



HHS Public Access

Author manuscript

Clin Gastroenterol Hepatol. Author manuscript; available in PMC 2023 October 01.

Published in final edited form as:

Clin Gastroenterol Hepatol. 2022 October ; 20(10): 2383–2392.e4. doi:10.1016/j.cgh.2022.01.054.

Cost effectiveness of mailed outreach programs for colorectal cancer screening: Analysis of a pragmatic, randomized trial

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Abstract

Background: Clinical guidelines for colorectal cancer (CRC) screening suggest use of either stool-based tests or colonoscopy – modalities that differ in recommended screening intervals, adherence, and costs. We know little about the long-term cost differences in population-health outreach strategies to promote these strategies.

Methods: We conducted a cost-effectiveness analysis to compare two mailed outreach strategies to increase CRC screening from a pragmatic, randomized clinical trial: mailed FIT kits vs. invitations to complete a screening colonoscopy. We built a 10-year Markov chain Monte Carlo microsimulation model to account for differences in screening intervals, adherence, and costs.

Results: Mailed FIT kits had a lower 10-year average per-person costs of screening than colonoscopy invitations (\$1139 vs. \$1725) but with 10.89 fewer months of compliance and 60 fewer advanced neoplasia detected (37 advanced adenomas and 23 CRC). Incremental cost effectiveness ratios (ICER) for colonoscopy invitations compared to mailed FIT kits were \$55.23,

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Author Contributions: Conceptualization: EH, CSS, CCM, AGS; acquisition of data: EH, NOS, ACL, AGS; methodology: KAK; analysis and interpretation of data: CCM, KAK; drafting of the manuscript: KAK; critical revision of the manuscript for important intellectual content: all authors; funding acquisition: EH, CSS.

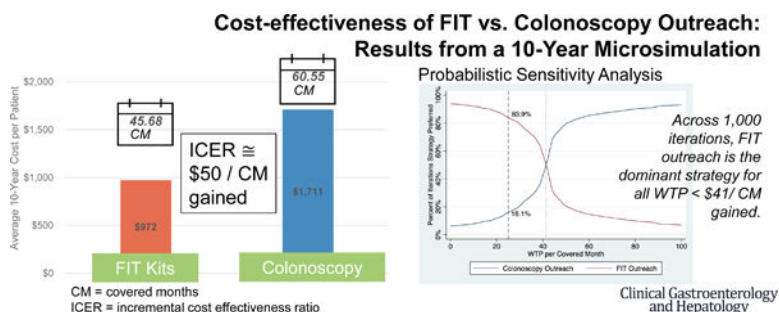
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Conflicts of interest: Dr. Singal has served as a member of scientific advisory boards with Exact Sciences. Dr. Murphy consults for Freenome. None of the other authors have any relevant conflicts of interest.

\$15.84, and \$25.48 per additional covered month, advanced adenoma, and CRC. Although FIT was the preferred strategy at low willingness to pay thresholds, the two strategies were equal at a willingness to pay threshold of \$41.31 per covered month gained.

Conclusion: Mailed FIT or colonoscopy invitations are both options to improve CRC screening completion and advanced neoplasia detection, and the choice of outreach strategy may differ by a health system's willingness to pay threshold. Mailed FIT kits are less expensive than colonoscopy invitations but result in fewer months of screening compliance and advanced neoplasia detected.

Graphical Abstract



Keywords

fecal immunochemical test; colonoscopy; safety-net health system

INTRODUCTION

Screening for colorectal cancer (CRC) with fecal immunochemical tests (FIT) or colonoscopy reduces mortality through early detection and removal of premalignant polyps. Screening has increased in the U.S.,¹ but participation lags behind other screening tests (e.g., mammogram, Pap test), particularly among racial and ethnic minority and uninsured populations.

The US Preventive Services Task Force (USPSTF) does not rank CRC screening modalities, noting that offering patients a choice of tests may increase adherence.² FIT is less invasive and requires less preparation and time off work but must be repeated annually and followed by diagnostic colonoscopy if positive. Colonoscopy, the most common modality,³ has higher sensitivity than FIT and facilitates removal of pre-malignant lesions.^{4, 5} In pragmatic randomized trials, one-time screening with FIT has been greater than colonoscopy, especially when FIT kits are mailed and among minority populations,^{6–12} however, adherence over time is low.^{13, 14}

There are few data comparing cost-effectiveness of population-level, mailed outreach strategies to increase CRC screening, particularly beyond one-time screening. Micro-costing studies have reported \$39.81 per returned FIT and \$32.38 per person screened.^{15, 16} However, we know little about the clinical and cost-effectiveness of mailed FIT kits versus mailed invitations to complete screening colonoscopy. A recent meta-analysis documented a significant increase in screening from mailed outreach, but most of this outreach has focused

on stool-based tests (including FITs).¹⁷ Although there are advantages to mailing FIT kits, especially during the COVID-19 pandemic,¹⁸ tests have to be repeated annually. Thus, the question remains as to whether a population-level outreach strategy inviting completion of a screening colonoscopy, which needs to be completed every 10 years if normal, would yield a better marginal cost.

Most studies on population-level outreach used one-time screening for modeling inputs, despite data showing adherence declines over time.^{19–21} Many have focused on cost per screen completed, failing to evaluate downstream outcomes, such as proportion of time up-to-date with screening or clinical outcomes (e.g., neoplasia detection). Finally, most cost-effectiveness studies have used data from clinical trials rather than real-world populations, particularly racial and ethnic minority and socioeconomically disadvantaged patients who have higher risk of CRC and lowest screening adherence.^{20, 21}

To address these gaps, we built a Markov chain Monte Carlo (MCMC) microsimulation model to conduct a robust cost effectiveness analysis using results from a large, pragmatic, randomized trial among a racially and ethnically diverse safety-net patient population, comparing two outreach strategies: mailed FIT kits vs. invitations to complete a screening colonoscopy.^{6, 22} Our model predicts annual adherence and screening outcomes over 10 years, allowing us to evaluate the extent to which the greater upfront direct costs of colonoscopy are offset by gains in longer-term cost-effectiveness, based on months covered and neoplasia detected. Because we are comparing these two outreach strategies to each other, and not to opportunistic, visit-based screening, we used the lowest cost strategy to set a minimum willingness to pay (WTP) threshold as a benchmark. The lowest total per patient cost of the FIT outreach strategy was approximately \$25 per month;⁶ we assumed healthcare systems willing to pay \$25 per month to mail FIT kits to gain a “covered month” should be willing to pay the same amount per month for other outreach approaches that result in a covered month.

