



Research Article

# Cost-Effectiveness of mt-sDNA versus Mailed FIT Outreach for Medicare Advantage Enrollees using the CRC-AIM Microsimulation Model

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## Abstract

**Background:** Despite proven effectiveness in reducing Colorectal Cancer (CRC) cases, screening for CRC remains underutilized. As the use of an outreach program may increase uptake and adherence to screening, we examined the cost-effectiveness of provider-ordered multi-target stool DNA (mt-sDNA) versus an outreach program with a mailed Fecal Immunochemical Test (FIT), in a Medicare Advantage population. **Methods:** Annual FIT, mailed as part of an outreach program, and triennial mt-sDNA were compared using the validated CRC-AIM microsimulation model over a lifetime horizon. Costs and clinical outcomes of 2 million average-risk individuals, free of diagnosed CRC at age 40, who initiated CRC screening at age 65, were simulated. Test sensitivity and specificity inputs were based on the 2021 United States Preventive Services Task Force modeling study; adherence rates were based on published real-world data for stool-based tests and follow-up colonoscopies (COLs). The cost of the outreach program, screening tests, COLs, complications, and CRC care were included. Discount rates (3%) and the perspective of Medicare Advantage were employed. Outcomes are reported in Life-Years Gained (LYG), Quality-Adjusted Life Years (QALY), Incidence Reduction (IR), mortality reduction (MR) and the incremental cost-effectiveness ratio. Scenario analyses explored alternate adherence rates. **Results:** In the base case, using real-world adherence rates, mt-sDNA had higher IR, MR and LYG; mt-sDNA was cost-effective at a willingness-to-pay threshold of \$50,000 per QALY compared to mailed FIT outreach. In scenario analyses, when assuming 100% adherence for both screening test and follow-up COL, mt-sDNA was dominated by mailed FIT outreach. mt-sDNA remained cost-effective versus outreach with mailed FIT in a scenario where FIT had 20% higher adherence than the base case. **Conclusions:** Adherence to CRC screening and follow-up COL greatly impacts clinical and cost-effectiveness outcomes. Future analyses should consider evidence-based, health plan-specific data to accurately reflect outcomes in order to aid payers in decision making.g.

**Keywords:** Colorectal cancer; Screening; Preventive health services; Medicare advantage

## Introduction

Colorectal Cancer (CRC) is the second most common cause of cancer deaths [1]. The United States Preventive Services Task Force (USPSTF) recommends screening for CRC among average-risk adults beginning at age 45 [2] as screening has long been established in reducing both the incidence of and death from CRC [3]. While recommended CRC screening use has increased since 2000 [4], rates remain below the National Colorectal Cancer Roundtable goal of screening 80% of eligible adults [5]. Despite studies estimating that increasing screening by 10 percentage points would reduce the number of deaths from CRC by 15 percentage points [6], CRC screening remains underutilized [2,7].

Multiple options for CRC screening are supported by evidence of net benefit, including stool-based tests [2]. Stool-based tests have multiple advantages: they are non-invasive; they are accessible in resource-constrained settings and they do not rely on traveling to a health centre to perform. Two commonly used stool-based tests include Fecal Immunochemical Test (FIT) and multi-target stool DNA (mt-sDNA). FIT is recommended to be performed annually while mt-sDNA is recommended to be repeated every three years [8] and includes patient navigation with every test [9], which has been found to be a key factor in increasing adherence [10]. While patient navigation is not routinely included with FIT tests, mailed outreach programs have been found to increase use and adherence to FIT among eligible screeners enrolled in Medicare Advantage [11].

CRC screening varies based on the type of insurance coverage, including Medicare with private insurance versus Medicare with no supplementary insurance or Medicare and Medicaid [12]. Medicare Advantage is provided through provide-sector health insurers and was chosen by nearly 40% of Medicare enrollees in 2020 [13]. Despite the inclusion of preventive health services within the Medicare Advantage program, CRC screening remains underutilized by enrollees. To better understand the health and economic consequences of mt-sDNA versus a FIT mailed outreach program, this study examined the cost-effectiveness of these stool-based screening tests in a Medicare Advantage

population due for screening using a microsimulation model.

## Methods

### Overview

This analysis examined the cost-effectiveness of mt-sDNA versus a FIT mailed outreach program from the perspective of Medicare Advantage. The validated CRC-AIM model was used [14,15], and included average-risk US adults aged 65 to 75 (Medicare Advantage eligible years for screening). Individuals were assumed to be due for CRC screening; that is, they were previously screened and it had been one year since their previous negative FIT test, 5 years after a previous normal sigmoidoscopy and/or 10 years after a previous normal colonoscopy. Screening modalities included in the model were either annual FIT, or triennial mt-sDNA until age 75, as per the latest guidelines [2]. Individuals who did not undergo follow-up colonoscopy in the model were assumed to be non-adherent until they become symptomatic. A lifetime horizon was chosen to assess the impact of screening; costs and Quality-Adjusted Life Years (QALYs) were discounted at 3% [16].

### Inputs

Screening strategies performance parameters were based on the 2021 USPSTF modeling study (Supplementary Table 1) [2]. Cost inputs were based on Medicare fee for service and were inflated to November 2021 using the Medical Care Services component of the Consumer Price Index (Supplementary Table 2) [17]. FIT does not include the cost of an outreach program, thus, the cost of outreach was taken from a randomized controlled trial, which consisted of a mailed postcard and call, followed by a mailed FIT kit, and then a reminder phone call if the kit was not returned [18]. As patient navigation is included with every mt-sDNA, no additional cost for outreach was necessary. Utility inputs for patients not experiencing colonoscopy complications or utility loss due to complications were included at baseline, adjusted for age, and based on general US population utility values (Supplementary Table 3) [19]. Utility loss for all colonoscopies and complications from colonoscopy were included as utility decrements per event [20]. Utility loss for CRC was stratified by the level of CRC care and stage of CRC; these utility decrements were applied on a per

patient per year basis [20].

