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Comparing Universal Lynch Syndrome Tumor Screening Programs to Evaluate Associations Between Implementation Strategies and Patient Follow-through

Deborah Cragun, MS, PhD[a], **Rita D. DeBate, PhD**[b], **Susan T. Vadaparampil, PhD**[a], **Julie Baldwin, PhD**[b], **Heather Hampel, MS**[c], and **Tuya Pal, MD**[a]

[a]Moffitt Cancer Center, Tampa, FL

[b]University of South Florida, Tampa, FL

[c]Ohio State University, Columbus, OH

Abstract

Purpose—Universal tumor screening (UTS) for all colorectal cancer (CRC) patients can improve the identification of Lynch syndrome, the most common cause of hereditary CRC. This multiple-case study explored how variability in UTS procedures influence patient follow-through (PF) with germline testing after a screen-positive result.

Methods—Data were obtained through web-based surveys and telephone interviews with institutional informants. Institutions were categorized as Low-PF (≤10% underwent germline testing), Medium-PF (11–40%), or High-PF (>40%). To identify implementation procedures (i.e., conditions) unique High-PF institutions, qualitative comparative analysis was performed.

Results—Twenty-one informants from fifteen institutions completed surveys and/or interviews. Conditions present among all five High-PF institutions included: 1) disclosure of screen-positive results to patients by genetic counselors (GCs); and 2) GCs either facilitate physician referrals to genetics or eliminated the need for referrals. Although both of these High-PF conditions were present among two Medium-PF institutions, automatic reflex testing was lacking and difficulty contacting screen-positive patients was a barrier. The three remaining Medium-PF and five Low-PF institutions lacked High-PF conditions.

Conclusion—Methods for streamlining UTS procedures, incorporating a high level of involvement of GCs in results tracking and communication, and reducing barriers to patient contact are reviewed within a broader discussion on maximizing the effectiveness and public health impact of UTS.

Keywords

Qualitative comparative analysis; RE-AIM; hereditary colorectal cancer; effectiveness; Public Health Genomics; Lynch syndrome

Corresponding author: Deborah Cragun, Department of Cancer Epidemiology, Moffitt Cancer Center, MRC-CANCONT, 12902 Magnolia Drive, Tampa, FL 33612, Phone: (813) 745-4668; Fax: (813) 745-6525; deborah.cragun@moffitt.org.

INTRODUCTION

Colorectal cancer (CRC) is the second leading cause of cancer-related death in the United States when men and women are considered together.[1] Lynch syndrome is the most common cause of hereditary CRC, affecting approximately 1 in every 35 CRC patients.[2] Individuals with Lynch syndrome have a 50–70% lifetime risk of CRC,[3–5] a 40–60% chance of endometrial cancer,[3,6] and increased risks for several other malignancies.[6,7] Fortunately, effective cancer risk reduction strategies are available when Lynch syndrome is identified.[8,9]

The importance of Lynch syndrome identification is reflected in the following Healthy People 2020 provisional objective: *"Increase the proportion of persons with newly diagnosed colorectal cancer who receive genetic testing to identify Lynch syndrome."* Systematic efforts to identify patients with LS are needed given the current estimate that less than 5% of individuals with LS have been diagnosed.[10,11] Relying on age or family history criteria to determine Lynch syndrome screening or testing eligibility misses between 25–70% of Lynch syndrome patients.[12–16] Therefore, several institutions are now adopting a universal tumor screening (UTS) approach to determine which patients should be offered genetic counseling and germline testing for Lynch syndrome.[17,18]

UTS programs are endorsed by the Centers for Disease Control and Prevention Office of Public Health Genomics based on evidence of analytic validity, clinical validity, and clinical utility.[19–21] Additionally, economic models have found UTS costs to be comparable to other preventive services adopted within the United States.[22,23] Furthermore, a large private healthcare system has implemented UTS after independently weighing costs and benefits.[24]

UTS procedures are known to vary across institutions.[17,18] Laboratory procedures for UTS include microsatellite instability (MSI) testing and/or immunohistochemical (IHC) testing to identify tumor mismatch repair (MMR) deficiency. On a subset of MMR deficient tumors, reflex BRAF and/or hypermethylation testing may be added to rule out patients who are unlikely to have Lynch syndrome.[18,20,25] Variations in results follow-up procedures include different methods for tracking and disclosing results. An additional procedural consideration is whether patient informed consent is obtained prior to screening or whether screening is implemented as part of standard procedure.