METHODS

Model Structure and Parameters

Our MCMC microsimulation model follows a hypothetical cohort of 10,000 patients annually over a 10-year period who receive outreach each year (when not up-to-date with screening) either as a mailed FIT kit or an invitation to complete a screening colonoscopy. The structure of our model is shown in Figure 1 and the key parameters are shown in Table 1. For Years 1–3, we used screening completion and detection of advanced adenoma (AA) and CRC from our 3-year pragmatic trial⁶ ([Clinicaltrials.gov NCT01710215](https://clinicaltrials.gov/ct2/show/study/NCT01710215)) of 5,999 patients ages 50–64 years who were not up-to-date with screening and receiving primary care at Dallas County’s integrated Parkland safety-net system. In the trial, patients were randomly assigned to receive usual care (n=1999), a mailed FIT kit (n=2400), or mailed invitation for colonoscopy (n=2400). Details of the study are reported elsewhere.^{6, 22}

FIT completion declined exponentially in Years 4 – 10, based on the observed decline in Years 1 – 3 during the pragmatic trial, but calibrated to match screening patterns reported in a longitudinal study in the Veterans Health Administration.²³ Colonoscopy completion

also declined exponentially over time. The probability of detecting AA and CRC were sampled from the distributions as shown in Table 1 for Years 4 onwards.^{24, 25} Those with an AA would be “due” for a surveillance colonoscopy in three years, but following the lower bounds of earlier studies,²⁶ we assumed 18% would complete surveillance colonoscopy as a base case.²⁶ Those who did not complete surveillance colonoscopy in year 3 have a chance of obtaining it in subsequent years (until completed). We conducted probabilistic sensitivity analyses (PSA) using second-order Monte Carlo simulations (1,000 iterations) to model parameter uncertainty. All analyses were completed in Amua.²⁷

We calculated costs of outreach from a health system perspective using actual personnel, materials, and program management costs from the pragmatic trial (see Appendix). Costs per patient screened shown in Table 1 reflect costs across all dimensions (personnel, materials, and program management). Note that in the trial, the costs varied slightly across the two outreach strategies within a given screening mode, we kept the unit costs constant. The key outcomes measured over the 10-year period of 10,000 simulated patients were: 1) screening yield measured as AAs and CRCs (added together as “AN” “any advanced neoplasia”); and 2) months of screening up-to-date (“covered months”), defined as 12 for patients with negative FIT, 6 for positive FIT without follow-up, and 120 for normal colonoscopy.^{28, 29} When an AA was detected, covered months were calculated as 36 – reflecting the need for a surveillance colonoscopy. When CRC was detected, covered months were calculated as 12 months. We focused on the marginal gain in covered months to avoid double-counting. For example, patients completing a normal colonoscopy in Year 1 contributed 120 covered months in Year 1; those covered months are not in counts for subsequent years, nor are patients counted as “eligible” in subsequent years. We did not use a measure of proportion of time covered because, to account for differences in intervals, the denominator would need to cover 20 years to account for individuals who obtain colonoscopy in simulation Year 10. Estimating costs per advanced neoplasia detected accounts for differences in detection rates and recommended screening intervals, whereas typical measures of cost per screening (e.g., per FIT returned) do not.

To calculate the ICER, we calculated the difference in costs between the two outreach strategies divided by the difference in screening yields. Note that to keep the model tractable and following other cost effectiveness studies that have examined screening yields (per screen or covered month) as the outcome, we are not assigning life expectancy gains.^{30–33} Model uncertainty was further investigated using the second order Monte-Carlo simulations.

RESULTS

Figure 2 shows the average number of covered months gained (solid lines) and detection (bars) for the mailed FIT kit and colonoscopy invitation strategies over the 10-year simulation period. The number of covered months gained is higher for colonoscopy invitations in Years 1 and 2 relative to FIT kits but then is lower from Years 3 – 6. From Year 7 onwards, more covered months are gained among the colonoscopy invitation strategy. Cumulatively, 60.54 covered months are gained per person, on average, among the colonoscopy invitations relative to 49.93 among mailed FIT kits. The number of AAs detected is greater for colonoscopy invitations until Year 6, however, the number of CRCs

detected is only greater for colonoscopy invitations in Years 1 and 2. Cumulatively, 457 AAs and 96 cases of CRC were detected in colonoscopy outreach, relative to 420.5 and 72.5, respectively, in FIT outreach.

Table 2 first shows the average cost of screening and outreach over the 10-year period for both FIT kits and colonoscopy invitations using the cohort of 10,000 patients. The average cost per patient in FIT outreach, adjusting for adherence, was \$1,139, whereas the average cost per patient in colonoscopy outreach was \$1,725, for a difference of \$586. Although the colonoscopy invitation strategy had greater costs on average, it also yielded an additional 10.89 in covered months, an additional 37 AAs and 23 CRCs detected. Using the number of covered months gained as the key outcome, the ICER was \$55.23 per additional covered month gained.

In addition, we compared the number of AAs and CRCs detected under the assumption that these detections would result in cases (and ultimately deaths) averted, but as noted above, we do not impute life expectancy gains directly. Overall, ICERs using AA and CRC detections as the outcomes, were \$15.84, \$25.48, \$9.77 per additional AA, CRC, and any advanced neoplasia (either AA or CRC) detected, respectively.

In **Panel A** of Figure 3, we show a scatterplot of the incremental cost of colonoscopy invitations relative to FIT kits on the Y-axis and the incremental increase in the number of covered months gained on the X-axis derived from the PSA. The solid black line represents the benchmark WTP threshold of \$25 per month gained as this is the lowest cost of obtaining an additional covered month based on our earlier pragmatic trial.⁶ In 1,000 iterations, 161 resulted in a ICER that was less than this threshold, implying that colonoscopy invitations were the dominant strategy in 16% of the iterations. To see how this varies by WTP threshold, **Panel B**, shows the cost acceptability curves. The dashed line shows the benchmark WTP of \$25 per covered month gained, where 16.1 percent of the iterations yielded colonoscopy outreach as the dominant strategy. At a WTP threshold of \$41.31 per covered month gained, we are indifferent between two strategies based on our modeling assumptions. The threshold costs at which we are indifferent between the two outreach strategies calculated per AA and CRC case detected are \$1,759 and \$35,294, respectively.

The PSA results in Table 3 show that the parameter uncertainty affects the estimates in significant ways. First, in FIT outreach strategy, estimates of the average costs, the average number of covered months gained, AAs detected, and CRCs detected are all sensitive to the distributional assumptions of the parameters. In Monte Carlo simulations, where all parameters were randomly drawn from their respective distributions, we found that the average costs, covered months gained, and neoplasia detections were all lower over the 10-year period than we found in our base case analysis. Second, there were some differences in colonoscopy outreach as well, but primarily among the detection of AAs and CRCs. Using the PSA results yields a slightly lower ICER at \$49.63 per covered month gain. The ICER for AAs detected from colonoscopy outreach was much lower at \$3.34, but the ICER for CRCs detected was higher at \$52.60.

DISCUSSION

In this cost analysis microsimulation study using data from a pragmatic trial, we predicted mailed FIT kits and mailed invitations to complete screening colonoscopy would result in 49.93 and 60.54 additional covered months, respectively; the colonoscopy outreach arm yielded additional AAs and cases of CRC detected. However, the average cost per patient among the FIT outreach patients was about 66% of the cost per patient in the colonoscopy outreach (or almost \$586 less per person over the 10 years). The results were qualitatively similar across a set of sensitivity analyses, although the incremental improvement in AAs and CRCs detected were sensitive to parameters chosen.

Our analysis innovatively models how a cohort of patients from a safety-net health system would fare if a population-level outreach program of mailed FIT kits and screening colonoscopy invitations were extended for a decade. Examining costs and outcomes over only the actual period of the 3-year trial is problematic because it ignores longer-term benefits of colonoscopy while accounting for greater up-front costs. Our approach addresses this by modeling screening adherence, yield, and costs over 10 years using a microsimulation model.