	Sensitivity			Cancer	Specificity
	Adenomas				
	<6mm	6-9mm	10mm+		
mt-sDNA <sup>a</sup>	0.15		0.42	0.94	0.91
FIT <sup>a</sup>	0.07		0.22	0.74	0.97
Colonoscopy <sup>b</sup>	0.75	0.85	0.95	0.95	0.86

<sup>a</sup>per person; <sup>b</sup>within reach, per lesion

**Supplementary Table 1:** Cross-sectional test performance parameters [21].

Parameter	Base Value	Distribution range	Source
	Medicare (65-75)		
Screening costs			
Colonoscopy <sup>a</sup>	\$1,528.12	± 10%	Pyenson [22]
mt-sDNA	\$508.87	± 10%	PAMA prices
FIT	\$18.05	± 10%	
FIT outreach program	\$25.92	± 10%	Somsouk [18]
Complications			
Gastrointestinal	\$9,069.21	± 10%	Hathway [23]
Serious gastrointestinal	\$25,854.81	± 10%	
Cardiovascular	\$11,627.29	± 10%	
CRC costs			

Stage I Initial Care	\$38,320.65	± 10%	Naber [24]
Stage I Continuous Care	\$3,086.02	± 10%	
Stage I Terminal Care, CRC death	\$78,545.77	± 10%	
Stage I Terminal Care, non-CRC death	\$19,195.38	± 10%	
Stage II Initial Care	\$54,344.95	± 10%	
Stage II Continuous Care	\$3,753.79	± 10%	
Stage II Terminal Care, CRC death	\$88,612.97	± 10%	
Stage II Terminal Care, non-CRC death	\$20,645.86	± 10%	
Stage III Initial Care	\$77,351.59	± 10%	
Stage III Continuous Care	\$6,043.31	± 10%	
Stage III Terminal Care, CRC death	\$91,684.05	± 10%	
Stage III Terminal Care, non-CRC death	\$28,722.38	± 10%	
Stage IV Initial Care	\$112,557.49	± 10%	
Stage IV Continuous Care	\$30,428.03	± 10%	
Stage IV Terminal Care, CRC death	\$114,079.23	± 10%	
Stage IV Terminal Care, non-CRC death	\$70,384.20	± 10%	
<sup>a</sup> Includes colonoscopies, diagnostic colonoscopies, surveillance colonoscopies and follow-up colonoscopies.			

**Supplementary Table 2: Cost inputs.**

	Base value		Distribution range	Source
Health State Utility	EQ-5D population norms		Not varied	Szende [19]
Utility loss per event				
Colonoscopy	-0.0055		± 10%	Goede [20]
Complication from colonoscopy, any	-0.0384		± 10%	Goede [20]
Utility loss per person per year of CRC care	Stage I-III	Stage IV		
Initial care	-0.15	-0.34	± 10%	Goede [20]
Continuous care	-0.10	-0.29	± 10%	Goede [20]
Terminal care, CRC death	-0.29	-0.29	± 10%	Goede [20]
Terminal care, non-CRC death	-0.10	-0.29	± 10%	Goede [20]

**Supplementary Table 3: Utility inputs.**

**Base case analysis**

The base case analysis used reported real-world adherence rates for both adherence to initial screening and follow-up colonoscopy after a positive stool-based screening test (Supplementary Table 4). Surveillance and symptom-related colonoscopies had an assumed adherence of 100% and were not varied in sensitivity analyses. Fixed adherence rates are assumed over time.

Parameter	Medicare Advantage	Distribution range	Source
	(65-75)		
Stool-based screening tests			
mt-sDNA	69.8%	± 10%	Miller-Wilson [25]
FIT + outreach	29.0%	± 10%	Issaka [11]
Colonoscopies			
Follow-up – mt-sDNA	71.5%	± 10%	Cooper [26]
Follow-up – FIT + outreach	53.0%	± 10%	Issaka [11]

**Supplementary Table 4:** Adherence parameters used in the model.

The primary outcome was clinical benefit reported as incidence reduction, mortality reduction and Life Years Gained (LYG) per 1,000 patients. Secondary outcomes included total costs (screening costs, the cost of CRC-related direct medical costs, and costs associated with colonoscopy complications), QALYs, LYG and the Incremental Cost-Effectiveness Ratio (ICER) of mt-sDNA versus FIT + outreach. Willingness to Pay (WTP) was based on commonly accepted thresholds in the United States (US) [16].

**Scenario analyses**

In order to explore the impact of adherence on outcomes, three alternate scenarios were considered:

- **Scenario 1:** 100% adherence to both the stool-based screening test and follow-up colonoscopy
- **Scenario 2:** reported real-world adherence for stool-based screening only with 100% adherence to follow-up colonoscopy
- **Scenario 3:** for FIT only, an assumption of 20% higher real-world reported adherence rates for both the screening test and follow-up colonoscopy

