Title: New Screening Tests, Same Challenge: An Early Look at Colonoscopic Follow-up After Abnormal Blood-Based Colorectal Cancer Screening Results in a Real World Setting

Authors: Timothy A. Zaki, MD[1]; Nicole J. Zhang, MPH[2]; Victoria M. Raymond, MS[2]; Nick Ioannou, MD, PhD, MHA[2]; Shaun P. Forbes, PhD[2]; Amar K. Das, MD, PhD[2]; Folasade P. May, MD, PhD, MPhil[1]

Affiliations:
1.   Vatche and Tamar Manoukian Division of Digestive Diseases, David Geffen School of Medicine at the University of California Los Angeles, Los Angeles, CA
2.   Guardant Health, Inc, Redwood City, CA

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Introduction: Blood-based screening tests for colorectal cancer (CRC) are becoming increasingly prevalent and have the potential to improve adherence with screening guidelines and overall CRC outcomes. As for all non-colonoscopic screening tests, abnormal blood-based test results require follow-up colonoscopy (FU-CY) to complete the screening process. We aimed to perform one of the first analyses of FU-CY rates after abnormal blood-based screening test results and determine predictors of follow-up.

Methods: We conducted a retrospective cohort study of average-risk individuals in the U.S., aged 45 and above, with health plan enrollment data available, who received a Shield™ LDT blood-based CRC screening test between 5/2022 and 9/2023. Shield, developed by Guardant Health, has 83% sensitivity and 90% specificity for detecting CRC in average-risk individuals. Anonymized results from consecutively tested individuals were securely linked to medical and pharmacy claims in a de-identified encounters database compliant with HIPAA. We determined a sub-population of individuals with at least 6 months of follow-up after a result and summarized sociodemographic characteristics and FU-CY rates. We then used multivariable logistic regression to determine predictors of FU-CY within 6 months of an abnormal result.

Results: A total of 5,888 individuals received a Shield test during the study period and met the inclusion criteria, of which 470 (8.0%) tested abnormal. Of those with an abnormal result, 339 (72.1%) had at least 6 months of follow-up, comprising the cohort of interest. The population had a mean age of 62.8 years (s.d. 9.9) and was 26% non-Hispanic White, 5% non-Hispanic Black, 5% non-Hispanic Asian or Pacific Islander, and 16% Hispanic (Figure 1). Of the 339 individuals in the final cohort, 149 (44%) received a FU-CY within 6 months and 156 (46%) received a FU-CY at any time following an abnormal result. Mean time to FU-CY was 68.9 days (s.d. 50.7). In adjusted analysis, individuals with Medicaid (aOR=0.31; 95% CI 0.14-0.70) or Medicare (aOR=0.44; 95% CI 0.20-0.95) were less likely to receive a FU-CY compared to those with private insurance. Race/ethnicity and U.S. census region did not predict FU-CY (Figure 2).

Discussion: Only 44% of individuals with an abnormal Shield blood-based screening test result completed colonoscopy within 6 months. This rate is similar to follow-up after abnormal stool-based screening in a recent publication using national claims data (51.4%). Notably, insurance type, but not race or ethnicity, was associated with lack of follow-up. Blood-based CRC screening technologies are inevitable, but we must prioritize strategies to ensure that timely follow-up occurs to prevent setbacks in progress made towards CRC prevention and control. Future analyses will assess follow-up rates in larger populations and for longer follow-up periods.

Figure 1. Sociodemographic characteristics of the study sample, stratified by follow-up colonoscopy status; n=339

	Total (n=339)		No follow-up colonoscopy (n=183)		Follow-up colonoscopy (n=156)	
Mean age, y (s.d.)	62.8 (9.9)		64.2 (9.7)		61.1 (9.8)	
Age	**n**	**%**	**n**	**%**	**n**	**%**
45 - 49	22	6.5	5	2.7	17	10.9
50 - 54	65	19.2	35	19.1	30	19.2
55 - 59	43	12.7	18	9.8	25	16.0
60 - 64	82	24.2	44	24.0	38	24.4
65 - 69	44	13.0	28	15.3	16	10.3
70 - 74	31	9.1	24	13.1	7	4.5
75 - 79	29	8.6	15	8.2	14	9.0
80 - 84	18	5.3	10	5.5	8	5.1
85+	5	1.0	4	2.2	1	0.6
Sex						
Female	199	58.7	106	57.9	93	59.6
Male	140	41.3	77	42.1	63	40.4
Race/ethnicity						
Hispanic or Latino	54	15.9	31	16.9	23	14.7
Asian or Pacific Islander	*2*	*0.6*	*1*	*0.5*	*1*	*0.6*
White	*12*	*3.5*	*6*	*3.3*	*6*	*3.8*
Other/Unknown	*40*	*11.8*	*24*	*13.1*	*16*	*10.3*
Not Hispanic or Latino	157	46.3	82	44.8	75	48.1
Asian or Pacific Islander	*16*	*4.7*	*8*	*4.4*	*8*	*5.1*
Black or African American	*17*	*5.0*	*12*	*6.6*	*5*	*3.2*
White	*87*	*25.7*	*43*	*23.5*	*44*	*28.2*
Other/Unknown	*37*	*10.9*	*19*	*10.4*	*18*	*11.5*
Unknown Hispanic or Latino	128	37.8	70	38.3	58	37.2
Asian or Pacific Islander	*6*	*1.8*	*2*	*1.1*	*4*	*2.6*
Black or African American	*10*	*2.9*	*9*	*4.9*	*1*	*0.6*
White	*45*	*13.3*	*29*	*15.8*	*16*	*10.3*
Other/Unknown	*67*	*19.8*	*30*	*16.4*	*37*	*23.7*
U.S. Census Region						
Midwest	26	7.7	13	7.1	13	8.3
Northeast	41	12.1	28	15.3	13	8.3
South	146	43.1	73	39.9	73	46.8
West	117	34.5	65	35.5	52	33.3
Unknown	9	2.7	4	2.2	5	3.2

Insurance						
Medicaid	54	15.9	38	20.8	16	10.3
Medicare	82	24.2	55	30.1	27	17.3
Private	191	56.3	82	44.8	109	69.9
Dual eligible	8	2.4	5	2.7	3	1.9
Other/Unknown	4	1.2	3	1.6	1	0.6

Figure 2. Predictors of timely follow-up colonoscopy after an abnormal Shield test result using multivariable logistic regression

	Adjusted Odds Ratio	95% Confidence Interval
Age	0.99	0.96 – 1.03
Race/ethnicity		
Non-Hispanic White	Reference	Reference
Non-Hispanic Black	0.39	0.14 – 1.09
Non-Hispanic Asian or Pacific Islander	1.30	0.46 – 3.69
Non-Hispanic Other/Unknown	0.82	0.28 – 2.42
Hispanic	0.95	0.45 – 2.01
Insurance		
Medicaid	**0.31**	**0.14 – 0.70**
Medicare	**0.44**	**0.20 – 0.95**
Private	Reference	Reference
Dual eligible	0.71	0.15 – 3.36
Other/Unknown	0.68	0.04 – 12.51
U.S. Census Region		
Midwest	1.16	0.43 – 3.18
Northeast	0.49	0.19 – 1.26
South	1.10	0.58 – 2.07
West	Reference	Reference

NOTE: bolded values indicate significance at the p<0.05 level; data from 246 out of 339 individuals were used in the above analysis due to missing responses from 93 individuals