In contrast to cost-effectiveness studies that focus on generating a cost per life year gained from early detection or prevention of CRC,^{34–36} we took as a given that CRC screening is “cost-effective” from a healthcare system and health policy perspective, and focused on comparing programmatic costs across two outreach strategies to boost suboptimal screening participation. In particular, we are not comparing these outreach strategies to the standard of care – opportunistic, visit-based screening. Our approach to evaluating costs by calculating cost per covered month and advanced neoplasia detected is important because typical measures of costs per screening do not account for significant differences in detection or recommended screening intervals (e.g., 1 vs. 10 years).

Several implications from our results can inform health system approaches to improving CRC screening. In our trial, we found higher initiation of FIT compared to colonoscopy; however, colonoscopy outreach yields more covered months gained, AAs, and CRCs detected. Colonoscopy outreach yielded 11 to 15 additional covered months, on average, per person for an additional \$586 to \$739 per patient per 10-year period. Our estimates of the incremental improvement in AAs detected are noisy statistically suggesting that we could see anywhere from 37 to 221 additional AAs with colonoscopy outreach. Interestingly, despite this significant variation, the improvement in CRCs detected is less noisy estimated at between 14 and 23 additional cancers detected.

Nonetheless, the additional costs associated with colonoscopy outreach may be problematic in environments with limited resources for outreach or limited colonoscopy capacity. For these reasons, several large, integrated health systems have embraced mailed FIT as the dominant population-based screening strategy and reported major increases in screening, early detection, and decreased mortality over time.^{37, 38} Similarly, the Canadian Task Force on Preventive Health Care recommends stool-based tests as the primary screening modality because colonoscopies require more resources (staffing and equipment), are more

difficult for patients to obtain, and confer longer wait time despite clinical benefits.³⁹ Thus, although there may be a physician preference for colonoscopies,⁴⁰ FITs may be preferred as a population health outreach strategy in some settings. Implementing FIT outreach must account for navigation of patients with positive results to diagnostic colonoscopy, given prior studies show this is a step prone to frequent failure.⁴¹

Our analyses have several limitations. We do not account for potential selection effects (e.g., if patients systematically choose a screening mode based on risk factors or other unobservable measures, our analysis will not capture those differences). We do not account for age-related changes in probability of cancer detection. Nor do we account for changes in potential treatment trajectories that might vary across outreach strategies (e.g., as colonoscopies include biopsy of cancerous and pre-cancerous polyps, progression may evolve differently for those who receive colonoscopies earlier relative to later or relative to another screening mode). Our clinical outcome was advanced neoplasia over 10 years, not CRC-specific mortality, or quality-related life-years gained. Finally, assumptions regarding adherence may not hold amid a pandemic. Data from the Health Care Cost Institute suggests use of screening colonoscopy in 2020 was 37% lower than in 2019 (through July) as a result of COVID-19,⁴² which may make mailed FIT kits even more attractive now. Finally, in our calculations over a 10-year horizon, we opted not to discount projected costs because we would also need to adjust for medical inflation, which has been significantly greater than typical discount factors used in health net present value calculations (e.g. Medicare trustees⁴³ assume 5.1% relative to a more common assumption of 1.5 to 3% discount factors).⁴⁴ In this case, as healthcare costs are typically projected to exceed inflation, costs incurred later would be more expensive in real dollars.

In conclusion, a MCMC model using screening participation and neoplasia detection from a pragmatic trial revealed an ICER per covered month gained around \$49 to \$55 per patient for colonoscopy invitations relative to FIT outreach. The choice of outreach strategy may depend upon the local context of a healthcare system, costs of outreach, or differ by the system's willingness to pay threshold.

Acknowledgements:

We thank the Parkland Health and Hospital System for partnership in our PROSPR research initiative. We also appreciate support from the Polymedco Corporation for providing FIT kits and reagents for the trial.

Financial support:

This study was conducted as part of the NCI-funded consortium Population-Based Research Optimizing Screening through Personalized Regiments (PROSPR) with support from NIH/NCI U54CA163308, UM1CA222035, UL1TR001105; U01 CA221940, and P30 CA142543 as well as CPRIT PP160075. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Appendix

Appendix Table 1.

Labor, material, and program management costs of mailed outreach

Activity	Cost
Labor	
Phone calls	
Invitation	RA time (\$22 per hour) × total call time
Positive FIT	RA time (\$22 per hour) × total call time
Cancelled FIT	RA time (\$22 per hour) × total call time
Colonoscopy reminder	RA time (\$22 per hour) × total call time
Letters	
FIT invitation letter	RA time (\$22 per hour) × 3 minutes per letter
Colonoscopy invitation letter	RA time (\$22 per hour) × 1 minute per letter
Results letter	NP time to generate (\$45 per hour) × 1 minute per letter RA time to send (\$22 per hour) × 1 minute per letter
FIT orders	NP time (\$45 per hour) × 1.5 minutes per order
Colonoscopy orders	NP time (\$45 per hour) × 2 minutes per order NP time to route (\$45 per hour) × 0.5 minutes per colonoscopy
Clinical review (for colonoscopy)	Clinical access coordinator time to review (\$42 per hour) × 5 minutes per colonoscopy NP time to enter data (\$45 per hour) × 1 minute per colonoscopy
GI lab processing (for FITs)	Med tech time (\$27 per hour) × 80 FITs per hour
Materials	
FIT invitation letter	\$1.54 (includes \$0.34 for paper and \$1.20 for postage)
Polymedco FIT	\$6.90 per test
FIT results letter	\$0.71 (includes \$0.22 for paper and \$0.49 for postage)
Colonoscopy invitation letter	\$0.71 (includes \$0.22 for paper and \$0.49 for postage)
Bowel preparation kit	\$21.05 (includes \$11.05 for supplies and \$10.00 for postage)
Colonoscopy	Per transaction data from EHR
Program management	
Data analyst (hourly)	\$40 per hour × 20 hours per year
Project coordinator (30% FTE)	\$19,800 per year (based on annual salary of \$66,000)

Abbreviations: RA, research assistant; NP, nurse practitioner; FIT, fecal immunochemical test; EHR, electronic health record; FTE, full time equivalent

Appendix Table 2:

Time and cost of outreach activities by year, FIT outreach

	Year 1 (n=2,396)			Year 2 (n=2,159)			Year 3 (n=2,057)		
	n (%)	Time per patient ^I	Cost per patient ^I	n (%)	Time per patient ^I	Cost per patient ^I	n (%)	Time per patient ^I	Cost per patient ^I
Personnel									