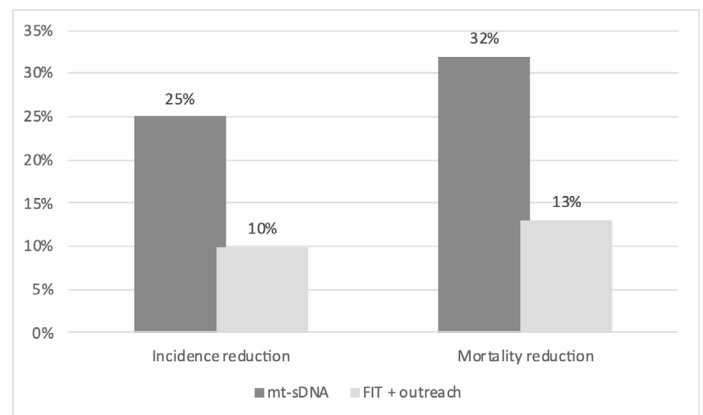
**Additional analyses**

In order to determine the impact of the inputs on results, a probabilistic sensitivity analysis, where all parameters were varied + / -10% of their base case values simultaneously, was undertaken. Threshold analyses were also undertaken to explore the robustness of the adherence inputs on the ICER. In the first threshold analysis, stool-based screening test adherence was varied from 0-100% while adherence to follow-up colonoscopy was held constant at 100%. In the second threshold analysis, adherence to the screening

test was held constant at the baseline reported real-world adherence rates, while adherence to follow-up colonoscopy was varied from 0-100%.

**Results**

In the base case analysis under reported real-world adherence rates for both stool-based screening tests and follow-up colonoscopies, use of mt-sDNA for screening resulted in a greater reduction in CRC incidence and mortality compared to a FIT + outreach program (Figure 1). Screening with mt-sDNA resulted in an incidence reduction of 25% and a mortality reduction of 32%, compared to 10% and 13%, respectively with FIT + outreach. Compared to FIT + outreach, screening with mt-sDNA resulted in greater LYG per 1,000 patients and lower CRC costs (Table 1).



**Figure 1:** CRC Incidence and mortality reduction under reported real-world adherence, base case analysis.

Strategy	Clinical			Costs					Utilities	
	Screening tests <sup>a</sup>	Lifetime COL <sup>a,b</sup>	LYG <sup>a</sup>	Screening <sup>c</sup>	Complications	Outreach	CRC	Lifetime costs <sup>d</sup>	Lifetime disutilities	Lifetime QALYs
No screening	0	81	0	\$88	\$21	\$0	\$6,490	\$6,600	-0.0524	9.3390
mt-sDNA	2,409	478	111	\$1,690	\$52	\$0	\$5,245	\$6,987	-0.0498	9.3828
FIT + outreach	2,361	187	49	\$267	\$23	\$54	\$6,007	\$6,351	-0.0519	9.3574

**COL:** Colonoscopy; **CRC:** Colorectal Cancer; **FIT:** Fecal Immunochemical Test; **LYG:** Life-Years Gained; **mt-sDNA:** multi-target stool DNA; **QALY:** Quality-Adjusted Life-Years. <sup>a</sup>per 1,000 patients; <sup>b</sup>includes any colonoscopy; <sup>c</sup>includes cost of colonoscopy; <sup>d</sup>lifetime costs include screening costs (stool-based screening costs and follow-up / diagnostic / surveillance colonoscopies, as relevant), complication costs, and CRC cost.

**Table 1:** Discounted clinical, cost and utility outcomes of screening, base case analysis.

### Scenario analyses

The highest reduction in incidence of and mortality from CRC were observed with perfect adherence to stool-based screening and follow-up colonoscopy (Scenario 1). In this scenario, FIT + outreach resulted in higher reduction in incidence and mortality from CRC compared to mt-sDNA (Table 2). The reduction in incidence and mortality from CRC, along with total QALYs, was lower in magnitude in Scenario 2 compared with Scenario 1 for both mt-sDNA and FIT + outreach when using reported real-world adherence for stool-based screening and perfect (100%) adherence for follow-up colonoscopy. mt-sDNA, however, still resulted in greater reduction in incidence and mortality from CRC compared to FIT (Scenario 2). When increasing the reported real-world adherence of FIT + outreach by 20% for both the stool-based test and follow-up colonoscopy (Scenario 3), mt-sDNA still resulted in greater reduction in incidence of and mortality from CRC as compared to FIT + outreach. Similar patterns were observed for life years gained, with the greatest life years gained observed for FIT + outreach under a perfect adherence scenario (Scenario 1), while mt-sDNA resulted in incrementally more life years gained under Scenario 2 and Scenario 3. Total lifetime costs were highest for both strategies under Scenario 3 and were lowest for mt-sDNA for Scenario 2 and for FIT + outreach under Scenario 1 (Table 3). Total QALYs were highest for both strategies under Scenario 1 and lowest under Scenario 3.

Strategy	Screening tests	Lifetime COLs <sup>a</sup>	Number of complications	Number of CRC cases	Number of CRC deaths	LYG	Incidence Reduction	Mortality Reduction
<b>Scenario 1</b>								
No screening	0	81	3	81	37	0	0%	0%
mt-sDNA	2,725	742	7	50	19	167	38.4%	47.7%
FIT + outreach	6,891	772	7	47	18	181	41.7%	52.2%
<b>Scenario 2</b>								
No screening	0	81	3	81	37	0	0%	0%
mt-sDNA	2,416	674	6	52	21	154	35.3%	44.3%
FIT + outreach	2,365	341	3	65	27	93	18.9%	26.2%
<b>Scenario 3</b>								
No screening	0	81	3	81	37	0	0%	0%
mt-sDNA	2,409	478	4	60	25	111	25.2%	31.6%
FIT + outreach	2,795	253	3	69	30	67	13.8%	18.7%

**Scenario 1:** 100% adherence to both the stool-based screening test and follow-up colonoscopy; **Scenario 2:** reported real-world adherence for stool-based screening only with 100% adherence to follow-up colonoscopy; **Scenario 3:** for FIT only, an assumption of 20% higher real-world reported adherence rates for both the screening test and follow-up colonoscopy; COL: Colonoscopy; CRC: Colorectal Cancer; FIT: Fecal Immunochemical Test; mt-sDNA: multi-target stool DNA; QALY: Quality-Adjusted Life-Years; <sup>a</sup>Lifetime COLs include surveillance colonoscopies, colonoscopies for symptoms and follow-up colonoscopies.

