false-positive FIT result. Because this would apply to both screening without surveillance and screening plus surveillance and we focused on the difference between these strategies, we expect no major effect on our results.

In conclusion, this study indicates that adding surveillance to FIT screening decreases CRC burden but is not cost-effective compared with screening without surveillance. Moreover, the colonoscopy demand associated with screening plus surveillance is considerably higher than that for screening without surveillance. This demand can be reduced without substantial loss of effectiveness if surveillance intervals are extended to 5 years.

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Note: The authors completed the CHEERS (Consolidated Health Economic Evaluation Reporting Standards) checklist (**Supplement**, available at Annals.org).

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Appendix Table 1. Overview of Natural History Parameters of the ASCCA Model*

Natural History Parameters	1-Year Transition Probabilities		Reference
Adenoma–carcinoma pathway			
Adenoma incidence in men (no adenoma to diminutive adenoma)			23, 63, 64
Age 20–39 y	0.003		
Age 40–49 y	0.007		
Age 50–54 y	0.019		
Age 55–59 y	0.022		
Age 60–64 y	0.024		
Age 65–69 y	0.028		
Age 70–74 y	0.033		
Age 75–90 y	0.035		
Adenoma incidence in women			23, 63, 64
Incidence factor	0.6†		
Personal risk index adenoma–carcinoma pathway			63, 64
Standard deviation	1.6†		
Progression in size			23, 64–66
Diminutive to small adenoma	0.07		
Small to large adenoma	0.10		
Regression in size			23, 64
Small to diminutive adenoma	0.25		
Large to small adenoma	0.15		
Dysplasia (low-grade to high-grade)			23, 64
Diminutive adenoma	0.004		
Small adenoma	0.009		
Large adenoma	0.010		
Villosity (tubular to tubulovillous/villous)			23, 64
Diminutive adenoma	0.004		
Small adenoma	0.025		
Large adenoma	0.085		
Progression from AA to CRC‡§	**Shape**	**Scale**	24
Men	2†	29†	
Women	2†	27†	
Serrated pathway	**SSA**	**HP**	
Serrated lesion incidence in men (no serrated lesion to small serrated lesion)			23, 64
Age 20–25 y	0.0001	0.001	
Age 25–29 y	0.0001	0.001	
Age 30–34 y	0.0001	0.002	
Age 35–39 y	0.0001	0.004	
Age 40–44 y	0.0006	0.007	
Age 45–49 y	0.0015	0.010	
Age 50–54 y	0.0016	0.010	
Age 55–59 y	0.0014	0.006	
Age 60–64 y	0.0008	0.004	
Age 65–69 y	0.0008	0.004	
Age 70–74 y	0.0007	0.002	
Age 75–79 y	0.0006	0.002	
Age 80–84 y	0.0005	0.002	
Age 85–90 y	0.0004	0.002	
Serrated lesion incidence in women			23, 64
Incidence factor SSA	0.7†		
Incidence factor HP	0.7†		
Personal risk index serrated pathway			23, 64
Standard deviation	1.7†		
Progression in size			23, 64
Small to large serrated lesion	0.028		
Regression in size			23, 64
Small HP to no serrated lesion	0.0		
Large HP to small HP	0.4		
Progression to CRC§	0.006		24

