

## Patient perceptions of stool DNA testing for pan-digestive cancer screening: A survey questionnaire

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### Abstract

**AIM:** To explore patient interest in a potential multi-organ stool-DNA test (MUST) for pan-digestive cancer screening.

**METHODS:** A questionnaire was designed and mailed to 1200 randomly-selected patients from the Mayo Clinic registry. The 29-item survey questionnaire included items related to demographics, knowledge of digestive cancers, personal and family history of cancer, personal concern of cancer, colorectal cancer (CRC) screening behavior, interest in MUST, importance of test features in a cancer screening tool, and compari-

son of MUST with available CRC screening tests. All responses were summarized descriptively.  $\chi^2$  and Rank Sum Test were used for categorical and continuous variables, respectively.

**RESULTS:** Completed surveys were returned by 434 (29% aged 50-59, 37% 60-69, 34% 70-79, 52% women). Most participants (98%) responded they would use MUST. In order of importance, respondents rated multi-cancer detection, absence of bowel preparation, safety and noninvasiveness as most attractive characteristics. For CRC screening, MUST was preferred over colorectal-only stool-DNA testing (53%), occult blood testing (75%), colonoscopy (84%), sigmoidoscopy (91%), and barium enema (95%),  $P < 0.0001$  for each. Among those not previously screened, most (96%) indicated they would use MUST if available. Respondents were confident in their ability to follow instructions to perform MUST (98%). Only 9% of respondents indicated that fear of finding cancer was a concern with MUST, and only 3% indicated unpleasantness of stool sampling as a potential barrier.

**CONCLUSION:** Patients are receptive to the concept of MUST, preferred MUST over conventional CRC screening modalities and valued its potential feature of multi-cancer detection.

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**Key words:** Stool-DNA testing; Colorectal cancer screening; Gastrointestinal cancer screening; Patient perceptions

**Core tip:** The value of stool DNA testing could be expanded beyond colorectal cancer screening by simultaneously targeting gastrointestinal cancers above the colon. Early data suggest technical feasibility for such pan-cancer detection. However, while multi-organ stool DNA testing (MUST) would seem intuitively to have broad appeal; patient perceptions have not been evalu-

ated. In this exploratory study, we demonstrate that patients were interested in using MUST if it was available to them. The potential unique ability to detect multiple cancers was its most distinguishing and attractive feature. General population surveys are warranted to corroborate these early findings.

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## INTRODUCTION

In aggregate, malignancies in the digestive track account for roughly 1/4 of all cancer deaths in the United States<sup>[1]</sup> and worldwide<sup>[2]</sup>. Although early stage detection and resection lead to a favorable prognosis with tumors at each gastrointestinal site, only colorectal cancer (CRC) is currently screened at the population level in most countries. It is remarkable that the common cancers above the colon remain unscreened despite the reality that their collective mortality substantially exceeds that of CRC alone<sup>[1]</sup>.

Early studies suggest that supra-colonic gastrointestinal cancers can be detected noninvasively by stool DNA testing. In 2009<sup>[3]</sup>, our research group evaluated the feasibility of stool-DNA testing for detection of common neoplasms throughout the gastrointestinal GI tract. We were able to detect specific mutations (TP53, KRAS, APC, CDH1, CTNNB1, BRAF, SMAD4, and P16) present in primary tumor tissue from matched stools of patients with diverse supra-colonic gastrointestinal malignancies. Target mutations were detected in stools from 71% (36/51) of patients with cancer overall [40% (2/5) with oropharyngeal, 65% (11/17) with esophageal, 100% (4/4) with gastric, 55% (6/11) with pancreatic, 75% (3/4) with biliary or gallbladder, and 100% (4/4) with colorectal], while none were detected in the matched-control groups. In the same year, a group from Japan<sup>[4]</sup> used a novel fecal DNA methylation assay to detect increased methylation of gene promoters in patients with gastric and colorectal tumors (57%-75%) as opposed to only 10% of subjects without neoplasms. More recently, using a similar approach, we evaluated aberrantly methylated genes as non-invasive markers by stool DNA testing for the detection of pancreatic cancer<sup>[5]</sup>. The results from this study demonstrated that at 90% specificity, methylated BMP3 detected 51% of pancreatic cancer, while a combined stool assay of methylated BMP3 and mutant KRAS increased pancreatic cancer detection to 67%. Overall, these early findings support the potential and feasibility of a non-invasive multi-organ gastrointestinal stool-DNA test for cancer screening.