	Year 1 (n=2,396)			Year 2 (n=2,159)			Year 3 (n=2,057)		
	n (%)	Time per patient ¹	Cost per patient ¹	n(%)	Time per patient ¹	Cost per patient ¹	n (%)	Time per patient ¹	Cost per patient ¹
Phone calls									
Invitation	1524 (63.6)	3.20	\$1.17	1682 (77.9)	2.67	\$0.98	1674 (81.4)	2.77	\$1.01
Positive FIT	72 (3.0)	5.52	\$2.02	29 (1.3)	6.56	\$2.37	18 (0.9)	6.75	\$2.48
Cancelled FIT	280 (11.7)	2.76	\$1.01	182 (8.4)	2.59	\$0.95	163 (7.9)	3.89	\$1.42
Colo. Reminder	44 (1.8)	6.91	\$2.53	18 (0.8)	6.52	\$2.39	11 (0.5)	10.14	\$3.72
Letters									
Invitation letter	2396 (100.0)	3.72	\$1.36	2159 (100.0)	3.51	\$1.29	2057 (100.0)	3.56	\$1.30
Results letter	1188 (49.6)	2.00	\$1.18	732 (33.9)	2.00	\$1.12	197 (9.6)	2.02	\$1.13
Test orders									
FIT	2014 (84.1)	2.19	\$1.64	2159 (100.0)	2.74	\$2.06	1166 (56.7)	1.80	\$1.35
Colonoscopy	459 (19.2)	1.82	\$1.37	266 (12.3)	1.65	\$1.24	102 (5.0)	1.39	\$1.04
Clinical review	60 (2.5)	2.60	\$1.86	22 (1.0)	5.68	\$4.05	13 (0.6)	6.50	\$4.63
Lab processing	1461 (61.0)	0.93	\$0.42	924 (42.8)	0.92	\$0.42	722 (35.1)	0.87	\$0.40
Materials									
Invitation letter	2396 (100.0)	--	\$1.91	2159 (100.0)	--	\$1.80	2057 (100.0)	--	\$1.83
Result letter	1188 (49.6)	--	\$0.71	731 (33.9)	--	\$0.71	197 (9.6)	--	\$0.71
FIT	2396 (100.0)	--	\$12.35	2159 (100.0)	--	\$10.81	2057 (100.0)	--	\$9.42
Bowel preparation	20 (0.8)	--	\$24.21	8 (0.4)	--	\$23.68	6 (0.3)	--	\$24.56
Colonoscopy	202 (8.4)	--	\$3038.50	91 (4.2)	--	\$3452.75	19 (0.9)	--	\$3697.16
Program management									
Data analyst	2396 (100.0)	0.25	\$0.17	2159 (100.0)	0.32	\$0.21	100.0	0.38	\$0.25
Program coordinator	2396 (100.0)	7.82	\$4.14	2159 (100.0)	9.96	\$5.27	100.0	11.85	\$6.27
Total Cost									
Cost per patient mailed	2396 (100.0)	--	\$275.83	2159 (100.0)	--	\$163.46	2057 (100.0)	--	\$55.43
Cost per screening ² completed	1433 (59.8)	--	\$461.18	880 (40.8)	--	\$401.04	642 (31.2)	--	\$177.62

¹ Mean time and cost per patient estimated among only patients who received the intervention component

² Screening completed defined as any FIT or colonoscopy completed at the end of the round, either through mailed outreach or usual care Year 1: April 2013 – Feb. 2015; Year 2: May 2014 – March 2016; Year 3: May 2015 – Jul. 2016

Appendix Table 3.

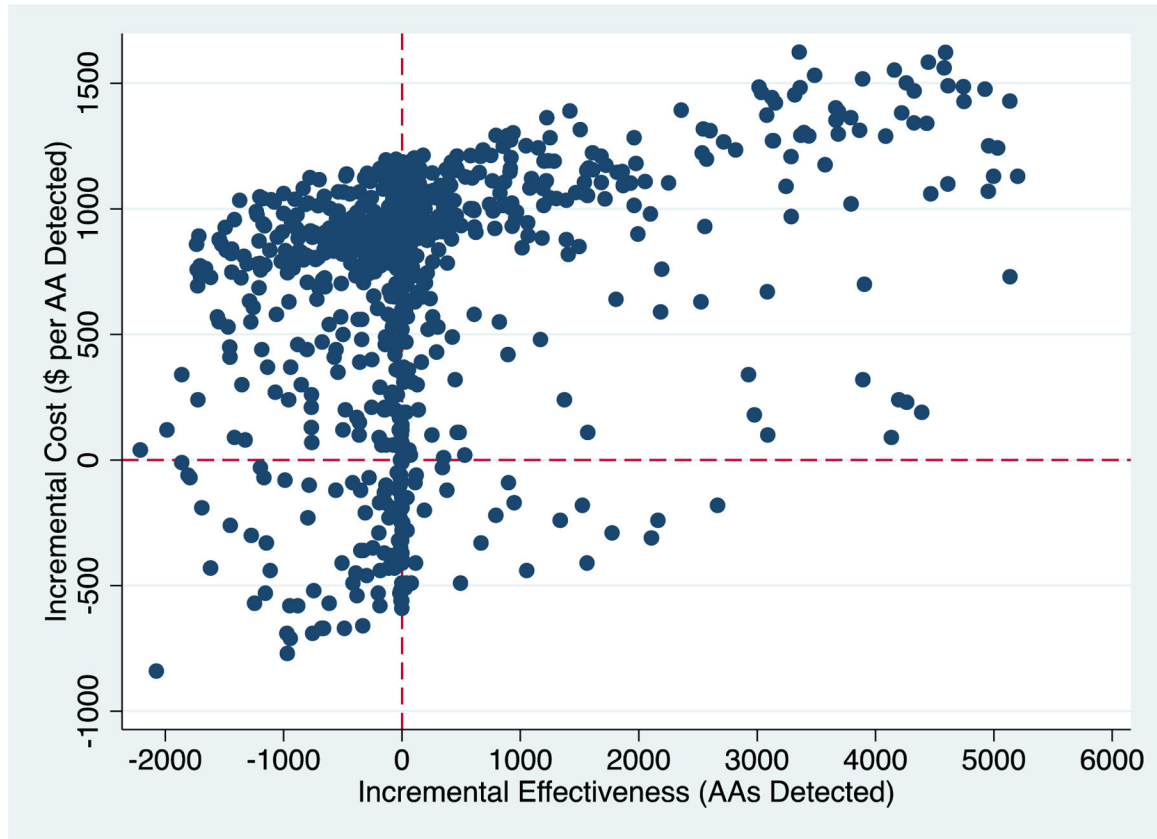
Time and cost of outreach activities by year, colonoscopy outreach