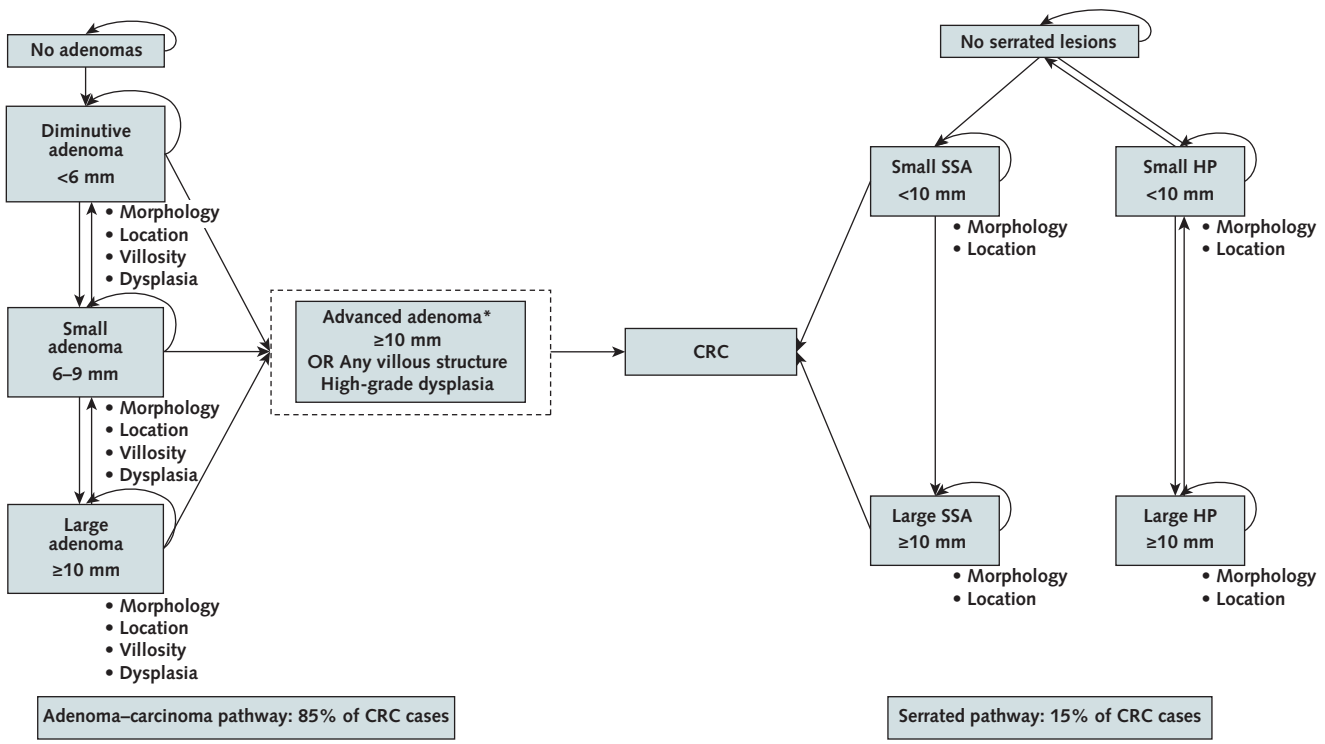
Continued on following page

Appendix Table 1–Continued

Natural History Parameters	1-Year Transition Probabilities		Reference
	Dwell Time, y‖	CRC Stage Distribution at Diagnosis	
CRC			67, 68
Stage I	2.5†	0.19†	
Stage II	2.0†	0.31†	
Stage III	1.5†	0.49†	
Stage IV	1.0†	0.01†	