Regardless of the chosen procedures, clinical benefits of UTS can only be realized if a high proportion of screen-positive patients (i.e., results suggest possible Lynch syndrome) follow through with genetic counseling and germline testing to confirm a diagnosis and obtain recommendations and options to prevent future cancers for themselves and their at-risk relatives. This multiple-case study compared UTS adoption, implementation and effectiveness across several existing UTS programs. Study objectives were to: 1) identify challenges and facilitators to UTS adoption; 2) further characterize similarities and differences in UTS procedures that have been implemented at different institutions; 3) identify suboptimal outcomes of UTS; and 4) develop a model to explain varying levels of patient follow-through (PF) with germline testing across institutions.

METHODS

Study Frameworks

Two complementary frameworks, RE-AIM[26–28] and the consolidated framework for implementation research (CFIR),[29] were used in study planning and the design of surveys and interview guides. The use of RE-AIM was expected to increase the quality, speed, and public health impact of stakeholder efforts to more effectively translate UTS into practice by considering the following five dimensions:[26–28] 1) *Reach* - the absolute number, proportion, and representativeness of CRC patients who are screened for Lynch syndrome; 2) *Effectiveness* - the impact of UTS procedures on patient follow-through and other outcomes, including potential negative effects; 3) *Adoption* - the absolute number, proportion, and representativeness of institutions and staff who adopt UTS, and the resources and expertise available to them; 4) *Implementation* - time and costs of UTS programs, and what adaptations are made to UTS in various settings; 5) *Maintenance* – extent to which UTS becomes part of routine practice and the effects of UTS over time. The CFIR, which is described in more detail in Supplemental Table A (available online), was used because it incorporates specific factors that may influence the decision to adopt an innovation (i.e., UTS) and includes several *Implementation* conditions that can influence overall *Effectiveness*.[29]

Study Design

Following IRB approval of this multiple-case study, key informants at institutions performing UTS completed an initial survey. Follow-up surveys and interviews were then conducted six-months later to obtain *Maintenance* data and inform the interpretation of earlier findings.

Participant recruitment, study procedures, and measures

Sampling frame—By June 2012, the Lynch Syndrome Screening Network (LSSN) membership consisted of over 70 institutions across the United States. Of these, 35 were actively screening all newly diagnosed CRC patients regardless of age or other factors (i.e., had adopted UTS). Given the current study's focus on system-level implementation rather than patient-level influences, institutions that were not performing UTS were excluded in order to reduce variation between the patient populations screened at different institutions.

Initial survey of key informants—LSSN representatives from institutions performing UTS were eligible and invited to participate in the initial survey via an e-mail invitation posted twice within a two month period on the LSSN listserv. Between mid-October through December 2012, interested representatives served as key informants by completing an online survey collecting information on: a) institutional characteristics; b) factors influencing the decision to adopt UTS; c) challenges and facilitators to UTS adoption; d) UTS procedures; e) percentage of patients who follow-through with germline testing after a positive screen (i.e., PF); and f) barriers or facilitators to PF. Prior to study initiation, the survey was reviewed for face and content validity by a medical geneticist, two genetic counselors (GCs), an epidemiologist, and a behavioral cancer scientist. The revised survey was piloted by two GCs and a nurse practitioner involved in UTS programs. The final online survey

included five open-ended questions and approximately 20 multi-part, closed-ended questions with an option to write in other responses.

Six-month follow-up with institutions—Key informants were e-mailed 1–2 requests asking them to provide additional information in all cases where the institution met the following more stringent inclusion criteria: 1) UTS had been fully implemented for 6 months or longer at the time of the initial survey; and 2) data on PF were available. In order to obtain additional UTS details, clarify information, and identify changes in UTS procedures, follow-up surveys and/or interviews were conducted with key informants and secondary informants. Surveys and semi-structured interview guides consisted of closed- and open-ended questions that had been reviewed for face and content validity by several specialists familiar with UTS. Although there was some overlap with questions from the initial survey, most questions included in follow-up surveys and interviews were designed to obtain additional UTS details, clarify information, and identify changes in UTS procedures. All interviews were audio recorded and notes were taken by the interviewer.

Primary Outcome and Conditions—The initial and follow-up surveys contained a question asking for the approximate percentage of patients with a screen-positive result who pursue germline testing. Response options were: 1 = ≤10%; 2 = 11–25%; 3 = 26–40%; 4 = 41–55%; 5 = 56–70%; 6 = 71–85%; and 7 = >85%. Ordinal responses to this question from the initial survey were used as the primary outcome (i.e., PF-score). Other questions from the initial survey measured the presence of implementation conditions hypothesized to influence the outcome. These questions are included in Table 1 along with select questions from follow-up surveys and interviews that aided in results interpretation.