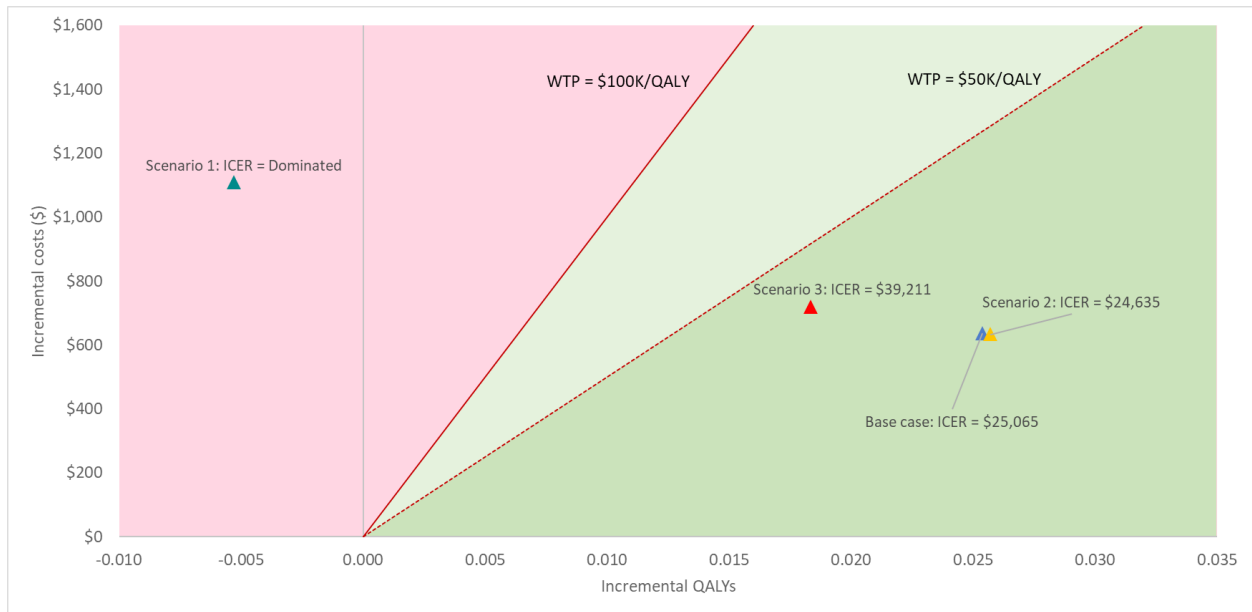
**Table 2:** Discounted clinical outcomes per 1,000 patients, scenario analyses.

Strategy	Screening	Costs				Disutilities			Total QALYs
		Complications	Outreach	CRC	Lifetime costs <sup>a</sup>	Screening	Complications	CRC	
<b>Scenario 1</b>									
No screening	\$88	\$21	\$0	\$6,490	\$6,600	-0.0003	-0.0001	-0.0520	9.3390
mt-sDNA	\$2,169	\$82	\$0	\$4,580	\$6,831	-0.0033	-0.0002	-0.0448	9.4056
FIT + outreach	\$1,061	\$83	\$158	\$4,421	\$5,723	-0.0034	-0.0002	-0.0446	9.4109
<b>Scenario 2</b>									
No screening	\$88	\$21	\$0	\$6,490	\$6,600	-0.0003	-0.0001	-0.0520	9.3390
mt-sDNA	\$1,934	\$71	\$0	\$4,742	\$6,747	-0.0030	-0.0002	-0.0456	9.4002
FIT + outreach	\$453	\$39	\$54	\$5,568	\$6,114	-0.0015	-0.0001	-0.0500	9.3745
<b>Scenario 3</b>									
No screening	\$88	\$21	\$0	\$6,490	\$6,600	-0.0003	-0.0001	-0.0520	9.3390
mt-sDNA	\$1,690	\$52	\$0	\$5,245	\$6,987	-0.0021	-0.0001	-0.0475	9.3828
FIT + outreach	\$354	\$30	\$64	\$5,820	\$6,268	-0.0011	-0.0001	-0.0504	9.3644

**Scenario 1:** 100% adherence to both the stool-based screening test and follow-up colonoscopy; **Scenario 2:** reported real-world adherence for stool-based screening only with 100% adherence to follow-up colonoscopy; **Scenario 3:** for FIT only, an assumption of 20% higher real-world reported adherence rates for both the screening test and follow-up colonoscopy; COL: Colonoscopy; CRC: Colorectal Cancer; FIT: Fecal Immunochemical Test; mt-sDNA: multi-target stool DNA; QALY: Quality-Adjusted Life-Years; <sup>a</sup>Lifetime costs include screening costs (stool-based and follow-up / symptom / surveillance colonoscopies, as relevant), cost of complications, cost of CRC.

