

**A Primary Care-Focused, Computer-Based Clinical
Decision Support Tool To Assess Patients' Risk for
Deleterious *BRCA* Mutations**

Appendixes

Appendix A. Workplans

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Work Plan for BRCA Clinical Decision Support Tools: BRCA1/2

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**Work Plan for BRCA Clinical Decision
Support Tools: BRCA1/2**

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1. Introduction

The purpose of this project is to develop and assess a clinical decision support (CDS) tool that effectively communicates information about BRCA1 and BRCA2 genetic mutations and the associated screening test to patients and providers and that promotes informed decisionmaking. For women with breast cancer, we will develop and assess a CDS tool that supports patients and providers as they make decisions about genetic expression profile (GEP) testing. To inform the design and development of the tools, our project team has conducted a literature review¹ and obtained input and guidance from our technical expert panel (TEP) members and the project's peer reviewers. This work plan outlines the process we are proposing to undertake for the BRCA1/2 tool; a separate work plan will address the GEP CDS tool.

This work plan describes the planned activities that will feed into BRCA1/2 tool development, the steps we will take in designing the tool, and our process for conducting a preliminary evaluation of its utility and effectiveness. The work plan is organized into five sections. Section 2 provides our plans for assessing the need for a BRCA1/2 tool from multiple perspectives by discussing plans to poll a limited number of physicians and by reviewing tools currently in existence. We also discuss feasibility issues related to integration into existing computer systems, namely information technology (IT) systems, Internet connectivity, and electronic medical records (EMRs). Section 3 provides information about the aims of the tools and introduces the likely content based on information at this time. In this section, we also present our conceptual framework and measures. Section 4 provides a discussion of our plans for implementation and preliminary evaluation. Section 6 concludes the report with the project timeline and next steps.

2. Needs Assessment

In this chapter, we discuss our plans for conducted a multifaceted needs assessment for the BRCA1/2 tool.

2.1 Primary Care Physician Assessment

A systematic review of CDS tools shows that integrating tool usage and recommendations into the natural clinical workflow is critical to a tool's effectiveness.² Consequently, to develop effective CDS tools, we need to understand how primary care physicians currently collect family history information (if at all) and how they identify patients for referral to genetic counseling and BRCA testing. We also need to understand, from a physician perspective, how accessible IT systems are used during patient encounters and how computer-based tools can best be integrated into the clinical workflow.

Because existing literature on these topics is scant—and because this information is critical to tool development—we plan to conduct informal telephone interviews with primary care physicians at each BRCA evaluation site ($n = 4$, given budget limitations). We will use these interviews to obtain a cursory understanding of physicians' current practices, identify barriers to family history collection and genetic testing referral, and pinpoint opportunities for integrating the CDS tools into the clinical workflow.

Ultimately, our goals for the primary care physician needs assessment are to:

- design CDS tools that enable physicians to efficiently gather and use cancer family history data to screen and appropriately refer patients, and

- understand how the CDS tools can be incorporated into the clinical workflow with minimal or no disruption.

With these objectives in mind, we increase the probability that physicians will find the CDS tools useful and adopt them in their practices.

We will interview eight primary care physicians from the evaluation sites (two from each site). Site managers will assist us in identifying appropriate physicians. The phone interviews will last approximately 60 minutes and will be conducted by a team member heavily involved in tool development. The proposed interview questions can be found in Exhibit 1.

After interviews are complete, we will summarize participant responses in a matrix and analyze the responses for trends. Specifically, we will identify the current family history collection and genetic testing referral practices, the perceived barriers to accurate family history reporting and appropriate referral, the accessibility of IT and computer systems during patient appointments, and the existing workflow. We will then use these findings to design CDS tools that enhance current practices and can be easily integrated into the clinical workflow.