Ideally, such multi-organ stool DNA testing (MUST) would have the potential to expand the value of stool

screening beyond that of CRC detection alone and address the existing gap in screening for upper gastrointestinal cancers. While the potential availability of MUST would seem intuitively to have broad patient appeal, there are no data on patient acceptability or perceptions of such an approach.

Endorsed by the American Cancer Society, the US Multi-society Task Force, and the American College of Radiology, stool DNA testing has emerged as an approach to CRC screening<sup>[6]</sup>. Stool DNA testing offers user-friendly features of noninvasiveness, avoidance of unpleasant bowel preparation associated with other approaches<sup>[7-12]</sup>, ease of access *via* off-site sample collection and shipping, single rather than multiple stool sampling per screen, no diet or medication restriction, and possibly reduced screen frequency because of its capacity to detect precursor lesions<sup>[13,14]</sup>. With advanced next generation technology, stool-DNA testing has proven highly accurate for detection of both CRC and advanced precancer<sup>[15,16]</sup>, and an automated test is currently under review by the FDA following evaluation in a general population<sup>[17]</sup>. In prior surveys, patients showed interest in using stool-DNA testing for CRC screening and appeared to prefer it over both fecal occult blood testing (FOBT) and colonoscopy<sup>[9,18-22]</sup>. However, it is not clear if an expanded capacity of stool-DNA testing for multi-cancer detection would enhance or impede participation in a CRC screening application.

Knowledge of patient perceptions and preferences regarding screening tools is important to understand compliance to screening<sup>[22-26]</sup>. For example, patient concern about pain, potential injury and discomfort with cathartic preparations are recognized barriers to routine screening with colonoscopy, flexible sigmoidoscopy, or barium enema<sup>[27,28]</sup>. While FOBT is a low risk and noninvasive screening alternative, the variability in cancer detection rates, inconvenient stool sampling, dietary restrictions, and poor sensitivity for precursor lesions, may limit its acceptance by some<sup>[29-32]</sup>. If MUST is to be further considered for a potential future pan-digestive cancer screening application, an early appraisal of patient attitudes would be instructive.

In this exploratory study, we designed a questionnaire to assess interest in and preferences for using MUST. We examined and compared perceptions and preferences for MUST against available CRC screening options.

## MATERIALS AND METHODS

### Study population and data collection

A total of 1200 patients were randomly selected within age and gender groups from the Mayo Clinic registry. Questionnaires were mailed to 400 candidates (200 men, 200 women) in each of 3 average-risk sub-groups between 50-79 years of age (50-59, 60-69, and 70-79 years).

**Sample size considerations:** In this exploratory study, we targeted a sample large enough to provide a 95%

confidence interval within  $\pm 10$  percentage points; and 100 respondents would yield such confidence. Based on 1200 candidates, we assumed that 1000 would have a current address, 500 would respond to the survey, and 100 respondents would not have undergone routine CRC screening.

### Questionnaire survey

Questionnaire mailing from the Survey Research Center included a cover letter explaining the nature and purpose of the study and inviting the subject to complete the survey and return it in the stamped, pre-addressed envelope provided. A waiver consent form was included with the mailing and required signature for participation. Only one mailing was sent per participant with no follow-ups attempted.

**Survey instrument:** The questionnaire was designed in collaboration with the Mayo Clinic Survey Research Center (Appendix). Question format was modeled after those developed in the Health Information National Trends Survey (HINTS) 2007 on perceived risk, screening behavior, knowledge and concern about cancer.