Data analysis

Descriptives—After arranging institutions in descending order by PF-scores, institutions were categorized into three groups: High-PF (>40%); Medium-PF (11–40%), Low-PF (≤10%). Frequencies and percentages were generated for responses to closed-ended survey questions. Open-ended responses and interview data were reviewed to identify commonalities and diversity across institutions and to characterize each RE-AIM dimension.

Implementation procedures associated with PF—Qualitative comparative analysis (QCA) is an analytic technique for performing cross-case comparisons to identify conditions that are “sufficient” for an outcome of interest to occur.[30,31] Although QCA is quite different from inferential statistics, conditions (i.e., implementation procedures) are analogous to independent variables hypothesized to influence the outcome of interest (i.e., PF). Using QCA, combinations of conditions uniquely associated with high- and low-PF were determined.

Prior to conducting QCA, conditions were coded as 1=condition present; 0=condition absent. PF was coded into two different variables for two separate QCA analyses: 1) High-PF=1 if institutional PF score was >40% and High-PF=0 for all other institutions; 2) Low-PF=1 if PF score was ≤10% and Low-PF=0 for all others. Specialized software (fsQCA 2.0) and the truth table approach[32] were used to identify combinations of conditions that were

unique to High-PF institutions and those unique to Low-PF institutions. Steps used to perform QCA are outlined in Supplemental Table B (available online). QCA solutions were obtained from Boolean simplification of the data matrix shown in Table 2; solutions were then triangulated with six-month follow-up data to formulate mechanistic models by which these conditions may influence PF.

RESULTS

Respondent and institution characteristics

Of 35 LSSN representatives at institutions performing UTS, 20 (57%) completed the initial survey, of which 15 institutions met stringent inclusion criteria for cross-case comparisons. All key informants were genetic counselors (GCs), except for 1 from an institution not meeting inclusion criteria. Additional information was collected at six-month follow-up via interviews and/or follow-up surveys completed by 12 of the 15 key informants whose institutions met inclusion criteria. Interviews were also completed with six secondary informants from four of the 15 institutions. Table 3 provides characteristics of all participating institutions, including the 5 for which PF data were not available. Table 3 also presents institutional characteristics according to PF. Four of the five High-PF institutions were National Cancer Institute-designated academic/research institutions. In contrast, 3 of the 5 Medium-PF and 3 of the 5 Low-PF institutions were non-academic/non-research institutions. Among the 15 institutions meeting stringent inclusion criteria, 11 had been performing UTS for over one year as of October 2012.

RE-AIM

Study findings within each of the five RE-AIM dimensions are presented in Table 4 and summarized in the following sections. Table 4 also highlights differences between High-PF and Low-PF institutions.

Patient Reach—Estimated numbers of newly diagnosed CRC patients undergoing tumor screening are listed in Table 3. Although the proportion of all newly diagnosed CRC patients screened was not assessed, it was believed to be nearly 100% at all participating institutions based on the following: 1) institutional procedures dictated that tumors from all newly diagnosed CRC patients were to be screened; and 2) no patients were reported to have opted out of screening. Nevertheless, it is possible that some tumors were missed.

Effectiveness—Patient follow-through (PF) with germline testing after a positive tumor screen varied widely (ranging from <10% to >85%) across institutions (Table 2). Negative outcomes related to UTS were uncommon, but included: 1) two patients who were unaware that tumor screening was part of their surgical informed consent; 2) a few patients who were concerned about their inability to pay for genetic counseling and/or germline testing; 3) the need to plan for handling results from prison inmates or deceased patients; 4) rare problems with reimbursement for tumor screening at two institutions; 5) one patient who, despite lack of interest, felt obligated to undergo germline testing; 6) difficulties deciding how to follow-up when results are equivocal or atypical; and 7) concerns that physicians were not always disclosing screening results to patients.

Adoption—GCs were the first to propose the idea of UTS at most institutions, but pathologists, surgeons, gastroenterologists, or oncologists were typically very important in the decision to adopt UTS. At non-academic institutions, administrators were often highly involved in decision-making, but less so at academic institutions. The most commonly cited facilitators to UTS adoption were collaborative relationships that existed across departments, guidance from other institutions performing UTS, and having an institutional champion support UTS. Commonly cited challenges included concerns about whether active patient informed consent was necessary and concerns about screening costs or reimbursement. Additional challenges, primarily reported among Low-PF and non-academic institutions, included: 1) difficulty convincing key stakeholders (e.g., administrators, healthcare providers, pathologists) why UTS is important, 2) general lack of knowledge by stakeholders, and 3) communication barriers between stakeholders.