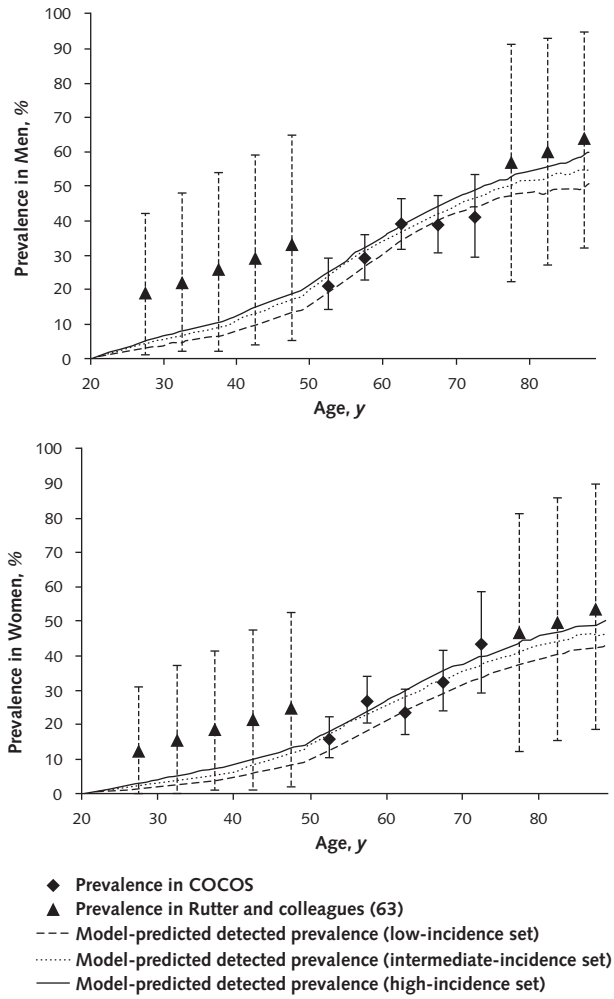
AA = advanced adenoma; ASCCA = Adenoma and Serrated pathway to Colorectal CAncer; CRC = colorectal cancer; HP = hyperplastic polyp; SSA = sessile serrated adenoma.
* The ASCCA model is programmed in C++ using the Boost library for the random-number generator (69).
† Parameter value instead of yearly transition probability.
‡ Weibull distribution.
§ This progression rate from polyp to CRC applies to the base-case analysis, in which we assumed an 85% contribution of the adenoma–carcinoma pathway and a 15% contribution of the serrated pathway to CRC incidence. This transition probability was recalibrated when assuming different contributions of each pathway to CRC incidence.
‖ Number of years a tumor spends in specific stage.

Appendix Figure 1. Flow chart of the ASCCA model.



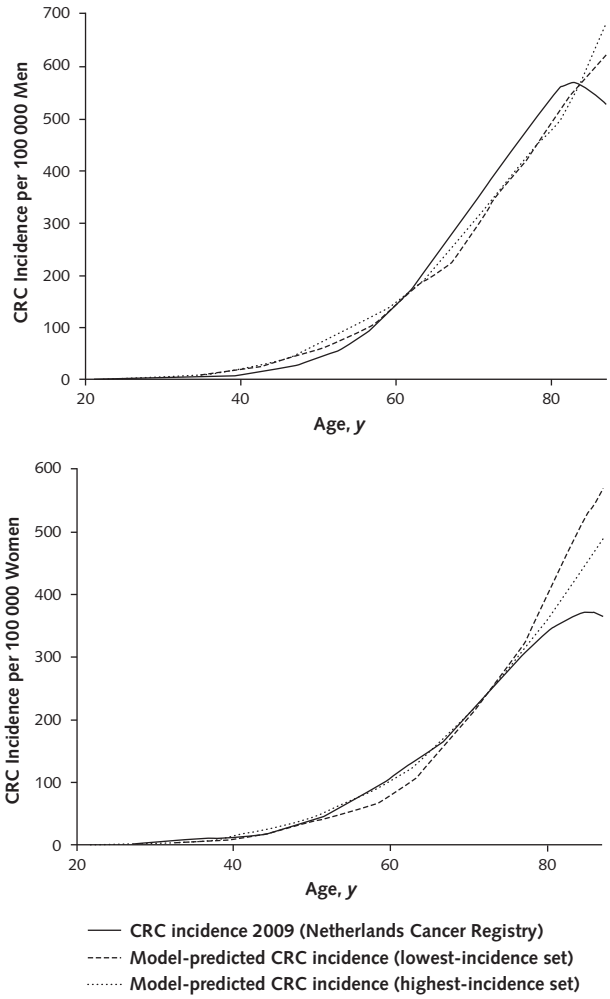
Adapted from Greuter and colleagues (15). ASCCA = Adenoma and Serrated pathway to Colorectal CAncer; CRC = colorectal cancer; HP = hyperplastic polyp; SSA = sessile serrated adenoma.
* Advanced adenoma is a definition and not a state in the model.

Appendix Figure 2. Model-predicted prevalence of detected adenomas in men (*top*) and women (*bottom*) for the lowest and highest fitting incidence set and an intermediate set.



Error bars indicate 95% CIs. Adapted from Greuter and colleagues (15). COCOS = COlonoscopy versus COlonography Screening trial.

