Critical Adherence to Blood-Based Versus Stool-Based Screening for Colorectal Cancer: A Scenario Analysis

Reinier G.S. Meester[1,2], Andy J. Piscitello[1], Karolina Kutnik[1], Lilian C. Lee[1], Lance Baldo[1], Peter Liang[3]

[1]Freenome Holdings Inc.; [2]Stanford University School of Medicine; [3]New York University Grossman School of Medicine

INTRODUCTION

Blood tests (BTs) are among the latest innovations in non-invasive colorectal cancer (CRC) screening. Large, representative, prospective studies with colonoscopy as the reference standard are intended to provide diagnostic performance estimates of the tests. Data suggest that in comparison to stool tests, certain BTs have greater sensitivity for CRC but lower sensitivity for advanced adenomas (AA). Additionally, BTs may be more acceptable to patients leading to higher adherence over time.

We investigate the impact of the differential performance of blood-based versus stool-based screening on long-term outcomes, and define critical adherence thresholds for similar benefit.

METHODS

- A Cancer Intervention and Surveillance Modeling Network (CISNET) model was replicated
- The model compared screening from 45-75y, using
  - Fecal immunochemical testing (FIT) every year
  - Stool-DNA/FIT (FIT-DNA) every 3 years
  - Low-sensitivity BT (lsBT) every 3 years, satisfying minimum U.S. coverage criteria
  - High-sensitivity BT (hsBT) every 3 years, reflecting the upper range of representative data

Test	Specificity	Sensitivity AA	Sensitivity CRC
FIT	96%	24%	74%
FIT-DNA	90%	42%	92%
lsBT	90%	10%	74%
hsBT	90%	20%	90%

- Starting with 100% adherence for all strategies, adherence to stool tests was decreased until predicted life-years gained (LYG) were equivalent to BT, which defines the relative **critical adherence** level.
- Regardless of BT adherence, if stool test adherence is lower than this critical value, BT will result in more LYG

RESULTS

- Among 1000 U.S. adults, there were an estimated 70.7 lifetime CRC cases and 27.1 CRC deaths
- With 100% assumed adherence, screening reduced CRC incidence by 43–75% and CRC mortality by 50–80% **(Table 1)**

Table 1. Results per 1000 adults in order of efficacy

Outcomes	No screen	lsBT	hsBT	FIT-DNA	FIT
Adherence	-	100%	100%	100%	100%
Screening tests	-	7620	7530	7262	18974
Colonoscopies	71	1531	1655	1933	2143
CRC cases	70.7	40.4	32.9	22.8	17.4
Cases averted	-	30.3	37.8	47.9	53.3
CRC deaths	27.1	13.5	10.7	7.5	5.4
Deaths averted	-	13.6	16.4	19.6	21.7
Life-years gained	-	158.2	191.7	227.4	252.5

- With real-world adherence for FIT and FIT-DNA, previously suggested at 42.6%[1] *vs.* 65.6%[2] (Exact Sciences[3]), hsBT would yield equivalent LYG to FIT-DNA at 77.8% adherence **(Table 2)**

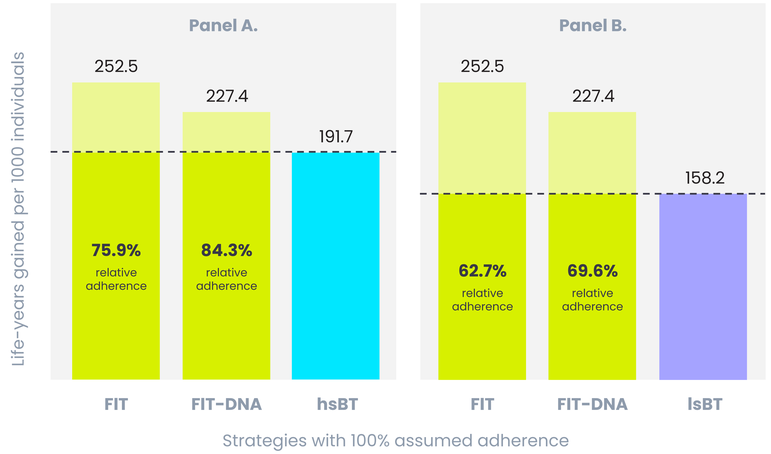
Table 2. Results per 1000 adults with realistic stool test adherence

Outcomes	No screen	lsBT	hsBT	FIT-DNA	FIT
Adherence	-	94.3%	77.8%	65.6%[2,3]	42.6%[1,3]
Screening tests	-	7185	5860	4016	6137
Colonoscopies	71	1444	1288	1069	693
CRC cases	70.7	42.1	41.3	52.3	59.9
Cases averted	-	28.6	29.4	18.4	10.8
CRC deaths	27.1	14.3	14.3	14.2	17.9
Deaths averted	-	12.8	12.8	12.9	9.2
Life-years gained	-	149.2	149.2	149.2	107.6

[1]Akram et al. (2017). Replacing Guaiac Fecal Occult Blood Test with Fecal Immunochemical Test in healthcare setting. Clin Gastroenterol Hepatol, 15(8), 1265–1270.e1.
[2]Miller-Wilson et al. (2021). Multi-target stool DNA test adherence in colorectal cancer screening. Int J Colorectal Dis, 36(11), 2471–2480.
[3]Fendrick et al. (2023). ASCO, Chicago IL. https://ascopubs.org/doi/abs/10.1200/JCO.2023.41.16_suppl.10580.

- With stool testing adherence below critical levels, BT would yield greater LYG **(Figure)**

Figure. Critical adherence levels for stool testing *vs.* hsBT (Panel A) and lsBT (Panel B)



- Inverted critical adherence levels for hsBT were
  - 1/84.3% = 118.6% (+18.6%) for hsBT *vs.* FIT-DNA
  - 1/75.9% = 131.7% (+31.7%) for hsBT *vs.* FIT

CONCLUSIONS

As a novel noninvasive CRC screening modality, blood tests have potential to improve CRC screening outcomes. Achieving life-year gains equal to or exceeding those of stool tests is feasible when patients prefer blood tests over those existing tests. Future research is needed to more firmly establish blood test performance and adherence over time for blood-based versus stool-based screening.