	Year 1 (n=2,392)			Year 2 (n=1,599)			Year 3 (n=1,103)		
	n (%)	Time per patient ^I	Cost per patient ^I	n(%)	Time per patient ^I	Cost per patient ^I	n (%)	Time per patient ^I	Cost per patient ^I
Labor									
Phone calls									
Invitation	2380 (99.5)	3.88	\$1.42	1568 (98.1)	3.26	\$1.20	1095 (99.3)	2.77	\$1.02
Positive FIT	--	--	--	--	--	--	--	--	--
Cancelled FIT	--	--	--	--	--	--	--	--	--
COL reminder	952 (39.8)	6.89	\$2.53	288 (18.0)	8.42	\$3.09	119 (10.8)	6.84	\$2.51
Letters									
Invitation letter	2392 (100.0)	1.05	\$0.38	1599 (100.0)	1.23	\$0.45	1103 (100.0)	1.00	\$0.37
Results letter	--	--	--	--	--	--	--	--	--
Test orders									
FIT	898 (37.5)	1.68	\$1.26	397 (24.8)	1.62	\$1.22	160 (14.5)	1.53	\$1.14
COL	1271 (53.1)	3.16	\$2.37	447 (28.0)	2.58	\$1.94	177 (16.1)	2.40	\$1.80
Clinical review	241 (10.1)	6.46	\$4.59	91 (5.7)	6.44	\$4.58	34 (3.1)	6.53	\$4.65
Lab processing	425 (17.8)	0.77	\$0.35	150 (9.4)	0.75	\$0.34	51 (4.6)	0.75	\$0.34
Materials									
Invitation letter	2392 (100.0)	--	\$0.74	1599 (100.0)	--	\$0.87	1103 (100.0)	--	\$0.71
Result letter	--	--	--	--	--	--	--	--	--
FIT	898 (37.5)	--	\$11.56	397 (24.8)	--	\$11.21	160 (14.5)	--	\$10.52
Bowel preparation	374 (15.6)	--	\$24.26	152 (9.5)	--	\$24.93	51 (4.6)	--	\$22.70
COL	724 (30.3)	--	\$2914.32	148 (9.3)	--	\$3362.41	45 (4.1)	--	\$3866.91
Program management									
Data analyst	2392 (100.0)	0.25	\$0.17	1599 (100.0)	0.32	\$0.21	100.0	0.38	\$0.25
Program coordinator	2392 (100.0)	7.82	\$4.14	1599 (100.0)	9.96	\$5.27	100.0	11.85	\$6.27
Total cost									
Cost per patient mailed	2392 (100.0)	--	\$896.03	100.0	--	\$320.56	1103 (100.0)	--	\$169.84

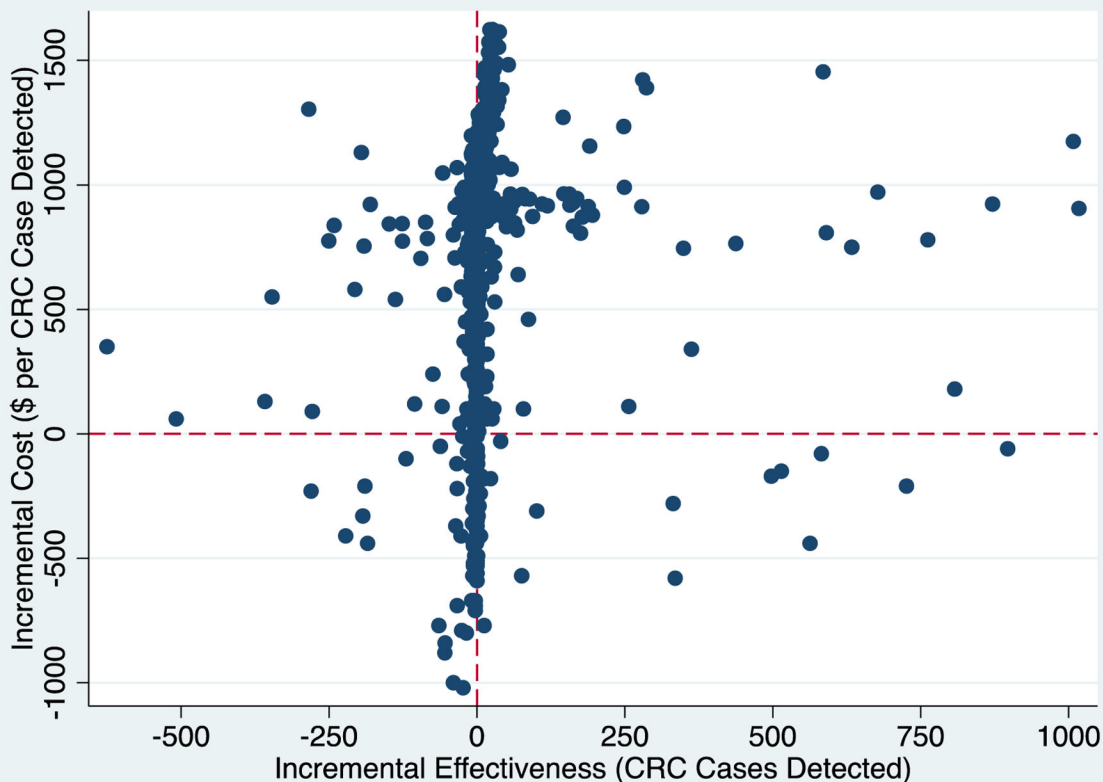
	Year 1 (n=2,392)			Year 2 (n=1,599)			Year 3 (n=1,103)		
	n (%)	Time per patient ¹	Cost per patient	n(%)	Time per patient ¹	Cost per patient	n (%)	Time per patient ¹	Cost per patient
Cost per screening completed ²	1058 (44.2)	--	\$2025.81	276 (17.3)	--	\$1857.17	116 (10.5)	--	\$1614.90

¹ Mean time and cost per patient estimated among only patients who received the intervention component

² Screening completed defined as any FIT or colonoscopy completed at the end of the round, either through mailed outreach or usual care Year 1: April 2013 – Feb. 2015; Year 2: May 2014 – March 2016; Year 3: May 2015 – Jul. 2016



Appendix Figure 1.
Incremental Costs vs. Incremental Effectiveness in AAs Detected



Appendix Figure 2.
Incremental Costs vs. Incremental Effectiveness in CRC Cases Detected

References

1. Ransohoff DF, Lang CA. Screening for colorectal cancer. *N Engl J Med* 1991;325:37–41. [PubMed: 1810273]
2. Bibbins-Domingo K, Grossman DC, Curry SJ, et al. Screening for colorectal cancer: Us preventive services task force recommendation statement. *JAMA* 2016;315:2564–2575. [PubMed: 27304597]
3. May FP, Yang L, Corona E, et al. Disparities in colorectal cancer screening in the united states before and after implementation of the affordable care act. *Clin Gastroenterol Hepatol* 2020;18:1796–1804.e2. [PubMed: 31525514]
4. Rex DK, Boland CR, Dominitz JA, et al. Colorectal cancer screening: Recommendations for physicians and patients from the u.S. Multi-society task force on colorectal cancer. *Am J Gastroenterol* 2017;112:1016–1030. [PubMed: 28555630]
5. Whitlock EP, Lin JS, Liles E, et al. Screening for colorectal cancer: A targeted, updated systematic review for the us preventive services task force. *Ann Intern Med* 2008;149:638–658. [PubMed: 18838718]
6. Singal AG, Gupta S, Skinner CS, et al. Effect of colonoscopy outreach vs fecal immunochemical test outreach on colorectal cancer screening completion: A randomized clinical trial. *JAMA* 2017;318:806–815. [PubMed: 28873161]
7. van Rossum LG, van Rijn AF, Laheij RJ, et al. Random comparison of guaiac and immunochemical fecal occult blood tests for colorectal cancer in a screening population. *Gastroenterology* 2008;135:82–90. [PubMed: 18482589]

