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COST-EFFECTIVENESS ANALYSIS OF A NOVEL RNA-FIT TEST AS A STRATEGY FOR CRC SCREENING IN AN AVERAGE RISK US POPULATION

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INTRODUCTION

- Colorectal cancer (CRC) is the 2nd leading cause of cancer-related deaths in the US, resulting in over 50,000 deaths annually. Early detection of CRC can lead to improvement in survival rates.
- US Clinical Guidelines recommend CRC screening for adults from Age 45.
- Colonoscopy, the gold-standard screening test, has a low compliance rate due to invasiveness, required bowel preparation, and procedure-associated time requirements.
- Non-invasive alternatives, including fecal immunochemical test (FIT) and multi-target stool DNA testing (mt-sDNA), are less reliable due to lower accuracy, especially regarding the detection of advanced adenomas.
- A novel RNA-FIT test was developed to accurately identify colorectal cancer and advanced adenomas by capturing the downstream effects of cancer-causing mutations.
- Early clinical trial results demonstrated a higher accuracy relative to existing non-invasive alternatives, particularly for detecting advanced adenomas (AA).
- In January 2020, this multi-target RNA-FIT biomarker stool test earned FDA breakthrough device designation for its high AA detection rate.

AIM

Assessment of differences between the RNA-FIT test, the mt-sDNA test, FIT, and colonoscopy with regards to total costs and health outcomes for patients undergoing colorectal cancer (CRC) screening.

METHODS

The Model:

- Compares triennial RNA-FIT screening, triennial mt-sDNA test screening, annual FIT, and ten-yearly colonoscopy in an average risk US population of 1,000 patients 45-75 years.
- Simulates CRC screening for a population of 1000 patients over a 30-year time horizon.
- Combines data on sensitivity, specificity, and compliance for each screening modality with the incidence and prevalence of colorectal cancer, advanced adenoma (AA), other precancerous adenomas (OPA), and benign polyps to assess the detection rates for each screening method (Table 1).
- Uses data on distribution across disease stages and five-year survival rates are used to determine long-term outcomes for patients with CRC.
- Accounts for cost of screening, complications associated with colonoscopy, surveillance programs, and the cost of CRC treatment (Table 2).
- Applies age and sex-specific general population mortality data to all patients at the end of each annual cycle.

The Assumptions:

- Compliance rates were used to categorize patients as compliant/non-compliant at the beginning of the analysis and remained in this status over a time horizon of the model.
- Patients were unable to develop CRC while in the surveillance health states.
- Patients who developed CRC were removed from the analysis in each annual cycle.

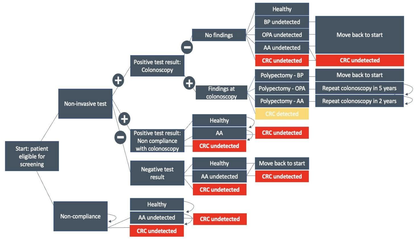

Figure 1. Model structure for non-invasive testing applies to a cohort of patients eligible for RNA-FIT test, the mt-sDNA test, and FIT.

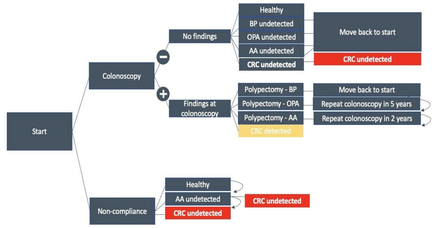

Figure 2. Model structure for Colonoscopy. Applies to cohort of patients that does not engage in non-invasive screening; only colonoscopy is considered.

	RNA-FIT		mt-sDNA		FIT	
Aspect	**Value**	**Source**	**Value**	**Source**	**Value**	**Source**
Compliance	88.3%	Assumption	88.3%	Prince 2017	34.2%	Quintero 2016
Screening interval	3	Geneoscopy	3	Prince 2017	1	Wolf 2018
Sensitivity CRC	95.0%	Geneoscopy	92.3%	FDA PMA P130017	73.8%	FDA PMA P130017
Sensitivity AA	60.0%	Geneoscopy	42.4%	FDA PMA P130017	23.8%	FDA PMA P130017
Sensitivity OPA	26.6%	Geneoscopy	17.2%	FDA PMA P130017	9.0%	FDA PMA P130017
Specificity BP	78.4%	Geneoscopy	84.7%	FDA PMA P130017	94.0%	FDA PMA P130017
Specificity Healthy	84.2%	Geneoscopy	89.8%	FDA PMA P130017	73.8%	FDA PMA P130017