Implementation and PF—QCA results, reported in Table 4, revealed that all High-PF institutions share a combination of implementation conditions. High-PF institutions perform automatic reflex testing on a subset of screen-positive patients. In addition, High-PF institutions either do not require screen-positive patients to be referred for genetic counseling or GCs contact physicians to request and assist in completing referrals. At all High-PF institutions patient disclosure of positive screening results is performed by a master's trained GC or a genetic nurse counselor on behalf of the treating physicians. Although GCs routinely disclosed screening results to patients at two Medium-PF institutions, these GCs reported difficulty contacting patients. In contrast, difficulty contacting patients was not selected as a barrier by informants from High-PF institutions; in fact, three of these informants indicated this barrier was overcome by having a GC or nurse meet the patient at an already scheduled follow-up appointment (e.g., surgical postoperative appointment). Interview data revealed that this approach is not feasible at some institutions due to a lack of time among genetics personnel or because follow-up appointments occur at several different locations that are not in close proximity to GCs (i.e., private practices). In fact, physical distance was reported as the impetus for having a genetics nurse disclose positive screening results during post-operative appointments at one High-PF institution.

As shown in Table 4, two different sets of conditions distinguished Low-PF from other institutions. Among all three non-academic Low-PF institutions, a higher proportion of adoption challenges to facilitators were reported. At both of the academic Low-PF institutions, GCs did not receive detailed information on screen-positive patients.

Maintenance and PF—Initial and follow-up survey results were largely consistent, but several institutions reported some degree of change in PF. The most striking change involved an increase in PF at one institution after initiating automatic BRAF reflex testing shortly after the initial survey. Over the six-month follow-up, this institution also noted an increase in physician referrals that institutional representatives attributed to two factors: 1) consistent attendance of a GC at biweekly case conferences with treating physicians; and 2) a high level of GC follow-up with physicians.

Although a few institutions moved either into or out of the Medium-PF group, no procedural changes were reported at the fourteen other institutions over the six-month time period.

Nevertheless, several institutions had modified UTS procedures prior to the current study; these included a few High-PF institutions that increased involvement of GCs and one Low-PF institution that decreased involvement of GCs.

Patient-level factors and PF

All key informants identified at least one patient-level factor that they believe influences PF at their institution. Factors most commonly reported include: patient concerns about cost or lack of insurance to cover genetic counseling and/or germline testing; lack of patient interest or failure to appreciate the importance of germline testing; and patients dealing with too many other issues.

DISCUSSION

To our knowledge this is the first study to systematically compare UTS outcomes across multiple institutions. Our study adds to limited outcomes data previously reported by only a few academic institutions,[33–36] and provides evidence that UTS programs can be successful, despite room for improvement at several participating institutions. Consistent with earlier survey research,[17,18] we found substantial variability in tumor screening implementation across different institutions. Advancing this understanding further, we provided evidence from 15 institutions to support how variability in UTS procedures may influence patient follow-through (PF) with germline testing among screen-positive patients. Specifically, our proposed model suggests that higher PF can be achieved when the following conditions are implemented: 1) streamlined UTS procedures (e.g., automatic reflex to BRAF or hypermethylation and elimination of the requirement for physician referral to genetics); 2) a high level of involvement of GCs in various UTS procedures (e.g., tracking screening results, facilitating physician referrals, following up with and/or communicating with treating physicians, directly disclosing positive tumor screening results to patients); and 3) methods for overcoming barriers to patient contact and facilitating follow-up (e.g., meeting patients at post-operative appointments).

Although this study was not designed to prove causality, plausible mechanisms exist to explain how or why key implementation conditions could improve or reduce PF. More specifically, implementing automatic reflex testing (i.e., BRAF or hypermethylation) on a subset of screen-positive tumors eliminates the need to order this testing on a case by case basis and reduces the need for follow-up among patients who do not likely have Lynch syndrome. Additionally, requiring a physician referral creates complexity and causes PF to be contingent upon multiple different health care providers' knowledge about the importance of genetic counseling and germline testing and their actions to both convey this to the patient and to complete a referral. Elimination of the need for referral altogether only occurred at institutions where GCs disclose positive screening results to patients. This latter condition could improve PF because GCs focus on hereditary cancer while physicians have many other competing demands that may interfere with time needed to discuss results with patients. Additionally, direct patient contact allows the GC to build rapport with patients early in the process and to convey to patients the importance of follow-up testing. Nevertheless, even if a GC discloses positive screening results, PF is logically contingent

upon successfully contacting patients. The presence of a higher ratio of adoption challenges to facilitators was a condition that helped distinguish non-academic Low-PF institutions from Medium-PF institutions. This difference may be indicative of several organizational challenges that could reduce PF (e.g., communication barriers within the institution, lack of knowledge regarding the importance of PF among physicians). Nevertheless, challenges to UTS adoption are insufficient to prevent institutions from eventually achieving relatively high PF, as evidenced by two participating institutions in the current study.