Appendix Figure 3. Model-predicted incidence of CRC in men (*top*) and women (*bottom*) for the lowest- and highest-prevalence parameter set that most closely approximates CRC incidence in 2009 according to the Netherlands Cancer Registry.



Incidence curves from other years are similar to this one. Adapted from Greuter and colleagues (15). CRC = colorectal cancer.

Appendix Figure 4. Impact inventory for determining perspective of economic evaluation (42).

Sector	Type of Impact (list category within each sector with unit of measure if relevant)*	Included in This Reference Case Analysis From ... Perspective?		Notes on Sources of Evidence
		Health Care Sector	Societal	
Formal Health Care Sector				
Health	Health outcomes (effects)			
	Longevity effects	■	☐	
	Health-related quality-of-life effects	☐	☐	
	Other health effects (e.g., adverse events and secondary transmissions of infections)	■	☐	
	Medical costs			
	Paid for by third-party payers	■	☐	
	Paid for by patients out-of-pocket	■	☐	
	Future related medical costs (payers and patients)	■	☐	
	Future unrelated medical costs (payers and patients)	☐	☐	
Informal Health Care Sector				
Health	Patient-time costs	NA	☐	
	Unpaid caregiver-time costs	NA	☐	
	Transportation costs	NA	☐	
Non–Health Care Sector (with examples of possible items)				
Productivity	Labor market earnings lost	NA	☐	
	Cost of unpaid lost productivity due to illness	NA	☐	
	Cost of uncompensated household production†	NA	☐	
Consumption	Future consumption unrelated to health	NA	☐	
Social Services	Cost of social services as part of intervention	NA	☐	
Legal or Criminal Justice	Number of crimes related to intervention	NA	☐	
	Cost of crimes related to intervention	NA	☐	
Education	Impact of intervention on educational achievement of population	NA	☐	
Housing	Cost of intervention on home improvements (e.g., removing lead paint)	NA	☐	
Environment	Production of toxic waste pollution by intervention	NA	☐	
Other (specify)	Other impacts	NA	☐	

NA = not applicable.
* Categories listed are intended as examples for analysts.
† Examples include such activities as food preparation, cooking, and cleanup; household management; shopping; obtaining services; and travel related to household activity.

Appendix Table 2. Results of 1-Way Sensitivity Analyses: CRC Burden and Colonoscopy Demand per 1000 Persons