The 29-item survey questionnaire included items related to demographics, knowledge of airway and digestive cancers, personal and family history of cancer, personal concern of cancer, CRC screening behavior, interest in MUST, importance of test features in a cancer screening tool, and comparison of MUST with available CRC screening tests.

Respondents' general knowledge of cancer was assessed by their ability to associate common risk factors (*i.e.*, age, smoking, obesity, alcohol consumption) with cancer development. Patients who specified a personal and/or family diagnosis of cancer (lung, breast, prostate, colon or rectal, esophageal, stomach, pancreatic, melanoma, and/or other) were considered to have a positive history of cancer. Personal concern of cancer was evaluated by asking how often (*i.e.*, all the time, often, sometimes, rarely or never) patients worried about developing any of the following cancers: lung, breast, colon or rectal, esophagus, stomach, pancreas, prostate.

Patients were asked about their likelihood of using MUST if it was available to them on a 5-point Likert-like scale with the following response options: very likely, likely, unlikely, and not sure. Seven items were also included describing possible reasons patients might choose MUST. Patients were again asked to rate these test features in terms of importance to them on a 5-point Likert-like scale.

Patients were asked to rank order their preferences for CRC screening tests among the following options: MUST, FOBT, colorectal-only stool-DNA testing, colonoscopy, flexible sigmoidoscopy, and barium enema. Patients were asked to rate the importance of test features (*i.e.*, ability to detect pre-cancerous lesions, accuracy, risk of injury, degree of discomfort, need for bowel preparation, cost) when choosing a regular CRC screening test

on a 5-point Likert-like scale.

### Statistical analysis

All responses were included for analysis when possible. If there was any confusion over the intent of an answer, the response was not included. All responses to surveys were summarized descriptively.  $\chi^2$  tests were performed to test for differences in baseline characteristics for all categorical characteristics. The Rank Sum Test was used to test for differences for all continuous characteristics. Since only a small subset of items were available for non-respondents, we also explored differences between early and later respondents in order to better understand the impact of potential non-response bias.  $\chi^2$  tests were used for these comparisons. In addition, the Wilcoxon Sign Rank Test was performed to compare the preference rank for MUST when compared to each of the other 5 colorectal screening tests. A *P* value of  $< 0.05$  was considered statistically significant.

## RESULTS

### Sample characteristics

Thirty-six percent (434 of 1200) of mailed out surveys were completed and returned between November 14<sup>th</sup>, 2008 and January 16<sup>th</sup>, 2009. When respondents were compared to non-respondents, there was no difference in median age (66.0 years *vs* 64.4 years, *P* = 0.64), or in the number of days since the patient was last seen at the Mayo Clinic (82.5 *vs* 89.0, *P* = 0.16). Women accounted for 52% of respondents compared to 49% of non-respondents (*P* = 0.34).

Demographic and baseline characteristics of the sample population are summarized (Table 1). The majority of respondents were white, from Minnesota, and with the equivalent of a college degree or higher. A personal history of cancer was reported by 44%, with 9% originating from the airway or digestive tract; and 67% indicated a history of cancer in a first-degree relative. Most respondents acknowledged a personal concern with cancer (74%).

### Knowledge about digestive and airway cancers

Most subjects correctly identified age over 50 years (85%), smoking (99%), alcohol consumption (74%) and obesity (76%) as factors that can increase a person's risk of developing cancer. Many understood that pain or other symptoms are generally absent at early curative stages of lung (65%), pancreas (60%), colorectal (63%), esophageal (47%) and stomach (50%) cancers.