2.2 IT Feasibility Assessment

Diversity in evaluation site IT systems, Internet connectivity, and EMRs is a potential barrier to physicians' adoption of the CDS tools. Different IT systems might require different CDS tool specifications, and EMR software might use different processes to read and integrate tool output. Moreover, IT security systems—such as firewalls, antivirus software, and Internet browser configuration—can block physicians from accessing the Web-based tools. Finally, physician and patient access to computers during the clinical encounter determines how the tools can be integrated into clinic workflow.

To address these potential barriers and to ensure the development of effective CDS tools, RTI will conduct informal telephone interviews with IT professionals at each evaluation site.

By conducting interviews (as opposed to a survey), not only can we collect basic information about each site's IT system and EMR usage, but we can also probe the IT professionals for specifics about their EMR software, computer accessibility, Internet connectivity, and opinions on tool integration.

Ultimately, our goals for the IT assessment are to:

- design CDS tools that will work within the sites' existing IT systems,
- design CDS tools that can be integrated with the sites' EMR software, and
- understand how the CDS tools can be incorporated into the IT workflow with minimal or no disruption.

Exhibit 1. Primary care physician needs assessment questions for provider interviews breast cancer CDS tools project

CURRENT PRACTICES

1. Do you routinely collect cancer family history from your patients? If so, when and how frequently do you collect this information (e.g., first visit only, specified intervals, annual/routine appointment)? Who usually collects the family history (e.g., primary care physician nurse)?
2. If you collect cancer family history, do you use a standard protocol for collecting and documenting the information? How well is this process working? What are the process' limitations?
3. Once you've collected the cancer family history or general family health history, how does your practice document and track the information (e.g., electronic medical records, hard copy patient questionnaires)? How do you use this information in your practice?
4. There are many different tools (e.g., worksheets, computerized tools) available to patients to gather their family health history and family cancer history. Does your practice use or recommend any family history collection tools? If so, which ones and why? How well is the tool serving your needs?
5. How do you determine if your patients are at high risk for familial breast cancer or BRCA1/2 mutations? Do you use any tools to help you make this determination? If so, which ones and why?
6. What type of education or information do you think primary care providers need to help them identify patients at high risk for BRCA1/2 mutations? How should this information be provided? Would it be helpful to have information about the calculations for determining BRCA1/2 genetic risk (e.g., risk factors, risk factor scoring)?
7. Have you ever referred a patient for BRCA1/2 genetic testing? If so, why did you decide to refer them? What was the referral process like?
8. How do primary care providers know when to refer high risk patients for genetic counseling?
9. Do you have access to genetic counselors for your patients? If so, how do you decide to which counselors patients should be referred? Is genetic counseling covered by insurance for most of your patients?

INPUT ON FUTURE TOOL

We understand that many primary care physicians do not currently screen women for risk of hereditary breast cancer. We are planning to develop a computer-based decision support tool for primary care providers to help them (1) collect cancer family history from their patients and (2) use the family history to identify women at high risk of a BRCA1/2 genetic mutation so they can be referred to genetic counseling.

We are envisioning that patients will enter their cancer family history into the tool, which would then calculate their risk for BRCA1/2 mutations. Physicians would have their own interface for the tool: They would review the patients' cancer family history and receive a recommendation about referral to genetic testing/counseling.

1. Would you and your colleagues use such a tool? Why or why not?
2. How might such a tool be integrated into the workflow at your practice? At what point would you review the patient's cancer family history? How would you like to receive the patient's cancer family history (e.g., incorporated into EMR, e-mail print out)? Where would you access the computer-based tool?
3. What would be the barriers to using this tool at your practice? How can we address these barriers?
4. What problems do you think your patients would have completing a cancer family history? What should the tool do to address these problems? Are there other resources that could be helpful?
5. Where should patients enter their cancer family history into the computer-based tool (e.g., private exam room, at home prior to appointment)?
6. What information should patients receive about cancer family history or BRCA1/2 mutations before using the tool? What information should they receive as a result of using the tool? For high risk patients, what would you want them to know before they see a genetic counselor?
7. What other pieces of information—besides cancer family history—would you like to have when deciding whether to refer a patient to genetic testing/counseling? How would you like to receive this information (e.g., paper report, online report, integrated into EMR)?
8. What else can we do to ensure this tool is effective? To ensure it is user-friendly for both physicians and patients?