8. Segnan N, Senore C, Andreoni B, et al. Comparing attendance and detection rate of colonoscopy with sigmoidoscopy and fit for colorectal cancer screening. *Gastroenterology* 2007;132:2304–2312. [PubMed: 17570205]
9. Gupta S, Halm EA, Rockey DC, et al. Comparative effectiveness of fecal immunochemical test outreach, colonoscopy outreach, and usual care for boosting colorectal cancer screening among the underserved: A randomized clinical trial. *JAMA Internal Medicine* 2013;173:1725–1732. [PubMed: 23921906]
10. Hoffman RM, Steel S, Yee EF, et al. Colorectal cancer screening adherence is higher with fecal immunochemical tests than guaiac-based fecal occult blood tests: A randomized, controlled trial. *Prev Med* 2010;50:297–299. [PubMed: 20307568]
11. van der Vlugt M, Grobbee EJ, Bossuyt PMM, et al. Adherence to colorectal cancer screening: Four rounds of faecal immunochemical test-based screening. *Br J Cancer* 2017;116:44–49. [PubMed: 27923037]
12. Issaka RB, Avila P, Whitaker E, et al. Population health interventions to improve colorectal cancer screening by fecal immunochemical tests: A systematic review. *Prev Med* 2019;118:113–121. [PubMed: 30367972]
13. Dougherty MK, Brenner AT, Crockett SD, et al. Evaluation of interventions intended to increase colorectal cancer screening rates in the united states: A systematic review and meta-analysis. *JAMA internal medicine* 2018;178:1645–1658. [PubMed: 30326005]
14. Cyhaniuk A, Coombes ME. Longitudinal adherence to colorectal cancer screening guidelines. *Am J Manag Care* 2016;22:105–111. [PubMed: 26885670]
15. Kemper KE, Glaze BL, Eastman CL, et al. Effectiveness and cost of multilayered colorectal cancer screening promotion interventions at federally qualified health centers in washington state. *Cancer* 2018;124:4121–4129. [PubMed: 30359468]
16. Guy GP Jr, Richardson LC, Pignone MP, et al. Costs and benefits of an organized fecal immunochemical test-based colorectal cancer screening program in the united states. *Cancer* 2014;120:2308–2315. [PubMed: 24737634]
17. Jager M, Demb J, Asghar A, et al. Mailed outreach is superior to usual care alone for colorectal cancer screening in the USA: A systematic review and meta-analysis. *Dig Dis Sci* 2019;64:2489–2496. [PubMed: 30915656]
18. Issaka RB, Somsouk M. Colorectal cancer screening and prevention in the covid-19 era. *JAMA health forum* 2020;1:e200588. [PubMed: 34532717]
19. Nodora JN, Gupta S, Howard N, et al. The covid-19 pandemic: Identifying adaptive solutions for colorectal cancer screening in underserved communities. *JNCI: Journal of the National Cancer Institute* 2020.
20. Singal AG, Corley DA, Kamineni A, et al. Patterns and predictors of repeat fecal occult blood test screening in four large health systems in the united states. *The American journal of gastroenterology* 2018;113:746. [PubMed: 29487413]
21. Murphy CC, Sen A, Watson B, et al. A systematic review of repeat fecal occult blood tests for colorectal cancer screening. *Cancer Epidemiology and Prevention Biomarkers* 2020;29:278–287.
22. Murphy CC, Ahn C, Pruitt SL, et al. Screening initiation with fit or colonoscopy: Post-hoc analysis of a pragmatic, randomized trial. *Prev Med* 2019;118:332–335. [PubMed: 30508552]
23. Fenton JJ, Elmore JG, Buist DS, et al. Longitudinal adherence with fecal occult blood test screening in community practice. *Ann Fam Med* 2010;8:397–401. [PubMed: 20843880]
24. Lieberman DA, Prindiville S, Weiss DG, et al. Risk factors for advanced colonic neoplasia and hyperplastic polyps in asymptomatic individuals. *JAMA* 2003;290:2959–67. [PubMed: 14665657]
25. Niv Y, Hazazi R, Levi Z, et al. Screening colonoscopy for colorectal cancer in asymptomatic people: A meta-analysis. *Dig Dis Sci* 2008;53:3049–54. [PubMed: 18463980]
26. Chubak J, McLerran D, Zheng Y, et al. Receipt of colonoscopy following diagnosis of advanced adenomas: An analysis within integrated healthcare delivery systems. *Cancer Epidemiol Biomarkers Prev* 2019;28:91–98. [PubMed: 30459208]
27. ZJ. W. Amua: An open source modeling framework, 2019.
28. Murphy CC, Sigel BM, Yang E, et al. Adherence to colorectal cancer screening measured as the proportion of time covered. *Gastrointest Endosc* 2018;88:323–331. e2. [PubMed: 29477302]

29. Murphy CC, Halm EA, Skinner CS, et al. Challenges and approaches to measuring repeat fecal immunochemical test for colorectal cancer screening. *Cancer Epidemiology Biomarkers & Prevention* 2020;29:1557–1563.
30. Pignone M, Lanier B, Kluz N, et al. Effectiveness and cost-effectiveness of mailed fit in a safety net clinic population. *J Gen Intern Med* 2021.
31. Meenan RT, Coronado GD, Petrik A, et al. A cost-effectiveness analysis of a colorectal cancer screening program in safety net clinics. *Prev Med* 2019;120:119–125. [PubMed: 30685318]
32. Lee JK, Groessl EJ, Ganiats TG, et al. Cost-effectiveness of a mailed educational reminder to increase colorectal cancer screening. *BMC Gastroenterol* 2011;11:93. [PubMed: 21867492]
33. Shankaran V, Luu TH, Nonzee N, et al. Costs and cost effectiveness of a health care provider-directed intervention to promote colorectal cancer screening. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* 2009;27:5370–5375. [PubMed: 19826133]
34. Lansdorp-Vogelaar I, Knudsen AB, Brenner H. Cost-effectiveness of colorectal cancer screening. *Epidemiol Rev* 2011;33:88–100. [PubMed: 21633092]
35. Zauber AG, Lansdorp-Vogelaar I, Knudsen AB, et al. Evaluating test strategies for colorectal cancer screening: A decision analysis for the us preventive services task force. *Ann Intern Med* 2008;149:659–669. [PubMed: 18838717]
36. Vanness DJ, Knudsen AB, Lansdorp-Vogelaar I, et al. Comparative economic evaluation of data from the acrin national ct colonography trial with three cancer intervention and surveillance modeling network microsimulations. *Radiology* 2011;261:487–498. [PubMed: 21813740]
37. Levin TR, Corley DA, Jensen CD, et al. Effects of organized colorectal cancer screening on cancer incidence and mortality in a large community-based population. *Gastroenterology* 2018;155:1383–1391. e5. [PubMed: 30031768]
38. Moiel D, Thompson J. Early detection of colon cancer—the kaiser permanente northwest 30-year history: How do we measure success? Is it the test, the number of tests, the stage, or the percentage of screen-detected patients? *The Permanente journal* 2011;15:30–38. [PubMed: 22319413]
39. Sanderson M, Allen P, Osipovic D. The regulation of competition in the national health service (nhs): What difference has the health and social care act 2012 made? *Health Economics, Policy and Law* 2016;FirstView:1–19.
40. Zapka J, Klabunde CN, Taplin S, et al. Screening colonoscopy in the us: Attitudes and practices of primary care physicians. *J Gen Intern Med* 2012;27:1150–8. [PubMed: 22539065]
41. Martin J, Halm EA, Tiro JA, et al. Reasons for lack of diagnostic colonoscopy after positive result on fecal immunochemical test in a safety-net health system. *Am J Med* 2017;130:93.e1–93.e7.
42. Martin K, Kurowski D, Given P, et al. The impact of covid-19 on the use of preventive health care, 2020.
43. 2020 annual report of the boards of trustees of the federal hospital insurance trust fund and the federal supplementary medical insurance trust fund: Centers for Medicare and Medicaid Services, 2020.
44. Claxton K, Paulden M, Gravelle H, et al. Discounting and decision making in the economic evaluation of health-care technologies. *Health Econ* 2011;20:2–15. [PubMed: 21154521]
45. Laiyemo AO, Pinsky PF, Marcus PM, et al. Utilization and yield of surveillance colonoscopy in the continued follow-up study of the polyp prevention trial. *Clin Gastroenterol Hepatol* 2009;7:562–567. [PubMed: 19138760]
46. Winawer SJ, Zauber AG, O'Brien MJ, et al. Randomized comparison of surveillance intervals after colonoscopic removal of newly diagnosed adenomatous polyps. *N Engl J Med* 1993;328:901–906. [PubMed: 8446136]