Strategy	CRC Cases, *n*	CRC Deaths, *n*	Colonoscopies, *n*	Negative Colonoscopy Results, %	CRC Cases, *n*	CRC Deaths, *n*	Colonoscopies, *n*	Negative Colonoscopy Results, %
	ESGE Guideline				**AGA Guideline**			
No screening or surveillance	68.8	28.2	NA	NA	68.8	28.2	NA	NA
Screening without surveillance	45.9	14.0	335	32	45.9	14.0	335	32
Screening plus surveillance	43.2	13.3	758	42	42.3	12.9	1100	63
	Low-Prevalence Parameter Set				**High-Prevalence Parameter Set**			
No screening or surveillance	69.8	28.4	NA	NA	68.2	28.3	NA	NA
Screening without surveillance	48.8	14.7	332	36	49.0	15.1	343	29
Screening plus surveillance								
Dutch guideline strategy	46.5	14.2	513	41	46.8	14.5	561	34
All intervals set at 5 y	46.9	14.2	458	39	47.1	14.6	493	32
Intervals set at 5 or 10 y*	47.5	14.4	405	36	47.7	14.8	434	30
All intervals set at 10 y	48.1	14.6	365	36	48.3	15.0	385	29
	5% Decrease in Surveillance Participation Rate				**5% Increase in Surveillance Participation Rate**			
No screening or surveillance	68.8	28.2	NA	NA	68.8	28.2	NA	NA
Screening without surveillance	45.9	14.0	335	32	45.9	14.0	335	32
Screening plus surveillance								
Dutch guideline strategy	43.9	13.5	529	37	43.9	13.4	556	38
All intervals set at 5 y	44.3	13.6	469	35	44.1	13.5	488	35
Intervals set at 5 or 10 y*	44.8	13.8	416	33	44.6	13.7	429	33
All intervals set at 10 y	45.3	13.9	372	32	45.1	13.8	379	32
	5% Decrease in Detection Rate of Colonoscopy				**5% Increase in Detection Rate of Colonoscopy**			
No screening or surveillance	68.8	28.2	NA	NA	68.8	28.2	NA	NA
Screening without surveillance	46.9	14.5	338	33	45.1	13.7	334	31
Screening plus surveillance								
Dutch guideline strategy	44.9	14.0	534	38	43.3	13.3	548	37
All intervals set at 5 y	45.1	14.1	473	36	43.4	13.3	482	34
Intervals set at 5 or 10 y*	45.8	14.3	418	34	43.9	13.5	425	32
All intervals set at 10 y	46.4	14.5	374	33	44.3	13.6	377	31
	10% Decrease in Detection Rate of Colonoscopy				**10% Increase in Detection Rate of Colonoscopy**			
No screening or surveillance	68.8	28.2	NA	NA	68.8	28.2	NA	NA
Screening without surveillance	47.9	15.1	340	35	45.1	13.7	334	31
Screening plus surveillance								
Dutch guideline strategy	45.8	14.5	524	39	43.3	13.3	548	37
All intervals set at 5 y	46.2	14.6	468	37	43.4	13.3	482	34
Intervals set at 5 or 10 y*	47.0	14.9	413	35	43.9	13.5	425	32
All intervals set at 10 y	47.6	15.2	372	35	44.3	13.6	377	31
	Colonoscopy Costs Halved				**Colonoscopy Costs Doubled**			
No screening or surveillance	68.8	28.2	NA	NA	68.8	28.2	NA	NA
Screening without surveillance	45.9	14.0	335	32	45.9	14.0	335	32
Screening plus surveillance								
Dutch guideline strategy	43.9	13.5	543	37	43.9	13.5	543	37
All intervals set at 5 y	44.2	13.6	478	35	44.2	13.6	478	35
Intervals set at 5 or 10 y*	44.7	13.7	422	33	44.7	13.7	422	33
All intervals set at 10 y	45.2	13.9	376	32	45.2	13.9	376	32
	0% Contribution of Serrated Pathway				**30% Contribution of Serrated Pathway**			
No screening or surveillance	69.1	28.3	NA	NA	68.5	28.6	NA	NA
Screening without surveillance	47.1	14.4	332	37	50.8	15.5	338	32
Screening plus surveillance								
Dutch guideline strategy	44.8	13.9	533	28	48.8	15.0	548	37
All intervals set at 5 y	45.1	14.0	472	27	49.1	15.0	482	35
Intervals set at 5 or 10 y*	45.7	14.2	416	25	49.6	15.2	426	33
All intervals set at 10 y	46.5	14.4	371	24	50.1	15.4	378	32

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Appendix Table 2–Continued

Strategy	CRC Cases, *n*	CRC Deaths, *n*	Colonoscopies, *n*	Negative Colonoscopy Results, %	CRC Cases, *n*	CRC Deaths, *n*	Colonoscopies, *n*	Negative Colonoscopy Results, %
	Colorectal Lesion Incidence Halved				Colorectal Lesion Incidence Doubled			
No screening or surveillance	37.8	15.2	NA	NA	118.1	49.3	NA	NA
Screening without surveillance	25.6	7.7	279	49	77.8	24.2	417	18
Screening plus surveillance								
Dutch guideline strategy	25.0	7.5	388	53	73.2	23.0	774	24
All intervals set at 5 y	25.0	7.5	361	51	73.9	23.1	644	22
Intervals set at 5 or 10 y*	25.2	7.6	325	50	74.9	23.5	569	19
All intervals set at 10 y	25.4	7.7	305	49	76.5	24.0	473	19

AGA = American Gastroenterological Association; CRC = colorectal cancer; ESGE = European Society of Gastrointestinal Endoscopy.
* 5 y for high-risk persons and 10 y for intermediate-risk persons.