Implementation complexity uncovered in this study helps to explain a discrepancy among limited data previously reported on outcomes of Lynch syndrome tumor screening. Two institutions have independently documented increases in PF after implementing a high level of involvement of GCs in follow-up and results disclosure to patients.[33,34] In contrast, results from a large national survey of cancer GCs found no association between who discloses screen positive results to patients (i.e., GC versus physicians) and problems with PF.[18] In our study, disclosure of screen-positive results by GCs was insufficient for high PF. Nevertheless, a high level of GC involvement was part of a more complex 'recipe' for attaining High-PF.

Although not the focus of the current study, informants identified several patient-level factors (such as insurance coverage) that were barriers to PF. Differences in patient populations may help to explain why certain institutions have reduced PF. For example, one Medium-PF institution is located in a socioeconomically disadvantaged, urban area where several patients reportedly do not even attend their post-operative appointments. Therefore, even if GCs were available to meet patients at these appointments, patient contact and PF may continue to be problematic.

Strengths of the current study include the use of methodologies for improving data credibility, reliability and validity.[37,38] First, follow-up data was gathered from 12 of the 15 key informants approximately six months after the initial survey. In addition, summaries were shared with informants and reviewed for accuracy by 11 of 15 informants. Nearly all informants reported having good tracking systems in place and were quite confident in the accuracy of the PF numbers they reported. Nevertheless, measurement limitations included self-reported data by institutional informants, the inability to collect uniform patient-level data, artificial division of institutions into three PF groups, fluctuations in PF over time, dichotomously measured conditions, and inability to prove causality. More specifically, responses from key informants (who were all GCs) could be inaccurate or biased in their favor. However, we have no reason to suspect this for the following two reasons: 1) key informants were simply asked about follow-up procedures in terms of who does what and how rather than asking questions about whether they thought involvement of GCs improved patient follow-through; and 2) the importance of GC involvement was confirmed when secondary informants (who were not GCs) from institutions with high PF were asked an open-ended interview question about what they believe contributes to their success.

Thus despite these limitations, open-ended survey responses and interview data all support the proposed model. Furthermore, previous reports from two institutions document

improvements in PF after making changes to UTS procedures, including implementation of BRAF reflex testing and/or increased involvement of GCs.[33,34]

As with other multiple-case studies, our model can serve as a mechanism for generalizing results.[38] Nevertheless, institutions participating in our study are not representative of all cancer centers and hospitals that treat CRC patients. Furthermore, we do not know how the participating institutions compare to the 15 non-participating LSSN institutions that were also performing UTS at the time of the study. Consequently, additional paths to improve PF may need to be identified or forged, particularly for institutions that do not employ GCs or are unable to implement conditions that were found to associate with high PF in our study.

Although the current study advances our understanding of UTS, we were unable to comprehensively measure all RE-AIM dimensions. The application of RE-AIM in future studies and surveillance efforts should contribute to a more complete assessment of the health impact of tumor screening to identify Lynch syndrome. Specifically, demographic data should be collected on all individuals screened and future efforts should take into account the reduction in patient *Reach* at those institutions where tumor screening is limited to a subset of patients. Additional measures of *Effectiveness* should include the proportion of family members who are subsequently identified as a result of tumor screening programs. This is important because cascade testing and prevention of cancers in family members determine a large portion of the public health and cost benefits of tumor screening programs.[22–24,39]

Widespread *Adoption* of routine tumor screening is critical because adoption influences the absolute number of patients who are ultimately reached. The current study focused on a relatively small number of institutions where GCs were involved in the adoption and implementation of UTS. Therefore future research will need to identify whether institutions that do not employ a GC have adopted UTS and characterize how UTS *Implementation* differs at these institutions. Given that academic/research institutions appear to have been quicker or more likely to adopt UTS,[17,18] health disparities could increase in rural areas or among minority populations unless UTS becomes more widely adopted. Our findings suggest that non-academic institutions may face a greater number of challenges and/or have fewer resources or expertise needed to facilitate UTS adoption. Given the many complexities associated with UTS adoption and implementation, institutions may find the freely available resources on the Lynch Syndrome Screening Network (LSSN) website (www.lynchscreening.net) helpful. In addition, LSSN members can access the active listserv to troubleshoot challenging cases or seek advice from members with expertise in Lynch syndrome.