**Table 3:** Discounted total costs and QALYs, scenario analyses.

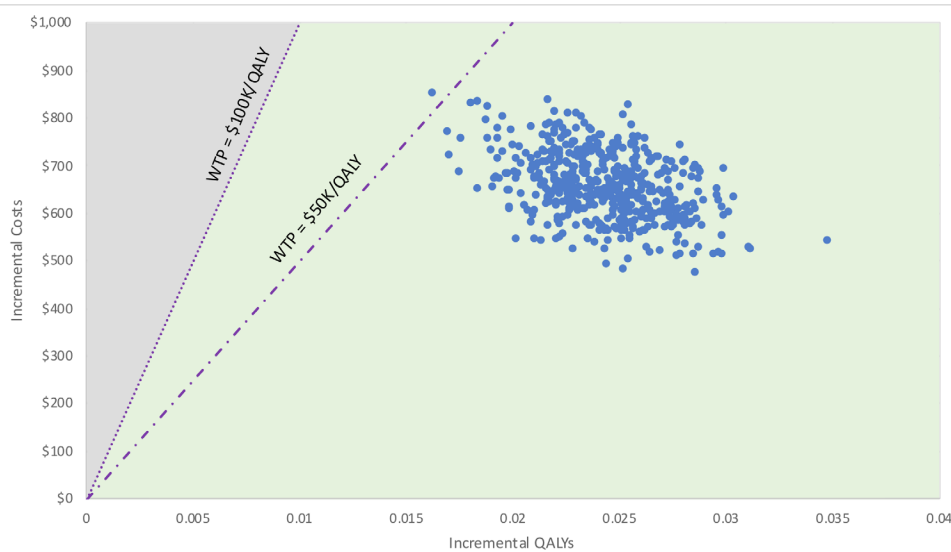
For the base case analysis, while total costs were higher when screening with mt-sDNA, due to increased QALY gains, mt-sDNA was cost-effective versus FIT + outreach with an ICER of \$25,065 / QALY. Under both Scenarios 2 and 3, mt-sDNA was cost-effective versus FIT + outreach at a WTP threshold of \$50,000 / QALY (Supplementary Figure 1).



**Supplementary Figure 1:** Incremental cost-effectiveness plane of mt-sDNA versus FIT + outreach.

**Additional analyses**

The probabilistic analysis found that 99.8% (499/500) of the iterations resulted in an ICER of no more than \$50K/QALY for mt-sDNA versus FIT; 100% of the runs resulted in ICERs less than \$100K/QALY (Supplementary Figure 2).



**Supplementary Figure 2:** Probabilistic sensitivity analysis of mt-sDNA versus FIT, base case.

The threshold analysis found that when varying the stool-based test adherence (while keeping the follow-up colonoscopy adherence rate fixed at 100%), adherence to both stool-based tests would need to be at least 75% for FIT to dominate mt-sDNA (Figure 2). When varying follow-up colonoscopy adherence rates (keeping adherence to stool-based screening rates fixed at baseline values), mt-sDNA is cost-effective against FIT at all levels of adherence to FIT (Figure 3).