“What You Need to Know”

Background:

Mailed outreach strategies are effective at promoting colorectal cancer screening process completion; however, there are limited data regarding cost-effectiveness of mailed FIT kits relative to mailed invitations to complete a colonoscopy.

Findings:

Mailed FIT kits had a lower 10-year average per-person costs of screening than colonoscopy invitations (\$1139 vs. \$1725) but with 10.89 fewer months of compliance and 60 fewer advanced neoplasia detected (37 advanced adenomas and 23 CRC). The ICER per covered month gained around was \$49 to \$55 per patient.

Implications for patient care:

Thus, although FIT outreach is less expensive and may be prioritized in resource-constrained healthcare settings, costs of colonoscopy outreach are only slightly greater with a more thorough accounting of differences. Based on these data, FIT and colonoscopy outreach both appear to be good options to improve screening completion and early CRC detection.

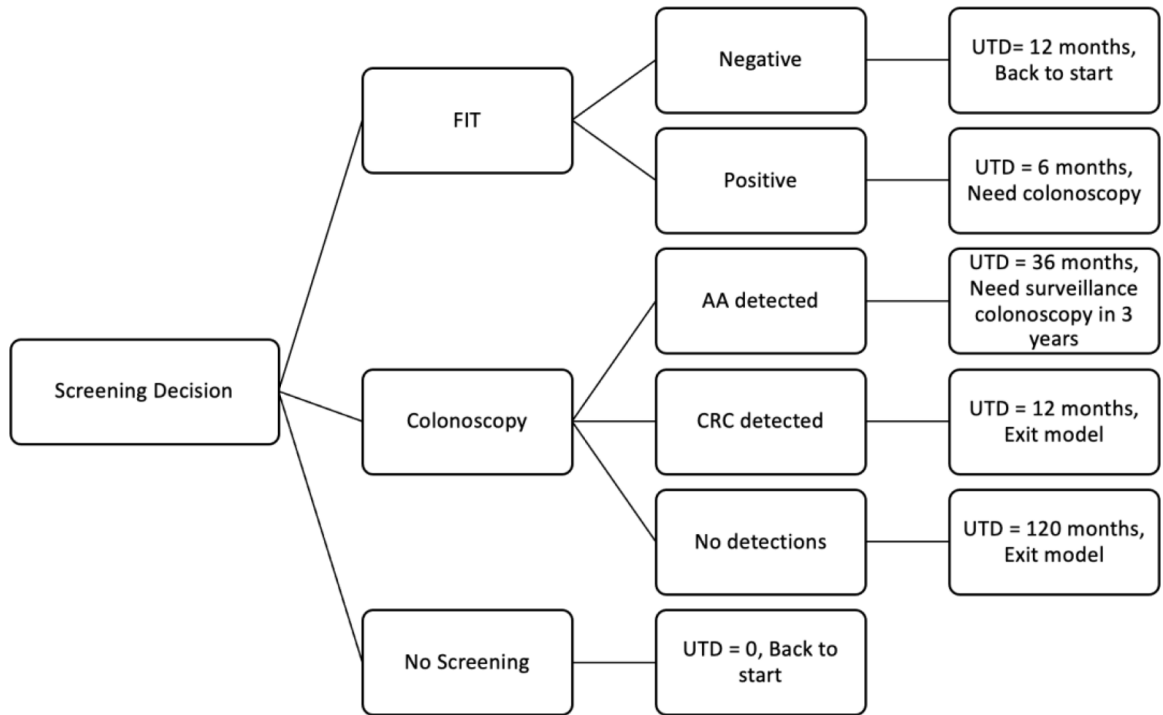


Figure 1.
Model State Transition Diagram
Notes: UTD = up-to-date defined by the number of covered months.

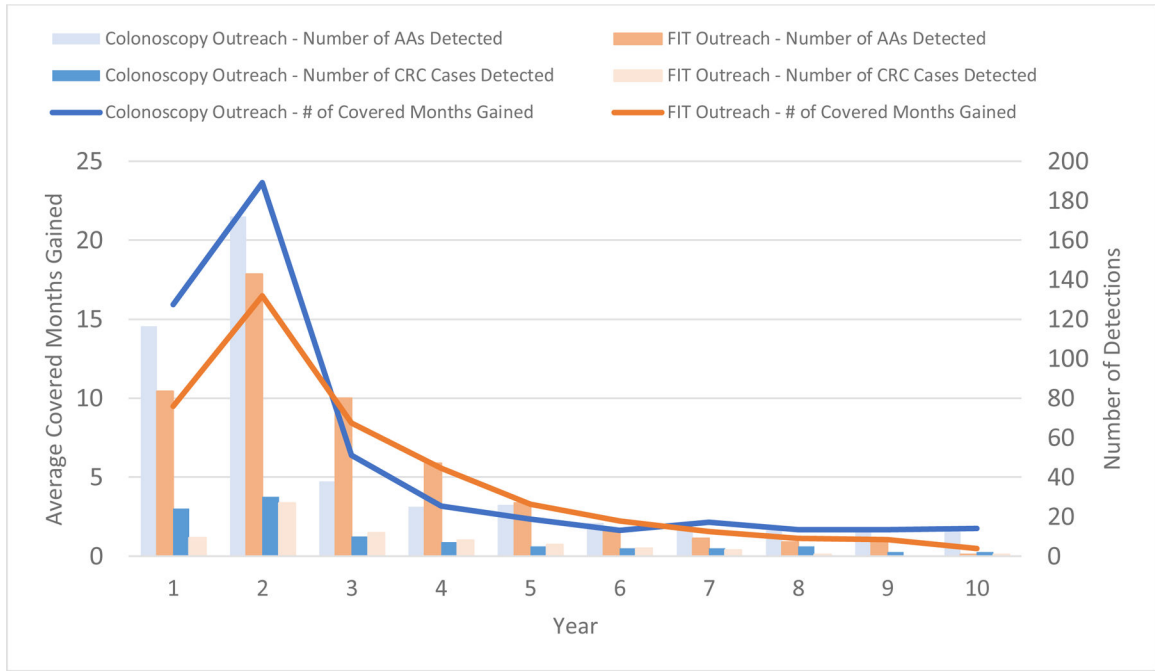


Figure 2. Average Number of Covered Months Gained and Number of AA/CRC Detected, by Outreach Strategy and Year
Notes: Based on actual data for years 1 to 3 and microsimulation estimates for years 4 to 10. The lines correspond to the average number of covered months gained in each year for each outreach strategy. The bars correspond to the average number of detections (AAs and CRC cases, separately) in each year for each outreach strategy.

