

Multi-target stool DNA based Colorectal Cancer Screening: Modeling the Impact of Inter-test Interval on Clinical Effectiveness

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INTRODUCTION

A unique, multi-target stool DNA (sDNA) test was recently approved by the U.S. FDA¹ for colorectal cancer (CRC) screening for men and women, 50 years of age or older, at average risk for CRC. Guidelines^{2,3} currently recommend a 3-year interval for sDNA testing, but longitudinal data to support the interval are not available. The aim of our study was to use clinical effectiveness modeling to assess the projected decrease in CRC incidence and related mortality with sDNA screening when used every 1, 3, or 5 years, to help inform the inter-test interval.

METHODS

We used the Archimedes Model (Archimedes Inc., San Francisco CA),⁴ a large-scale simulation model of human physiology, diseases, and healthcare delivery processes, to conduct a virtual five-arm clinical study of 200,000 virtual patients. We compared Cologuard at 1, 3 and 5 year intervals to colonoscopy at 10-year intervals and to no screening with 100% screening and follow-up test adherence. Screening began at age 50 and screening benefits accrued until death or 30 years elapsed from a patient's study entry. Cologuard performance was from Imperiale et al⁵ with sensitivity of 92% for colorectal cancer, 69% for high-grade dysplasia, 42% of advanced adenoma overall and 87% specificity. Colonoscopy sensitivity was 95% for CRC and 90% for advanced adenoma.⁶ Study endpoints were decreased CRC incidence and related mortality. Follow up diagnostic colonoscopy for a positive sDNA test cost \$1500. Medicare payment for the Cologuard test for average risk screening of beneficiaries age 50-85 years of age (HCPCS G0464) is \$493, once every three years with no copay or deductible for the beneficiary.⁷ The list price of Cologuard is \$649. An average societal "cost" of \$600/per test was modeled. Cost-effectiveness ratios compared with no screening were calculated for context.

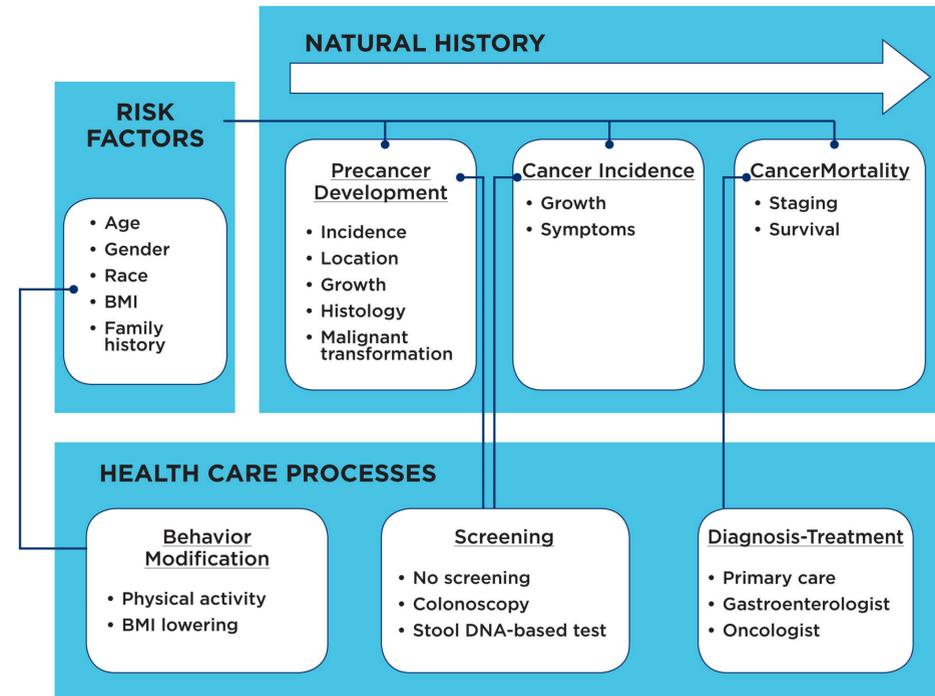


Fig. The Archimedes Model. The model evaluates virtual people who can experience one or more disease states, get screened and/or develop symptoms, seek care, and receive diagnosis and treatment. BMI = body mass index.

CRC Screening Strategy	Screening age 50–85 years		
	% Decrease in CRC incidence	% Decrease in CRC mortality	QALYs gained relative to no screening
No screening	0	0	0
Colonoscopy every 10 years	65%	73%	0.1330
sDNA annually	63%	72%	0.1290
sDNA every 3 years	57%	67%	0.1160
sDNA every 5 years	52%	62%	0.1050

CRC = colorectal cancer
 QALY = quality-adjusted life year
 sDNA = stool DNA

Table 1. Effect of Screening Strategies on CRC Incidence and Related Mortality Compared with no Screening.

Table 2. CERs of Multitarget sDNA Screening at Intervals of 1, 3, and 5 Years compared with no screening and in relation to other cancer screening tests with limited or no other alternative screening strategies.

CRC Screening Strategy	CER (\$/QALY)
No screening	\$0
sDNA annually	\$20,178
sDNA every 3 years	\$11,313
sDNA every 5 years	\$7,388
Cervical (Pap Smear) and Breast Cancer (Mammography) Screening Strategy	CER (\$/QALY)
Pap smear, annual [8]	\$23,900
Pap smear, triennial [8]	\$15,500
Mammography, biennial, age 50–75 years [9]	\$30,000
Mammography, biennial, age 40–80 years [9]	\$32,307
Mammography, annual, ge 40–80 years [9]	\$39,210

RESULTS

Compared to every 10-year colonoscopy, annual screening with sDNA produced similar theoretical reductions in CRC incidence (65% vs. 63%, respectively) and CRC-related mortality (73% vs. 72% respectively). Screening with Cologuard at 3-year intervals reduced CRC incidence by 57% and CRC mortality 67% and at 5-year intervals reduced CRC incidence by 52% and CRC mortality 62%. At an average cost of \$600/Cologuard test and a colonoscopy cost of \$1500 for each diagnostic colonoscopy performed for a positive Cologuard test, annual, 3-year and 5-year sDNA screening cost \$20,178, \$11,313, and \$7,388 per quality adjusted life year respectively compared with no screening.

CONCLUSIONS

This Archimedes modeling study suggests that screening every 3 years with the multi-target sDNA-based test provides reasonable performance at acceptable cost, with potentially lower patient, clinician and administrative burdens compared to annual screening and with improved clinical performance compared to 5-year screening. These results support the expert opinion based 3-year screening interval for sDNA-based tests included in the colorectal cancer screening guidelines of the American College of Gastroenterology and the American Cancer Society.

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