In conclusion, results of this study are expected to help inform decision-making by stakeholders and guide future research that is needed to assess the public health impact of Lynch syndrome tumor screening programs. The current study provides compelling evidence that tumor screening implementation influences patient follow-through (PF). Our model, which illustrates procedures that are expected to maximize PF, should be tested among a broader set of institutions that have implemented routine tumor screening. This model will likely need to be revised as additional methods of improving tumor screening

effectiveness are identified. Ultimately, a larger-scale, multi-institution study is needed to evaluate patient-level factors and determine the relative influence of patient versus system-level factors on the effectiveness of tumor screening programs. Additionally, this study highlights the importance of assessing system-level implementation conditions when future genomic technologies are integrated into healthcare settings.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Sample of select study questions and responses along with their relation to RE-AIM dimensions and/or constructs from the Consolidated Framework for Implementation Research (CFIR)

Initial Survey Questions **response options**	**RE-AIM Dimension** ***CFIR construct***
Approximately how many colorectal cancer patients have been screened at your institution in the past six months (or less if you have recently implemented universal tumor screening)?	**Reach**
What were the primary reasons for implementing UTS at your institution? (check all that apply)	**Adoption**
• UTS was recommended in 2009 by the Evaluation of Genomic Applications in Practice and Prevention (EGAPP) working group	*External policy*
• To improve the identification of patients with Lynch syndrome • To reduce cancer mortality • To benefit relatives of individuals with Lynch syndrome • To generate increased revenue	*Relative advantages*
• To "keep up" with other institutions that were already performing UTS	*Peer pressure*
What barriers (if any) did your institution face when planning UTS? (check all that apply)	**Adoption**
• No real barriers	Not applicable
• Difficulty convincing key stakeholders (e.g., administrators, healthcare providers, etc.) why UTS was important	*Knowledge & beliefs*
• Arranging time when individuals could meet to discuss UTS was challenging • Lack of laboratory expertise/resources	*Resources*
• Concerns were raised regarding the need for informed consent	*Patient needs*
• Difficulty deciding which screening method to use (i.e., IHC versus MSI) • Disagreement occurred about how results should be handled	*Complexity & planning*
• Concerns about the cost of screening were raised	*Cost*
• One or more individuals tried to prevent UTS implementation	*Engagement*
• Communication barriers existed between key stakeholders (e.g., administrators, pathologists, healthcare providers, etc.)	*Communication*
• Perceptions that other screening algorithms are more cost effective or superior to UTS	*Relative advantage*
What factors were helpful when planning and implementing universal tumor screening (UTS) at your institution? (check all that apply)	**Adoption**
• Prior to UTS, my institution was already routinely screening a subset of colorectal tumors	*Trialability*
• An "institutional champion" worked hard to implement UTS • A high-level administrator or supervisor supported UTS	*Engagement*
• Collaborative relationships existed across departments and/or working groups	*Networks & communication*

Initial Survey Questions **response options**	**RE-AIM Dimension** ***CFIR construct***
• Protected time was provided for planning UTS	*Resources*
• Useful information was obtained from another institution that was already performing UTS	*Access to information*
• Multiple planning meetings helped facilitate UTS implementation	*Planning*
Who is responsible for disclosing abnormal screening results to the patients?	*Executing*
How are abnormal screening results usually disclosed to patients? (e.g. phone, in-person)	*Executing*
What do you think may be preventing some colorectal cancer patients from receiving germline testing after an abnormal tumor screen at your institution? (check all that apply)	**Effectiveness**
• Lack of adequate insurance coverage and/or financial difficulties	*Patient resources*
• Healthcare providers fail to recognize the need for germline testing	*Beliefs & knowledge*
• Referral to genetics by other healthcare provider is required	*Executing*
• Inconvenient for patients to arrange and/or attend a separate genetics appointment	*Patient needs*
• Difficulty contacting patients to set up germline testing	*Executing*
• Lack of patient understanding about the importance of genetic counseling	Not applicable
• Patients are dealing with too many other issues at the time of diagnosis	Not applicable
• Patients don't want to face the possibility that others in their family may be at increased risk for cancer	Not applicable
• Patients are concerned about genetic discrimination	Not applicable
Of those colorectal cancer patients who have an abnormal tumor screen, approximately what percentage do you think provide a blood or saliva sample for germline testing?	**Effectiveness**
How often have patients at your institution expressed concerns or responded negatively to tumor screening?	**Effectiveness**
Has your institution experienced any problems or unanticipated outcomes related to universal colorectal tumor screening?	**Effectiveness**
Follow-up Survey Questions	
How often does someone meet the patient at a routine follow-up visit (i.e., surgical follow-up) to discuss germline testing when indicated (Likert-type scale for response)	*Executing*
Under your current screening protocol, consider the total number of colorectal cancer patients who screen positive and indicate what percentage receives germline testing? NOTE: If BRAF or hypermethylation is performed, only include those who need germline testing.	**Maintenance Effectiveness**
Interview Questions	
Have you made any changes to your UTS procedures over time? Why, why not?	**Maintenance** *Executing*
Why do you think you have difficulty contacting patients?	*Executing*
Thinking about your UTS program, what kinds of communications take place that are important for making the program work?	*Networks and communication*
How certain are you about the accuracy of the percentage of patients who follow-through with germline testing at your institution?	**Effectiveness**