### Perceptions of and interest in MUST

Responses regarding the likelihood of using MUST are summarized (Table 2). Overall, most (98%) were interested in MUST and would likely use it, irrespective of physician recommendation. Subgroup comparisons were performed to assess whether likelihood of using MUST varied by age, gender, prior CRC screening, or personal

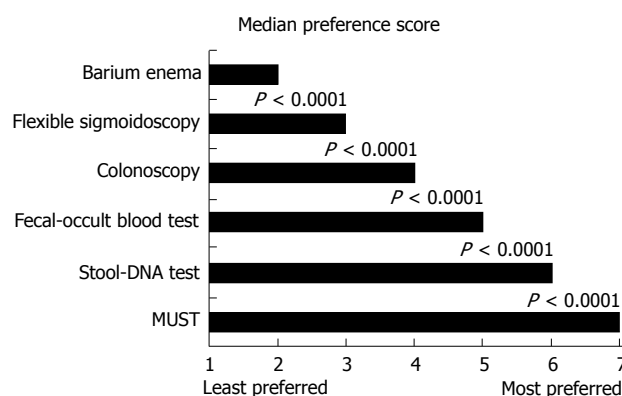
**Table 1** Demographics and baseline characteristics of sample population *n* (%)

Characteristics	Value
Age (yr)	
50-59	122 (28.6)
60-69	159 (37.2)
70-79	146 (34.2)
Sex	
Female	225 (51.8)
Male	209 (48.6)
Race/ethnicity	
White	424 (98.4)
Non-white	7 (1.6)
Education	
Some high school	11 (2.6)
High school graduate or GED	108 (25.2)
Vocational, technical or business school	40 (9.3)
Some college or associate's degree	98 (22.9)
4-yr college graduate or Bachelor's degree	76 (18.8)
Graduate or professional school	95 (22.2)
Region	
Minnesota	251 (57.8)
Other	183 (42.2)
Positive personal history of cancer	
Aero-digestive cancer <sup>1</sup>	38 (8.8)
Other <sup>2</sup>	152 (35.0)
No	244 (56.2)
Positive familial history of cancer	
Yes	278 (66.8)
No	125 (30.0)
Not sure	13 (3.1)
CRC screening history	
Yes	355 (84.9)
No	50 (12.0)
Not sure	13 (3.1)
Personal concern with cancer <sup>3</sup>	
Yes	311 (73.5)
No	112 (26.5)

<sup>1</sup>Includes responses from subjects who specified they had been diagnosed with cancer from any of the following: lung, esophagus, stomach, pancreas, colon or rectum; <sup>2</sup>Includes responses from subjects who specified they had been diagnosed with cancer from any of the following: breast, prostate, skin (melanoma only), or specified as other. <sup>3</sup>Defined as subjects who responded "all the time" or "often" when asked how often they worry about getting one or all of the following cancers: lung, breast, colon or rectal, esophagus, stomach, pancreas, prostate. GED: General equivalent diploma; CRC: Colorectal cancer.

concern with cancer. "Very likely" and "likely" categories were combined and considered a positive response towards likelihood of using MUST. Interest in using MUST was high across all subgroups, and no statistically significant differences were observed.

MUST features rated as very important included its multi-cancer detection (95%), noninvasiveness (85%), avoidance of bowel preparation (81%), ability to perform the test at home (74%), and other features (Table 3). Subjects were provided with a description of the steps required to complete MUST. Most (98%) were confident in their ability to follow the instructions to complete the test. Reasons for not choosing MUST included uncertainty about physician recommendation (21%), not enough information on MUST (12%), and fear of finding cancer (9%). Only 3% responded that the unpleasantness of



**Figure 1** Median preference score for colorectal cancer screening. Scores were assigned from 1 (least preferred) to 7 (most preferred) for currently used screening approaches and for multi-organ stool-DNA test (MUST).  $P < 0.0001$  using Wilcoxon sign rank test.

stool sampling represented a barrier to using MUST.