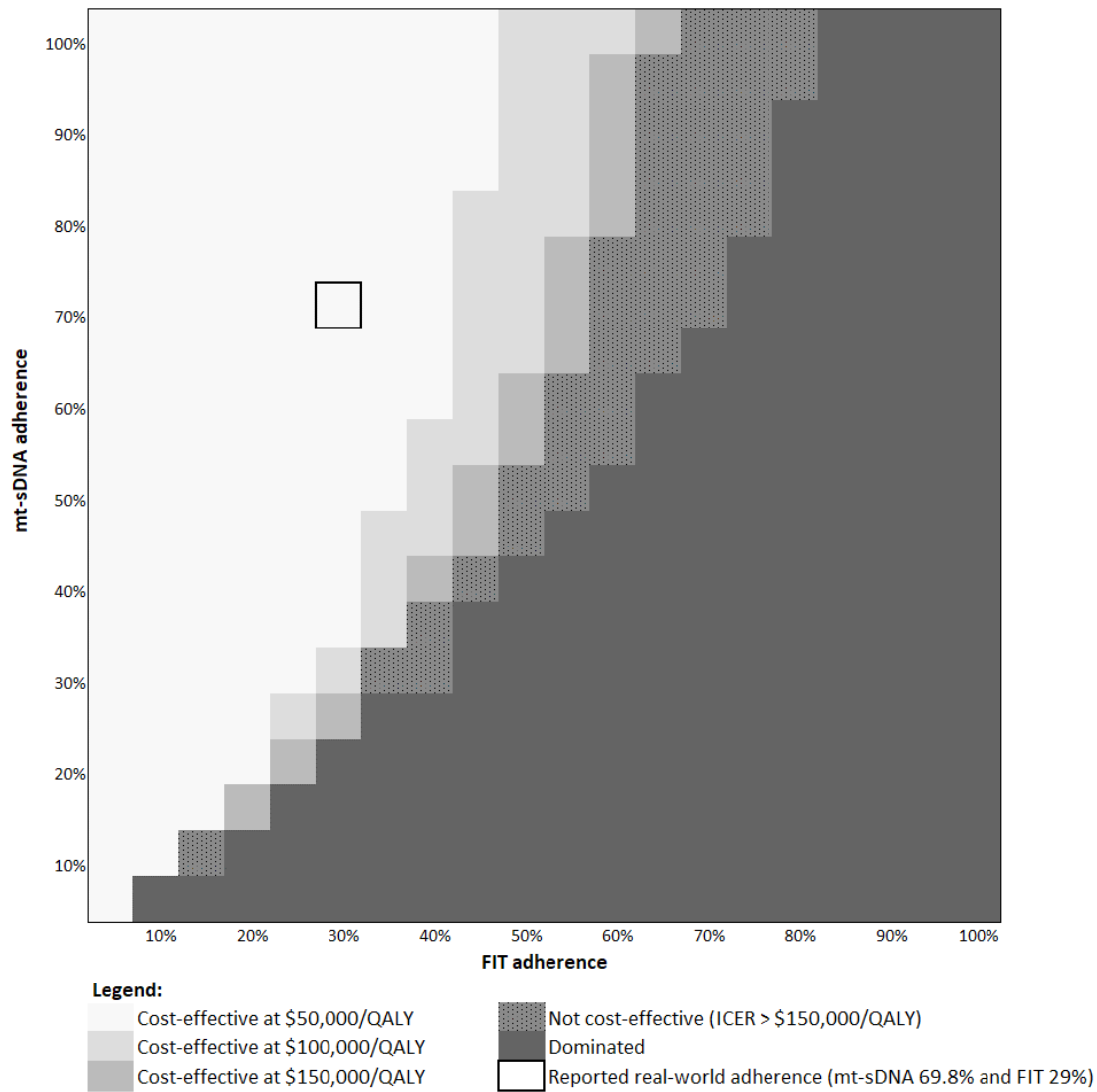
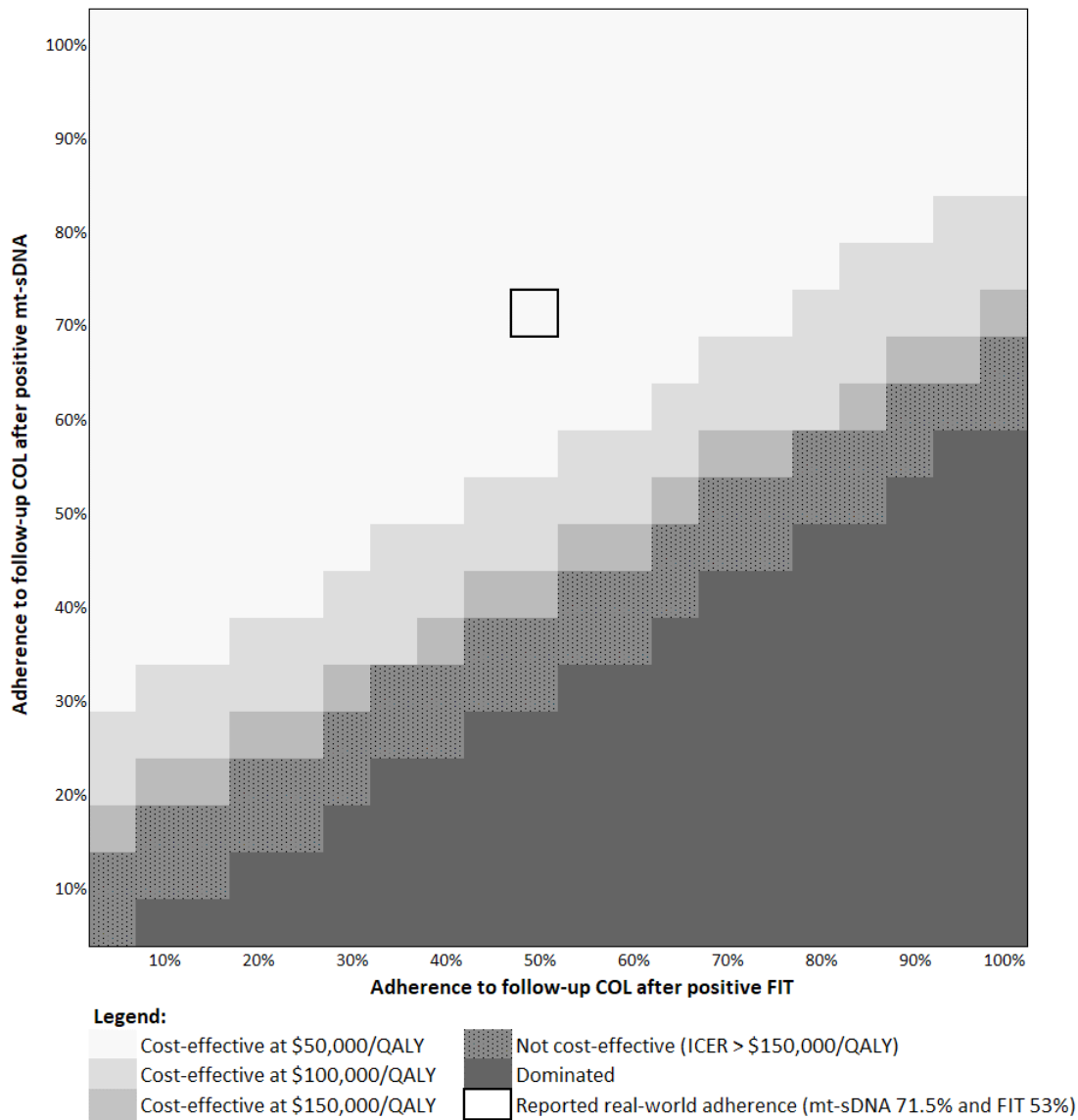


Figure 2: Heatmap of mt-sDNA versus FIT when varying screening test rates (follow-up colonoscopy adherence fixed at 100%).



**Figure 3:** Heatmap of mt-sDNA versus FIT when varying follow-up colonoscopy rates (stool-based screening adherence fixed at baseline values).

## Discussion

Ensuring eligible patients remain up to date with screening is essential to reducing the burden of CRC. Our results found that under reported real-world adherence rates, screening with mt-sDNA resulted in greater incidence and mortality reduction compared to FIT + outreach, in a Medicare Advantage population. While total costs were higher when screening with mt-sDNA due to increased QALY gains, use of mt-sDNA was found to be cost-effective versus FIT + outreach at a WTP threshold of \$50,000 / QALY. Similar results were observed with scenario analyses exploring perfect adherence for follow-up colonoscopy as well as when increasing the adherence to FIT + outreach by 20%. These results highlight the need for robust cost-effectiveness analyses, including the use of real-world adherence rates, when determining the value of a test.