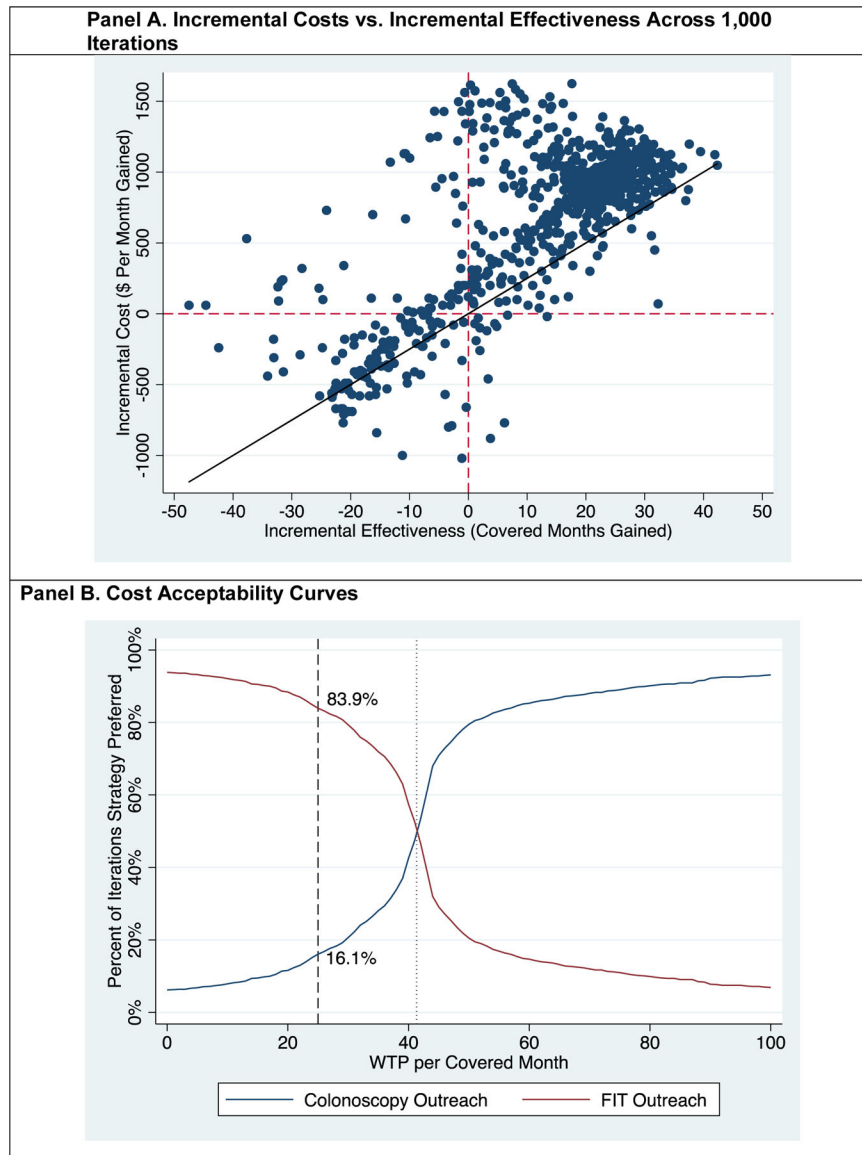


Figure 3. Incremental Costs, Incremental Covered Months Gained, and Willingness to Pay

Table 1.

Modeling Parameters, by Outreach Strategy

	FIT			Colonoscopy		
	Base case	Dist.	Ref.	Base case	Dist.	Ref.
<i>Completion Rates</i>						
Pr(FIT) ^a	0.61	Triangle	22	0.18	Triangle	22
Pr(Colonoscopy) ^a	0.02	Beta	22	0.26	Beta	22
Pr (No Screening)	0.37	Beta	22	0.56	Beta	22
<i>Detection Rates</i>						
Pr (FIT neg) ^b	0.93	Beta	22	0.93	Beta	22
Pr (AA colon) ^c	0.12	Beta	22	0.09	Beta	22
Pr (CRC colon) ^d	0.03	Beta	22	0.03	Beta	22
<i>Follow-up Colonoscopy Rates</i>						
Pr(Surveill at 3 Years) ^e	0.18	Triangle	26	0.18	Triangle	26
Pr(AA surveill colon)	0.35	Beta	45	0.35	Beta	45
Pr(CRC surveill colon)	0.03	Beta	46	0.03	Beta	46
<i>Costs, per Patient Screened</i>						
Negative FIT test	\$25	Gamma	22	\$25	Gamma	22
Positive FIT test	\$28	Gamma	22	\$28	Gamma	(20) ²⁰
Colonoscopy	\$3,065	Gamma	22	\$3,065	Gamma	22

Table 2.

Average per Patient Costs and Screening Yields from Base Case

	FIT outreach	Colonoscopy outreach	Difference	ICER
Costs				
Average Cost per 10-Years	\$1,139 (\$1,113, \$1,165)	\$1,725 (\$1,699, \$1,751)	\$586	
Outcomes				
Average Number of Covered Months	49.93 (49.05, 50.81)	60.54 (60.25, 62.23)	10.89	\$55.23
Average Number of AAs Detected	420 (379.86, 460.14)	457 (415.92, 498.08)	37	\$15.84
Average Number of CRC Cases Detected	73 (56.99, 89.01)	96 (78.3, 113.7)	23	\$25.48
Average Number of Any Advanced Neoplasia (AA or CRC) Detected	493 (449.74, 536.26)	553 (508.19, 597.81)	60	\$9.77

Table 3.

Probabilistic Sensitivity Analyses (PSA) Results

	FIT outreach	Colonoscopy outreach	Difference	ICER
Costs				
Average Cost per 10-Years	\$972 (\$943, 1,001)	\$1,711 (\$1,701, \$1,721)	\$739 (\$708, 769)	
Outcomes				
Average Number of Covered Months	45.68 (44.86, 46.51)	60.55 (60.12, 60.98)	14.89 (13.94, 15.80)	\$49.63
Average Number of AAs Detected	313.39 (277.69, 349.10)	534.72 (461.78, 607.65)	221.32 (137.97, 304.68)	\$3.34
Average Number of CRC Cases Detected	39.89 (28.61, 51.17)	53.95 (36.15, 71.75)	14.05 (-1.21, 29.33)	\$52.60

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