Initial Survey Questions **response options**	**RE-AIM Dimension** ***CFIR construct***
Can you please clarify discrepancies in _____ between initial and follow-up surveys?	Not applicable

Note: UTS=universal tumor screening for colorectal cancer.

Questions on both the initial and follow-up survey asked several other detailed questions about how UTS procedures are executed.

Table 2

Data matrix of patient follow-through (PF)[a] with germline genetic testing after a positive screen and conditions showing patterns associated with High- and Low-PF.

Outcome			Conditions						Intermediary step
PF genetic testing	**High PF[b]**	**Low PF[b]**	**Challenges to adoption ≥ facilitators[c]**	**Automatic reflex test of screen positive tumors (e.g., BRAF)[c]**	**GC[d] receives positive screen results[c]**	**GC[d] discloses screening result to patient[c]**	**Difficulty contacting patients[c]**	**Need for physician referral is barrier[c]**	**Follow-through with genetic counseling[d]**
>85%	1			1	1	1			41–55%
71–85%	1			1	1	1			71–85%
56–70%	1			1	1	1			56–70%
41–55%	1			1	1	1			>85%
41–55%	1		1	1	1	1			71–85%
26–40%					1	1	1		56–70%
26–40%				1	1		1	1	41–55%
26–40%					1	1	1		26–40%
26–40%				1	1			1	11–25%
11–25%				1	1			1	41–55%
≤10%		1	1		1			1	11–25%
≤10%		1	1		1			1	11–25%
≤10%		1	1	1	1			1	≤10%
≤10%		1		1				1	≤10%
≤10%		1						1	≤10%

Notes:

[a] PF was determined from ordinal response options to a question on the initial survey asking about the percentage of patients who follow-through with germline testing after a positive screen suggestive of Lynch syndrome. Responses ranged from 1(<10%) to 7 (>85%).

[b] The presence of each outcome used in qualitative comparative analysis (QCA) is indicated with “1”.

[c] The presence of each condition used in QCA is indicated with “1”.

[d] GC refers to a master’s trained genetic counselor or a nurse with extensive genetic counseling experience.

[d] The percentage of patients who follow-through with genetic counseling was asked (without specifying whether or not it had to be performed by a GC). Response options were the same as for PF. Responses to this question were ultimately not used as part of the outcome or as a condition because genetic counseling could be considered an intermediary step.

Table 3

Characteristics of institutions and their respective universal tumor screening (UTS) programs

Characteristics	**All institutions (N=20)**	**High-PF (n=5)**	**Med-PF (n=5)**	**Low-PF (n=5)**	**PF data not available (n=5)**
	n (%)	**n**	**n**	**n**	**n**
Institution type					
Academic/research	8 (40)	4	2	2	0
Non-academic	12 (60)	1	3	3	5
Designations[a]					
Member National Comprehensive Cancer Network (NCCN)	4 (20)	2	1	1	0
NCI comprehensive cancer center	6 (30)	3	2	1	0
NCI cancer center	2 (10)	1	0	0	0
Screening implemented					
<3 months ago	1 (5)	0	0	0	1
3–5 months ago	1 (5)	0	0	0	1
6–12 months ago	5 (25)	0	2	2	1
>1 year ago	13 (65)	5	3	3	2
# patients screened in 6 months [b]					
<10	1 (5)	0	0	0	1
10–29	3 (15)	1	0	0	2
30–49	5 (25)	0	3	1	1
50–69	2 (10)	1	0	1	0
70–89	3 (15)	0	1	2	0
≥90	5 (25)	3	0	1	1
Uncertain	1 (5)	0	1	0	0
# screen-positive patients in 6 months [b]					
0	2 (10)	0	0	0	2
1–5	6 (30)	1	2	2	1
6–15	9 (45)	3	2	3	1
≥16	2 (10)	1	1	0	0
Uncertain	1 (5)	0	0	0	1

Notes: PF = patient follow-through with germline testing.