This is the first study to explore the cost-effectiveness of stool-based tests in a Medicare Advantage population. Medicare Advantage has been found to deliver significantly better quality of care, with better health outcomes [21]. One study found that Medicare Advantage

beneficiaries were more likely to receive mammography screening compared with a Medicare fee for service population [22]. Medicare Advantage may be considered to be more efficient than Medicare fee-for-service, as it offers improved disease management, care coordination and supplemental benefits, all factors that may impact the uptake of CRC screening. Despite these differences, this analysis extends the generalizability of the results observed with mt-sDNA in other insured populations [23,24].

Multiple factors affect adherence to CRC screening. The top barriers to screening identified among respondents who had previously used stool-based screening options were lack of provider recommendations and lack of knowledge [25]. In order to address these barriers and increase adherence to screening, different outreach strategies have been proposed; these organized outreach programs have been shown to be effective to various degrees [26]. The results of this cost-effectiveness analysis are based on a mailed outreach program for FIT that included eligible Medicare Advantage patients receiving a letter containing information about CRC screening, along with a FIT kit where adherence to screening with outreach was found to be 29.0% [11]. This adherence is lower than the 69.8% reported among Medicare Advantage patients using mt-sDNA, which may be due to the fully integrated patient navigation for completion of the stool-based test which is integrated with every mt-sDNA test, including the universal outreach available in over 240 languages [9]. While a previous study in an integrated healthcare delivery system (Kaiser Permanente Northern California) found that the initiation of an organized CRC screening program significantly increased the up to date screening status from 39.0% to 82.7% over 15 years ( $p < 0.01$ ) [27], a claims analysis of multiple health plans found that only 23.4% of patients were adherent to FIT at year 2, and 10.6% were adherent at year 3 [28]. Outreach strategies to increase adherence to screening, including follow-up colonoscopy, need to be explored further, to determine the barriers and facilitators of screening across various populations.

Results of this study should be interpreted in the context of the assumptions. This analysis was based on the use of the CRC-AIM microsimulation model, which has previously been validated [29]. In addition, reported population-specific real-world data was used to inform adherence for both stool-based screening tests (mt-sDNA and FIT), along with the respective adherence to follow-up colonoscopies. However, as Medicare Advantage-specific adherence data are not available for the fecal occult blood test, it was excluded from this analysis. Further, only non-invasive stool tests were explored in this analysis. This analysis also only considered cross-sectional adherence rates; the impact of intermittent or longitudinal adherence on the cost-effectiveness of screening strategies was not explored. While the inputs of this analysis were based on a limited number of studies, these were tested through scenario and sensitivity analyses and results

remained robust.

## Conclusions

Adherence to initial stool-based CRC screening tests and follow-up colonoscopies impact both clinical and cost-effectiveness outcomes. The choice of test and patient outreach can favourably impact patient adherence, thus further contributing towards the goal of attaining 80% CRC screening adherence. Future analyses should consider population-specific real-world evidence, including those living in supportive care facilities and those with chronic conditions, as well as comparisons with colonoscopies, in order to aid payer decision making.

## Funding Source

This study was funded by Exact Sciences Corporation.

## Competing Interests

Dr. Fendrick reports having been a consultant and expert witness for Exact Sciences, he is also a consultant for Abbvie, Amgen, Bayer, the California Health Care Foundation, CareFirst Blue Cross Blue Shield, Centivo, the Community Oncology Association, EmblemHealth, Exact Sciences, GRAIL, Health[at]Scale Technologies, HealthCorum, MedZed, Merck, Mother Goose Health, Pfizer, Sempre Health, SilverFern Healthcare, the State of Minnesota, Teladoc Health, the U.S. Department of Defense, the Virginia Center for Health Innovation, Wellth, Yale University, and Zansors, being a partner in VBIDHEALTH, and receiving research support from the Agency for Healthcare Research and Quality, Arnold Ventures, the National Pharmaceutical Council, the PatientCentered Outcomes Research Institute, Pharmaceutical Research and Manufacturers of America, the Robert Wood Johnson Foundation, the State of Michigan, West Health Policy Center, and the Centers for Medicare and Medicaid Services. Dr. Chen, Dr. Vahdat, Dr. Brooks and Dr. Ozbay were full-time employees of Exact Sciences Corporation during the conduct of the study. Dr. Bhatt as nothing to disclose. Dr. Lieberman reports being part of the Safety Advisory Board for Genescopy, Colowrap and UDX; he also reports having received consultant fees for Freenome and Ironwood. Dr. Karlitz has provided consulting services to Exact Sciences and has an equity position and is Chief Medical Officer for Gastro Girl and GI OnDEMAND.

## Author's Contributions

All authors contributed to the conception of the work, the interpretation of the data and contributed to the draft of the manuscript. JVC and VV contributed to the data analysis. All authors have approved the final version of the manuscript. All authors agree to be both personally accountable for their own contributions.

## Acknowledgments

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## Data Availability Statement

The data inputs for the analysis are contained within the manuscript; the modeling approach has been detailed in a prior manuscript.