We will conduct the interviews with evaluation site IT professionals (n = 4) as well as several IT experts and consultants (n = 2). Sites will refer us to their IT professionals. The phone interviews will last 30 to 60 minutes, and our in-house IT expert will conduct or participate in all the sessions. A second staff member will also attend the interviews to serve as a dedicated notetaker. The proposed interview questions are highlighted in Exhibit 2.

Exhibit 2. IT feasibility assessment questions

1. Please describe your site's IT system. How do you use computers and IT at your site? How do you use computers/IT to store patient health information or medical records?
2. Tell me more about the computers and basic software that providers use at your site. What types of computers do providers use (i.e., PC or Mac)? What operating systems are used (e.g., Windows 2000, Windows XP, Macintosh OS-X, UNIX)?
3. Do providers have consistent Internet access? If so, do the computers connect individually or through a local area network? What Web browsers are installed on the computers (e.g., Internet Explorer, Netscape, Firefox)? Do providers have authority to upgrade Web browsers on their computers? Does your site have any policies or software that prevent staff from accessing certain Web sites?
4. If you store patient health information or medical records electronically, what type of software do you use? What do you think are the advantages and disadvantages of the current software?
5. How is information in the EMRs extracted and collectively examined? What type of software do you use for this extraction?
6. How do you incorporate information being sent from third-party systems (i.e., lab test results, pharmacy alerts) into EMRs?
7. Do patients have electronic access to their EMRs? If so, how do they access the records? Are patients able to electronically communicate with providers about their EMRs? How many patients use these features?
8. Imagine that physicians at your site want to use a computer-based decision aid and want to store the decision aid recommendations in patient EMRs. What level of effort—time and expense—would be required to integrate the EMRs and decision aids? What factors would influence the time and expense required?
9. Does the site ever e-mail patients (e.g., appointment reminders)? If so, for what purposes? How are patient e-mail addresses collected and stored?
10. How often do physicians have access to a computer during clinic hours? Do physicians have computer access during patient appointments and/or between patient appointments?
11. Do patients and visitors have access to the Internet at your site? If so, is this WiFi access (i.e., patients use own laptops) or is access granted through an on-site computer/kiosk?

Once interviews are complete, we will summarize the responses and identify themes that emerge. Specifically, we will identify the basic IT infrastructure of each site and pinpoint any major barriers to tool integration (e.g., limited physician computer access during clinic hours, unreliable Internet connectivity, unfamiliar EMR software). We will then use these findings to design CDS tools that are compatible with site IT systems, can address the identified barriers, and can be easily integrated into the clinic workflow.

2.3 Review of Existing Tools

This section describes the family history tools available today, some of their pros and cons, and how they can inform the development of the tool for this project. There are currently six Web-based and three paper-based tools available for collecting family history of cancer^a (see Exhibit 3). None of these tools are designed for use by both the patient and the provider. Instead,

^aOne of the TEP members referred us to the Utah Health Family Tree. However the Web site was not available and was listed as “coming soon” (1/18/2009).

they are designed for information to be collected by the patient and brought to an appointment with a physician or other health care provider for discussion. The online tool, MyGenerations (available at: <http://www.northshore.org/clinicalservices/medicalgenetics/mygenerations/>)—one of the few tools that provides a personalized risk assessment—may serve as a useful model or platform for designing the decision support tool for this project. Although MyGenerations is designed for use only by the patient, it includes many of the basic features necessary for a well-designed, user-friendly tool for collecting family history.