### Perceptions and preferences regarding colorectal cancer screening

Most respondents (85%) indicated that they had previously undergone CRC screening, including by colonoscopy (79%), FOBT (41%), flexible sigmoidoscopy (38%), barium enema (28%), and/or stool-DNA testing (3%). Among the respondent subset without prior CRC screening, most (> 95%) indicated that they would likely use MUST if it was available. The most commonly cited barriers against CRC screening by those who had no prior CRC screening and those who had been screened, but did not intend to do so again, included the perceived low risk of cancer in the absence of symptoms (57%), lack of physician recommendation (56%), bowel preparation (38%), unpleasant or embarrassing elements of the test (29%), and concern about complications such as bleeding, perforation, or injury (22%).

Respondents were asked to rank different tests for regular CRC screening, irrespective of cost or insurance coverage in their decision-making process, by assigning a number from 1 to 7 (1 representing the least preferred and 7 the most preferred). Median preference score was highest for MUST (7.0) and lowest for barium enema (2.0), as shown in Figure 1. MUST was preferred over colorectal-only stool-DNA testing by 53% of respondents, over occult blood testing by 75%, over colonoscopy by 84%, over sigmoidoscopy by 91%, and over barium enema by 95%,  $P < 0.0001$  for each. Most indicated the ability of a test to detect pre-cancerous lesions (97%), test sensitivity (95%), test specificity (94%), insurance coverage (62%) and risk of injury (56%) as very important test features when choosing the type of screening test (Table 3).

### Assessment of potential response bias

To evaluate the potential for response bias, participants were stratified into early respondents (returned the survey in < 3 mo) and late respondents (returned survey > 3 mo). Early respondents were predominantly women (55% *vs* 44%,  $P = 0.04$ ) and from Minnesota (63% *vs* 46%,  $P$

**Table 2** Likelihood of using multi-organ stool-DNA test

Characteristic (n)	Very likely	Likely	Unlikely	Very unlikely	Not sure	P value <sup>1</sup>
Age (yr)						
50-59 (121)	69.4%	25.6%	3.3%	1.7%	0.0%	0.56
60-69 (157)	82.2%	15.3%	1.3%	0.0%	1.2%	
70-79 (145)	75.2%	20.7%	2.1%	0.0%	2.0%	
Sex						
Female (219)	76.2%	20.1%	1.8%	0.5%	1.4%	0.89
Male (204)	76.0%	20.0%	2.5%	0.5%	1.0%	
Prior CRC screening						
Yes (352)	75.6%	20.5%	2.6%	0.6%	0.9%	0.66
No (49)	75.5%	20.4%	0.0%	0.0%	4.1%	
Do not know (13)	76.9%	23.1%	0.0%	0.0%	0.0%	
Personal concern with cancer						
Yes (311)	79.1%	16.7%	2.6%	0.3%	1.3%	0.48
No (112)	67.9%	29.4%	0.9%	0.9%	0.9%	
Respondents <sup>2</sup>						
Early (303)	76.6%	19.1%	3.0%	0.0%	1.3%	0.38
Late (120)	75.0%	22.5%	0.0%	1.7%	0.8%	

CRC: Colorectal cancer. <sup>1</sup> $\chi^2$  test; <sup>2</sup>Comparing the likelihood of using a multi-organ stool-DNA test between early and late respondents.

**Table 3** Respondents' rating of test features in multi-organ stool-DNA test and routine screening tool

	Very important	Somewhat important	Not at all important	Not sure
Stool-DNA test				
Detects multiple cancers with single test	95.1%	4.2	0.0	0.7
Safe noninvasive test	85.0%	13.3	0.7	1.0
No need for bowel preparation	80.8%	15.7	3.0	0.5
No need for sedation	77.8%	18.7	3.0	0.5
No need to change diet or medications	75.4%	22.0	1.9	0.7
Performed in the privacy of home	73.8%	21.5	4.2	0.5
No need to take time off from work	56.8%	15.2	27.3	0.7
A routine screening tool				
Ability of test to detect pre-cancer or change in body before it becomes cancer	96.5%	3.0	0.2	0.2
Accuracy of the test to say there is a cancer when there really is a cancer	94.7%	4.6	0.0	0.7
Accuracy of the test to say there really is no cancer when there is no cancer	93.3%	5.3	0.5	0.9
Whether test is covered by insurance	62.2%	27.7	8.5	1.6
Risk of injury with test	55.6%	31.4	10.2	2.8
How often the test has to be done	34.9%	43.1	19.2	2.8
The cost of the test	34.0%	44.4	17.8	3.8
Use of laxatives and/or enemas for bowel preparation	27.8%	46.5	22.9	2.8
Discomfort associated with the test	24.9%	48.2	24.2	2.6