## References

1. American Cancer Society (2021) Key Statistics for Colorectal Cancer.
2. Davidson KW, Barry MJ, Mangione CM, Cabana M, Caughey AB, et al. (2021) Screening for Colorectal Cancer: US Preventive Services Task Force Recommendation Statement. *JAMA* 325: 1965-1977.
3. Edwards BK, Ward E, Kohler BA, Ehemann C, Zaubler AG, et al. (2010) Annual report to the nation on the status of cancer, 1975-2006, featuring colorectal cancer trends and impact of interventions (risk factors, screening, and treatment) to reduce future rates. *Cancer* 116: 544-573.
4. Surveillance Epidemiology and End Results (2020) Cancer Stat Facts: Colorectal Cancer.
5. National Colorectal Cancer Roundtable (2022) 80% in every community strategic plan.
6. Sharma KP, Grosse SD, Maciosek MV, Joseph D, Roy K, et al. (2020) Preventing Breast, Cervical, and Colorectal Cancer Deaths: Assessing the Impact of Increased Screening. *Prev Chronic Dis* 17: E123.
7. Davis MM, Renfro S, Pham R, Lich KH, Shannon J, et al. (2017) Geographic and population-level disparities in colorectal cancer testing: A multilevel analysis of Medicaid and commercial claims data. *Prev Med* 101: 44-52.
8. Rex DK, Boland CR, Dominitz JA, Giardiello FM, Johnson DA, et al. (2017) Colorectal Cancer Screening: Recommendations for Physicians and Patients from the U.S. Multi-Society Task Force on Colorectal Cancer. *Am J Gastroenterol* 112: 1016-1030.
9. Weiser E, Parks PD, Swartz RK, Thomme JV, Lavin PT, et al. (2020) Cross-sectional adherence with the multi-target stool DNA test for colorectal cancer screening: Real-world data from a large cohort of older adults. *J Med Screen* 28: 18-24.
10. Sunny A, Rustveld L (2018) The Role of Patient Navigation on Colorectal Cancer Screening Completion and Education: a Review of the Literature. *J Cancer Educ* 33: 251-259.
11. Issaka RB, Akinsoto NO, Strait E, Chaudhari V, Flum DR, et al. (2020) Effectiveness of a mailed fecal immunochemical test outreach: a Medicare Advantage pilot study. *Therap Adv Gastroenterol* 13: 1756284820945388.
12. de Moor JS, Cohen RA, Shapiro JA, Nadel MR, Sabatino SA, et al. (2018) Colorectal cancer screening in the United States: Trends from 2008 to 2015 and variation by health insurance coverage. *Prev Med* 112: 199-206.
13. Freed M, Damico A, Neuman T (2021) A Dozen Facts About Medicare Advantage in 2020.
14. Piscitello A, Saoud L, Fendrick AM, Borah BJ, Lich KH, et al. (2020) Estimating the impact of differential adherence on the comparative effectiveness of stool-based colorectal cancer screening using the CRC-AIM microsimulation model. *PLoS One* 15: e0244431.
15. Piscitello A, Saoud L, Matney M, Borah BJ, Fendrick AM, et al. (2020) Description and validation of the novel Colorectal Cancer and Adenoma Incidence & Mortality (CRC-AIM) Microsimulation model.
16. Gold MR SJ, Russell LB, Weinstein MC (1996) Cost effectiveness in health and medicine. New York, NY: Oxford University Press.
17. Consumer Price Index (2021) Medical Care Services.
18. Somsouk M, Rachocki C, Mannalithara A, Garcia D, Laleau V, et al. (2020) Effectiveness and Cost of Organized Outreach for Colorectal Cancer Screening: A Randomized, Controlled Trial. *J Natl Cancer Inst* 112: 305-313.
19. Szende A, Janssen B, Cabases J (2014) Self-Reported Population Health: An International Perspective based on EQ-5D. Dordrecht (NL): Springer.
20. Goede SL, Rabeneck L, van Ballegooijen M, Zaubler AG, Paszat LF, et al. (2017) Harms, benefits and costs of fecal immunochemical testing versus guaiac fecal occult blood testing for colorectal cancer screening. *PLoS One* 12: e0172864.
21. DuGoff E, Tabak R, Diduch T, Garth V (2021) Quality, Health, and Spending in Medicare Advantage and Traditional Medicare. *Am J Manag Care* 27: 395-400.
22. Hung A, Stuart B, Harris I (2016) The effect of Medicare Advantage enrollment on mammographic screening. *Am J Manag Care* 22: e53-e59.
23. Karlitz JJ, Fendrick AM, Bhatt J, Coronado GD, Jeyakumar S, et al. (2021) Cost-Effectiveness of Outreach Strategies for Stool-Based Colorectal Cancer Screening in a Medicaid Population. *Popul Health Manag* 25: 343-351.
24. Fisher DA, Karlitz JJ, Jeyakumar S, Smith N, Limburg P, et al. (2021) Real-world cost-effectiveness of stool-based colorectal cancer screening in a Medicare population. *J Med Econ* 24: 654-664.
25. Zhu X, Parks PD, Weiser E, Jacobson DJ, Limburg PJ, et al. (2021) Barriers to utilization of three colorectal cancer screening options – Data from a national survey. *Prev Med Rep* 24: 101508.
26. Dougherty MK, Brenner AT, Crockett SD, Gupta S, Wheeler SB, et al. (2018) Evaluation of Interventions Intended to Increase Colorectal Cancer Screening Rates in the United States: A Systematic Review and Meta-analysis. *JAMA Intern Med* 178: 1645-1658.
27. Levin TR, Corley DA, Jensen CD, Schottinger JE, Quinn VP, et al. (2018) Effects of Organized Colorectal Cancer Screening on Cancer Incidence and Mortality in a Large Community-Based Population. *Gastroenterology* 155: 1383-1391.e5.
28. Fisher DA, Princic N, Miller-Wilson LA, Wilson K, DeYoung K, et al. (2022) Adherence to fecal immunochemical test screening among adults at average risk for colorectal cancer. *Int J Colorectal Dis* 37: 719-721.
29. Piscitello A, Saoud L, Fendrick AM, Borah BJ, Lich KH, et al. (2020) Estimating the impact of differential adherence on the comparative effectiveness of stool-based colorectal cancer screening using the CRC-AIM microsimulation model. *PLoS One* 15: e0244431.