Table 1. Screening inputs: Non-invasive tests. The table shows compliance rates, screening interval, and sensitivity/specificity inputs for each screening method are outlined in the table above. *AA: Advanced Adenoma, BP: Benign Polyp, CRC: Colorectal cancer, OPA: Other pre-cancerous adenoma (<1cm)*

Input	As initial screening method	Following positive non-invasive test	Source
Compliance with colonoscopy for those on a colonoscopy only screening program	58%	96.1%	Prince 2017
Screening interval for those on a colonoscopy only screening program	10 years	N/A	American Cancer Society, Wolf 2018
Detection rate - CRC	96.5%		Than 2015
Detection rate – AA	94.6%	95.5%	Johnson, 2017
Detection rate - OPA	83.0%	87.2%	Johnson, 2017
Detection rate - BP	83.2%	87.4%	Johnson, 2017
% Perforation	0.07%		Zauber 2010
% Serosal burn	0.03%		Zauber 2010
% Bleed with transfusion	0.04%		Zauber 2010
% Bleed without transfusion	0.11%		Zauber 2010

Table 2. Screening inputs: Colonoscopy:
The table shows the compliance rates and detection rates for colonoscopy as an initial screening method and following a positive non-invasive test result. The detection rates for colonoscopy are assumed to be higher following a positive result from a non-invasive test based on findings from a published study (Johnson, 2017). The table also shows the frequency of complications associated with colonoscopy.

RESULTS

- Use of the RNA-FIT results in a 17.6%, 59.5%, and 43.2% reduction in CRC cases versus mt-sDNA, FIT, and colonoscopy, respectively.
- RNA-FIT screening strategy results in an 18.1%, 60.6%, and 45.3% reduction in CRC-related deaths versus mt-sDNA, FIT, and colonoscopy, respectively.
- Compared to a colonoscopy-only screening program, RNA-FIT is associated with fewer colonoscopies, and colonoscopies that detected AA or CRC increased from 14% to 35%.
- Due to the higher number of pre-cancerous adenomas detected, analysis shows RNA-FIT test increases the number of screening colonoscopies following a positive test result by 362 and 919 versus mt-sDNA and FIT, respectively.
- The analysis demonstrated that RNA-FIT is comparable to mt-sDNA at an additional $207 per patient over a 30-year time horizon due to higher colonoscopy and surveillance costs. This was offset by lower costs associated with CRC diagnosis.
- RNA-FIT screening program was more costly than a screening program with FIT or colonoscopy alone per patient over a 30-year time horizon due to higher costs associated with non-invasive testing, screening colonoscopies, and surveillance colonoscopies. This was offset by lower costs associated with CRC diagnosis.

RNA-FIT vs. no screening

Over a 30-year time horizon, per 1000 individuals:
- 31 CRC cases were prevented
- 10 CRC-related deaths were prevented

CRC Cases Prevented

RNA-FIT test showed an incremental reduction in annual CRC cases:
- 17.6% vs. mt-sDNA
- 59.5% vs. FIT
- 43.2% vs. colonoscopy

Reduction in CRC-related deaths

RNA-FIT test showed incremental reduction in CRC-related deaths of:
- 18.1% vs. mt-sDNA
- 60.6% vs. FIT
- 45.3% vs. colonoscopy alone

Cost impact per 1000 individuals

RNA-FIT test demonstrated incremental cost of:
- $207 vs. mt-sDNA per patient ($7 increase per patient per year)
- $2,767 vs. FIT per patient ($92 increase per patient per year)
- $1,939 vs. colonoscopy ($65 increase per patient per year)

Cost per outcome avoided

	Cost/ CRC prevented	Cost/ Death prevented
RNA-FIT	$157,292	$529,391
mt-sDNA	$164,258	$551,706
FIT	$188,092	$617,098
Colonoscopy	$143,608	$489,365

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CONCLUSION AND FUTURE WORK

This early analysis shows that the RNA-FIT test could serve as a valuable and cost-effective colorectal cancer screening strategy option in the average-risk population. A future Markov model, which adds natural disease history, updated inputs, and customization is currently under development to build upon the work presented here.