= 0.001) when compared to late respondents (Table 4). There was no difference in race/ethnicity or educational background between early and late respondents. Interest in using MUST was high in both early and late respondents, and no statistical significant difference was observed (Table 2).

## DISCUSSION

This study found that most respondents to a survey questionnaire were interested in using MUST if it was available to them. The likelihood of using MUST did not vary significantly on the basis of age, gender, prior history of CRC screening, or personal concern with cancer. The potential to simultaneously screen cancer at multiple organ sites was the most attractive feature of MUST. Our results suggest that the concept of screening for multiple digestive cancers with a stool test is an incentive to its po-

tential use, and stool sampling *per se* was not perceived as a barrier

Of note, MUST was perceived as the preferred test for CRC screening, including a subset of respondents who had not previously undergone routine CRC screening. The concept of a stool test with capacity to detect both supra-colonic cancers and colorectal cancer was highly rated by respondents when asked to choose a CRC screening method. The majority of respondents identified accuracy, low risk of injury, and avoidance of bowel preparation and sedation as very important features when choosing a screening test. In this survey, noninvasive tests (MUST, colorectal-only stool-DNA testing, and FOBT) were preferred over invasive tests (colonoscopy, flexible sigmoidoscopy, and barium enema). However, it was the feature of multi-cancer detection that was most distinguishing in favoring MUST. These results suggest that multi-cancer detection is perceived as a value-add

**Table 4** Demographics of early versus late respondents

Characteristics	Early respondents	Late respondents	P value <sup>1</sup>
Sex			0.040
Female	55.0%	44.0%	
Male	45.0%	56.0%	
Race/ethnicity			0.400
White	98.7%	97.6%	
Non-white	1.3%	2.4%	
Education			0.340
Some high school	2.9%	1.6%	
High school graduate or GED	25.2%	25.4%	
Vocational, technical or business school	10.8%	5.7%	
Some college or associate's degree	23.5%	21.3%	
4-year college graduate or Bachelor's degree	17.7%	18.0%	
Graduate or professional school	19.9%	27.9%	
Region			0.001
Minnesota	62.8%	45.6%	
Other	37.2%	54.4%	

<sup>1</sup> $\chi^2$  test. GED: General equivalent diploma.

and that implementation of MUST has the potential to enhance patient participation in CRC screening.

Barriers to screening must be considered with the application of any new methods. Previous studies have identified lack of physician recommendation, lack of awareness of cancer, absence of symptoms and fear of finding cancer as common barriers to screening<sup>[7,9,18,19,21-28,33-35]</sup>. In our study, absence of provider recommendation was cited by some as a potential reason for not choosing MUST, highlighting the influential role of physicians in patient adherence to cancer screening. Whether personal concern with cancer would negatively impact patients' attitudes towards multi-cancer screening has not been previously assessed. In this study, fear of finding cancer did not appear to be an obstacle to using MUST, and the concept of multi-cancer detection was positively perceived. Furthermore, nearly all respondents indicated that stool sampling and collection per se was not a barrier.

In this study, respondents identified other specific test attributes, such as the ability to detect precancerous lesions and accuracy for cancer detection as key features when choosing a CRC screening tool. Recent studies have demonstrated that next-generation stool DNA testing can detect curable stage CRC and large precancerous lesions with high sensitivity, irrespective of neoplasm site in the colorectum<sup>[15,16]</sup>. In light of these advances in stool DNA technology, recent studies have evaluated the possibility of detecting supra-colonic gastrointestinal cancers in the stool<sup>[3-5]</sup>. Clearly, more clinical studies will be required to further develop and validate stool DNA testing for pan-digestive cancer detection. The results of our survey suggest that this expanded detection capacity of stool-DNA testing appeals to patients and that there are no obvious perceptual barriers to pan-cancer screening.