Appendix Table 3. Results of the Cost-Effectiveness Analysis per 1000 Persons*

Strategy	Discounted Costs	Discounted LYs	ICER, *€/LYG*	ICER, *$/LYG*
Costs/QALY†				
Screening without surveillance	€1 176 000/$1 329 000	16 334.9§	Reference	Reference
Screening plus surveillance				
All intervals set at 10 y	€1 183 000/$1 337 000	16 334.6§	Dominated§	Dominated§
Intervals set at 5 or 10 y‡	€1 198 000/$1 354 000	16 335.3§	55 000§	62 500§
All intervals set at 5 y	€1 218 000/$1 376 000	16 335.4§	200 000§	220 000§
Dutch guideline strategy	€1 243 000/$1 405 000	16 335.3§	Dominated§	Dominated§
No screening or surveillance	€1 436 000/$1 623 000	16 304.8§	Dominated§	Dominated§
ESGE guideline				
Screening without surveillance	€1 176 000/$1 329 000	19 470.5	Reference	Reference
Screening plus surveillance as in ESGE guideline	€1 324 000/$1 496 000	19 471.5	148 000	167 000
No screening or surveillance	€1 436 000/$1 623 000	19 412.4	Dominated	Dominated
AGA guideline				
Screening without surveillance	€1 176 000/$1 329 000	19 470.5	Reference	Reference
Screening plus surveillance as in AGA guideline	€1 430 000/$1 616 000	19 472.4	133 684	151 053
No screening or surveillance	€1 436 000/$1 623 000	19 412.4	Dominated	Dominated
Low-prevalence parameter set				
Screening without surveillance	€1 203 000/$1 359 000	19 467.3	Reference	Reference
Screening plus surveillance				
All intervals set at 10 y	€1 207 000/$1 364 000	19 467.5	Dominated‖	Dominated‖
Intervals set at 5 or 10 y‡	€1 216 000/$1 374 000	19 468.1	16 250	18 750
All intervals set at 5 y	€1 232 000/$1 392 000	19 468.4	Dominated‖	Dominated‖
Dutch guideline strategy	€1 252 000/$1 415 000	19 468.9	45 000	51 250
No screening or surveillance	€1 436 000/$1 623 000	19 411.1	Dominated	Dominated
High-prevalence parameter set				
Screening without surveillance	€1 237 000/$1 398 000	19 456.1	Reference	Reference
Screening plus surveillance				
All intervals set at 10 y	€1 247 000/$1 409 000	19 455.6	Dominated	Dominated
Intervals set at 5 or 10 y‡	€1 260 000/$1 424 000	19 456.4	Dominated‖	Dominated‖
All intervals set at 5 y	€1 280 000/$1 446 000	19 456.9	53 750	60 000
Dutch guideline strategy	€1 308 000/$1 478 000	19 457.2	93 333	106 667
No screening or surveillance	€1 428 000/$1 614 000	19 389.0	Dominated	Dominated
5% decrease in surveillance participation rate				
Screening without surveillance	€1 176 000/$1 329 000	19 470.5	Reference	Reference
Screening plus surveillance				
All intervals set at 10 y	€1 183 000/$1 337 000	19 470.4	Dominated	Dominated
Intervals set at 5 or 10 y‡	€1 198 000/$1 354 000	19 470.4	Dominated	Dominated
All intervals set at 5 y	€1 214 000/$1 372 000	19 471.0	38 000	43 000
Dutch guideline strategy	€1 239 000/$1 400 000	19 471.4	Dominated	Dominated
No screening or surveillance	€1 436 000/$1 623 000	19 412.4	Dominated	Dominated
5% increase in surveillance participation rate				
Screening without surveillance	€1 176 000/$1 329 000	19 470.5	Reference	Reference
Screening plus surveillance				
All intervals set at 10 y	€1 184 000/$1 338 000	19 470.5	Dominated	Dominated
Intervals set at 5 or 10 y‡	€1 200 000/$1 356 000	19 470.9	60 000	67 500
All intervals set at 5 y	€1 221 000/$1 380 000	19 471.0	Dominated‖	Dominated‖
Dutch guideline strategy	€1 250 000/$1 413 000	19 471.6	71 429	81 429
No screening or surveillance	€1 436 000/$1 623 000	19 412.4	Dominated	Dominated
5% decrease in detection rate of colonoscopy				
Screening without surveillance	€1 197 000/$1 353 000	19 468.1	Reference	Reference
Screening plus surveillance				
All intervals set at 10 y	€1 205 000/$1 362 000	19 467.8	Dominated	Dominated
Intervals set at 5 or 10 y‡	€1 218 000/$1 376 000	19 468.2	Dominated‖	Dominated‖
All intervals set at 5 y	€1 233 000/$1 393 000	19 468.9	45 000	50 000
Dutch guideline strategy	€1 258 000/$1 422 000	19 469.1	125 000	145 000
No screening or surveillance	€1 436 000/$1 623 000	19 412.4	Dominated	Dominated