[a] NCCN and NCI designations are independent and some centers have both designations.

[b] # within the last 6 months or less if screening was implemented under 6 months ago.

Table 4

Summary of study findings within the RE-AIM framework

RE-AIM Dimension Description	General Findings, Observations, or Future Research Considerations	High Patient Follow-through (High-PF) Institutions	Low Patient Follow-through (Low-PF) Institutions
Reach The absolute number, proportion, and representativeness of CRC patients screened	Absolute number of newly diagnosed CRC patients whose tumors were screened to determine who should be offered germline testing varies across institutions (Table 3) Proportion screened is uncertain, but estimated to approach 100%	No consistent patterns related to PF were discerned	No consistent patterns related to PF were discerned
Effectiveness The impact of UTS procedures on patient follow-through and other outcomes, including potential negative effects	• Patient follow-through with germline testing (PF) after a positive screen was highly variable ranging from ≤10% to >85% • Institutions were grouped into 3 categories according to PF (High-, Medium-, and Low-PF) • Few unexpected or negative outcomes have been encountered • Only two institutions reported rare difficulties with reimbursement for tumor screening; others did not know or had no reimbursement issues	PF-score >40% Two High-PF institutions reported past concerns that physicians were not consistently disclosing screen-positive results or referring patients; this prompted changes to procedures that were made prior to the current study	PF-score ≤10% All Low-PF institutions were concerned about difficulties with PF Additional concerns: • reflex tests may be interpreted incorrectly or not seen on pathology addendum • liability risks from failure to disclose screen-positive results
Adoption The absolute number, proportion, and representativeness of institutions and staff who adopt UTS, and the resources and expertise available to them	• Prior studies suggest academic institutions are more likely to adopt UTS • GCs usually raised the idea for UTS, but multiple stakeholders were involved in the decision to adopt • Common reasons for UTS adoption were to improve identification of Lynch syndrome patients and benefit their family members • Cost was a key characteristic considered in decision to adopt UTS	• All but one of the High-PF institutions were academic-research institutions • The only non-academic High-PF institution reported a greater number of challenges than facilitators to UTS adoption	• Two of the five Low-PF institutions were academic institutions • All non-academic Low-PF institutions reported a greater number of challenges than facilitators to UTS adoption
Implementation Time and costs of UTS programs, and what adaptations are made to UTS in various settings	• Substantial heterogeneity in UTS implementation exists across institutions • Several differences are NOT consistently associated with PF (i.e., method of screening IHC versus MSI, and	QCA revealed that High- PF institutions have all of the following unique conditions: **1** Automatic reflex testing (i.e., BRAF) is performed on subset of screen positive tumors	QCA revealed that Low-PF institutions have either of the following unique sets of conditions: GC does NOT disclose results AND adoption challenges ≥ facilitators OR

RE-AIM Dimension Description	General Findings, Observations, or Future Research Considerations	High Patient Follow-through (High-PF) Institutions	Low Patient Follow-through (Low-PF) Institutions
	whether results are disclosed by phone or in person) • High- and Low-PF were consistently associated with specific combinations of *Implementation* conditions based on qualitative comparative analysis (QCA)	**2** GC discloses positive results **3** contacting patients is NOT a major barrier **4** obtaining a referral from physician is NOT a barrier Several adaptations have been made to overcome barriers: • Lack of referral overcome by GC reminding physician and assisting with the referral • Meeting patients at a follow-up appointment helped overcome contact barrier	GC does NOT receive screening results Difficulty overcoming barriers to improve PF: • Resistance among physicians to direct patient contact by GC or HIPAA concerns • Too many physicians to build rapport with and educate about importance of GC and testing • Not logistically feasible for GCs to meet patients at follow-up appointments (e.g., lack of GC personnel, geographic distance of appointments)
Maintenance Extent to which UTS becomes part of routine practice and the effects of UTS over time	• Some institutions have modified their lab procedures (e.g., making BRAF or hypermethylation testing automatic for a subset of tumors) • Institutions have also changed their follow-up procedures over time (e.g., increased involvement of GCs)	• At least 3 High-PF institutions have changed their procedures to streamline the process and increase involvement of GCs; these changes reportedly increased PF	• One Low-PF institution used to have a GC call out results and reported higher PF before changing procedures so that GC no longer received screening results

CRC = colorectal cancer; UTS = universal tumor screening; GC = genetic counselor (nurse with GC experience)