This exploratory survey study has several limitations

and the findings may not be generalizable. First, as a majority of those contacted did not participate, response bias may have influenced our results. However, the similarity in demographics between respondents and non-respondents as well as the striking similarities in baseline characteristics, perceptions, and preferences between early and late respondents may be evidence against a major response bias. Second, the study population of this exploratory survey questionnaire lacked the demographic diversity reflective of the general population. Third, while this study was adequately powered for its objectives, the small sample size did not allow definitive co-variate analyses by demographic subsets. Fourth, our study population was well-informed. Their educational level and knowledge of cancer characteristics may have contributed to the overall positive response to using MUST. Fifth, this study was designed as an exploratory questionnaire survey and thus, the survey tool was not piloted and reliability analysis was not performed. Last, MUST is a hypothetical rather than an actual product at this point. Further research and development are needed before it can be offered for screening. Our survey can only assess perceptions, attitudes and likelihood of using a hypothetical MUST in comparison to already available CRC screening modalities. As such, respondents' perceptions of MUST may have been affected by its conceptual appeal and the lack of definite information on actual performance on cancer screening. Whether the overall positive response to MUST will translate to utilization once it is available remains to be determined; however, these results encourage further development and testing of MUST.

In conclusion, this study found that our population was interested in using MUST if it was available to them. The potential unique ability to detect multiple cancers was its most distinguishing and attractive feature. Other highly valued test characteristics included its noninvasiveness, absence of bowel preparation and sedation, avoidance of medication or dietary changes, and convenience of performing the test at home. MUST was preferred over conventional screening tools for routine CRC testing. Further studies are needed to determine whether a more diverse ethnic and socioeconomic population would express similar perceptions and preferences for MUST and CRC screening options.

## COMMENTS

### Background

The value of stool DNA testing could be expanded beyond colorectal cancer (CRC) screening by simultaneously targeting gastrointestinal cancers above the colon. Early data suggest technical feasibility for such pan-cancer detection.

### Research frontiers

Knowledge of patient perceptions and preferences regarding screening tools is important to understand compliance to screening. While a multi-organ stool DNA test (MUST) would seem intuitively to have broad appeal; patient perceptions have not been evaluated. In this exploratory study, the authors demonstrate that patients are interested in using MUST if it was available to them.

### Innovations and breakthroughs

Prior studies have shown patients' interest and preference in using stool DNA testing over both fecal occult blood testing and colonoscopy for colorectal can-

cer screening. This is the first study to evaluate patients' perceptions and preference for a MUST if it was available to them. The potential to simultaneously screen cancer at multiple organ sites was highly regarded by patients. MUST was preferred over conventional screening tools for routine CRC testing.

### Applications

This study highlights the potential ability to detect multiple cancers by MUST as its most distinguishing and attractive feature. Patients valued the noninvasive test characteristics of MUST, and stool sampling was not considered a barrier for screening. Further studies are needed to corroborate these initial findings and to determine receptiveness of such a test in the general population.

### Terminology

Stool-DNA testing: biological rationale of targeting DNA alterations (tumor markers, mutations) exfoliated from cancer cells arising in the gastrointestinal tract into stool. A MUST represents a potential noninvasive test that can detect different neoplasms in the GI tract based on multiple target DNA alterations. The concept of a MUST is based on the feasibility of stool-DNA testing for the detection of common supracolonic GI malignancies.

### Peer review

This paper evaluates stool DNA testing for pan-digestive cancer screening. This is a well-designed study of survey questionnaire. This manuscript is interesting and most parts of the paper are clearly detailed.

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