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Appendix Table 3–Continued

Strategy	Discounted Costs	Discounted LYs	ICER, *€/LYG*	ICER, *$/LYG*
5% increase in detection rate of colonoscopy				
Screening without surveillance	€1 160 000/$1 311 000	19 471.6	Reference	Reference
Screening plus surveillance				
All intervals set at 10 y	€1 168 000/$1 320 000	19 471.3	Dominated	Dominated
Intervals set at 5 or 10 y‡	€1 185 000/$1 339 000	19 471.5	Dominated	Dominated
All intervals set at 5 y	€1 206 000/$1 363 000	19 472.3	65 714	74 286
Dutch guideline strategy	€1 237 000/$1 398 000	19 471.9	Dominated	Dominated
No screening or surveillance	€1 436 000/$1 623 000	19 412.4	Dominated	Dominated
10% decrease in detection rate of colonoscopy				
Screening without surveillance	€1 217 000/$1 375 000	19 465.7	Reference	Reference
Screening plus surveillance				
All intervals set at 10 y	€1 228 000/$1 388 000	19 465.1	Dominated	Dominated
Intervals set at 5 or 10 y‡	€1 238 000/$1 399 000	19 465.7	Dominated	Dominated
All intervals set at 5 y	€1 252 000/$1 415 000	19 466.2	Dominated‖	Dominated‖
Dutch guideline strategy	€1 274 000/$1 440 000	19 466.8	51 818	59 091
No screening or surveillance	€1 436 000/$1 623 000	19 412.4	Dominated	Dominated
10% increase in detection rate of colonoscopy				
Screening without surveillance	€1 151 000/$1 301 000	19 471.6	Reference	Reference
Screening plus surveillance				
All intervals set at 10 y	€1 159 000/$1 310 000	19 471.3	Dominated	Dominated
Intervals set at 5 or 10 y‡	€1 176 000/$1 329 000	19 471.5	Dominated	Dominated
All intervals set at 5 y	€1 201 000/$1 357 000	19 472.3	71 429	80 000
Dutch guideline strategy	€1 232 000/$1 392 000	19 472.2	Dominated	Dominated
No screening or surveillance	€1 436 000/$1 623 000	19 412.4	Dominated	Dominated
0% contribution of serrated pathway				
Screening without surveillance	€1 170 000/$1 322 000	19 464.1	Reference	Reference
Screening plus surveillance				
All intervals set at 10 y	€1 182 000/$1 336 000	19 463.1	Dominated	Dominated
Intervals set at 5 or 10 y‡	€1 197 000/$1 353 000	19 464.1	Dominated	Dominated
All intervals set at 5 y	€1 215 000/$1 373 000	19 464.7	Dominated‖	Dominated‖
Dutch guideline strategy	€1 240 000/$1 401 000	19 465.1	70 000	79 000
No screening or surveillance	€1 424 000/$1 609 000	19 405.7	Dominated	Dominated
30% contribution of serrated pathway				
Screening without surveillance	€1 286 000/$1 453 000	19 456.2	Reference	Reference
Screening plus surveillance				
All intervals set at 10 y	€1 293 000/$1 461 000	19 454.8	Dominated	Dominated
Intervals set at 5 or 10 y‡	€1 308 000/$1 478 000	19 455.5	Dominated	Dominated
All intervals set at 5 y	€1 327 000/$1 500 000	19 456.0	Dominated	Dominated
Dutch guideline strategy	€1 355 000/$1 531 000	19 456.0	Dominated	Dominated
No screening or surveillance	€1 453 000/$1 642 000	19 397.8	Dominated	Dominated
Colonoscopy costs halved				
Screening plus surveillance, all intervals set at 10 y	€1 077 000/$1 217 000	19 470.4	Reference	Reference
Screening without surveillance	€1 079 000/$1 219 000	19 470.5	Dominated‖	Dominated‖
Screening plus surveillance, intervals set at 5 or 10 y‡	€1 080 000/$1 220 000	19 470.9	6000	6000
Screening plus surveillance, all intervals set at 5 y	€1 086 000/$1 227 000	19 471.1	30 000	35 000
Screening plus surveillance, Dutch guideline strategy	€1 095 000/$1 237 000	19 471.4	30 000	33 333
No screening or surveillance	€1 436 000/$1 623 000	19 412.4	Dominated	Dominated
Colonoscopy costs doubled				
Screening without surveillance	€1 273 000/$1 438 000	19 470.5	Reference	Reference
Screening plus surveillance				
All intervals set at 10 y	€1 289 000/$1 457 000	19 470.4	Dominated	Dominated
Intervals set at 5 or 10 y‡	€1 316 000/$1 487 000	19 470.9	107 500	122 500
All intervals set at 5 y	€1 351 000/$1 527 000	19 471.1	Dominated‖	Dominated‖
Dutch guideline strategy	€1 391 000/$1 572 000	19 471.4	150 000	170 000
No screening or surveillance	€1 436 000/$1 623 000	19 412.4	Dominated	Dominated

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Appendix Table 3–Continued

Strategy	Discounted Costs	Discounted LYs	ICER, *€/LYG*	ICER, *$/LYG*
Colorectal lesion incidence halved				
Screening without surveillance	€704 000/$796 000	19 521.7	Reference	Reference
Screening plus surveillance				
All intervals set at 10 y	€711 000/$803 000	19 521.9	35 000	35 000
Intervals set at 5 or 10 y‡	€718 000/$811 000	19 521.9	Dominated	Dominated
All intervals set at 5 y	€732 000/$827 000	19 522.1	105 000	120 000
Dutch guideline strategy	€744 000/$841 000	19 522.2	120 000	140 000
No screening or surveillance	€780 000/$881 000	19 491.4	Dominated	Dominated
Colorectal lesion incidence doubled				
Screening without surveillance	€1 928 000/$2 179 000	19 378.3	Reference	Reference
Screening plus surveillance				
All intervals set at 10 y	€1 936 000/$2 188 000	19 377.8	Dominated	Dominated
Intervals set at 5 or 10 y‡	€1 959 000/$2 214 000	19 379.7	22 143	25 000
All intervals set at 5 y	€1 981 000/$2 239 000	19 380.5	27 500	31 250
Dutch guideline strategy	€2 036 000/$2 301 000	19 380.7	275 000	310 000
No screening or surveillance	€2 505 000/$2 831 000	19 270.5	Dominated	Dominated

AGA = American Gastroenterological Association; ESGE = European Society of Gastrointestinal Endoscopy; ICER = incremental cost-effectiveness ratio; LY = life-year; LYG = life-year gained; QALY = quality-adjusted life-year.

* Strategies are ordered according to increasing discounted total costs. When strategies have equal total costs, they are ordered according to decreasing LYs. The ICER is calculated using the nearest cheaper strategy that is not dominated as the reference. The reference strategy is the comparator strategy. Dominated strategies led to fewer LYs at higher or equal costs than the comparator strategy.

† We used the following utilities (46): healthy: 0.84; colorectal cancer stage I: 0.74; colorectal cancer stage II: 0.69; colorectal cancer stage III: 0.64; colorectal cancer stage IV: 0.25. For screening and surveillance procedures, available data were too limited to estimate utility losses. Because the utility losses are likely to be extremely small due to the short time span of screening procedures, we assumed that screening and surveillance did not influence quality of life.

‡ 5 y for high-risk persons and 10 y for intermediate-risk persons.

§ Discounted QALY and costs per QALY gained.

‖ Subject to extended dominance.