2.3.1 Interactive Tools

Interactive Cancer Family Tree, University of Nebraska Medical Center

This tool presents the likelihood of having an inherited cancer by asking about the incidence of cancer among family members. It includes a comprehensive list of different types of cancer. However, Interactive Cancer Family Tree is not very user-friendly. The instructions are heavily text-oriented. Use of this tool also requires a high level of health literacy. It is not possible to return to the home page with instructions after beginning to enter data. It also uses pop-ups, which are easy to miss, for entering the age of relatives. Also, it does not allow the user to edit previously entered information or to save information to update later. This tool follows the American College of Medical Genetics (ACMG) guidelines for collecting family history. It does not provide a risk assessment.

MyGenerations, NorthShore University Health System's Center for Medical Genetics, Illinois

This tool collects family history of all cancers. It has some desirable features. The text is simple and easy to read. The presentation is more user-friendly than most tools. It is possible to save information to update later. It is also possible to send a report to your physician if you are a patient with the NorthShore University Health System. MyGenerations follows the ACMG guidelines for collecting family history. It provides the user with a personalized risk assessment and information on screening based on level of risk; it also provides a substantial amount of information about genetic screening.

Family HealthLink, The Ohio State University Medical Center

This tool collects family history information about a variety of cancers and coronary heart disease. It excludes relatives who have not had cancer or heart disease. This tool does not create a graphical family tree for the user and does not allow the user to save information to update later. Family HealthLink does not follow ACMG guidelines for collecting family history because it does not collect information on unaffected relatives. It provides a risk assessment as well as tips for what the user can do to reduce his or her risk.

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Exhibit 3. Currently available tools for collecting family history of cancer

Computer patient tool	URL	Source or developer	Key educational messages/features/limitations	Conditions addressed	Able to enter at least three generations of history?	Meets the ACMG guidelines for collecting family history (http://www.health.state.ny.us/nysdoh/cancer/obcancer/pp27-35.htm)	Based on which guidelines?
Interactive Cancer Family Tree (ICFT)	http://app1.unmc.edu/gencancer/	University of Nebraska Medical Center	Presents likelihood of having an inherited cancer	All cancers, includes multifactorial factors	Yes	Yes	
MyGenerations	http://www.enh.org/clinicalservices/medicalgenetics/mygenerations/default.aspx?id=4411	Center for Medical Genetics NorthShore University Health System, IL	Presents information on screening based on level of risk	All cancers	Yes	Yes	American Cancer Society (ACS)
Family HealthLink	https://familyhealthlink.osumc.edu/Notice.aspx#Start%20SessionIt	Ohio State University Medical Center	Gives respondent tips for "what you can do" to decrease risk	Cancer, coronary heart disease	Yes, but cannot enter information on unaffected relatives	No	ACS mentioned as a source and reference
Norwich Union Health Tree	http://www.norwichunion.com/healthtree/index.htm	Aviva—UK insurer	Other cancers must be added one at a time	All cancers and other related conditions	Yes, but does not collect information on age at diagnosis or vital status		
My Family Health Portrait	https://familyhistory.hhs.gov/	Department of Health and Human Services	Links to family health Web sites, educational components	Asks for info on breast, colon, ovarian cancers, diabetes, stroke, and heart disease; users can add other conditions	Yes, but doesn't ask about second-degree relatives other than grandparents and doesn't ask for age of living relatives	No	

Exhibit 3. Currently available tools for collecting family history of cancer (continued)

Computer patient tool	URL	Source or developer	Key educational messages/features/limitations	Conditions addressed	Able to enter at least three generations of history?	Meets the ACMG guidelines for collecting family history (http://www.health.state.ny.us/nysdoh/cancer/obcancer/pp27-35.htm)	Based on which guidelines?
New My Family Health Portrait (launched 1/2009)	https://familyhistory.hhs.gov/fhh-web/home.action	Department of Health and Human Services	Does not address disease risk or health promotion, screening, or treatment	All major cancers and other health conditions using a drop-down menu	Yes, asks about third-degree relatives, age for living and deceased relatives	Yes	
Myriad Cancer History Guide	http://www.myriadtests.com/cancerhistory.htm#	Myriad Genetic Laboratories, Genetic Testing Company	Good way to organize information on relatives and their illnesses; gives very little information about personal cancer risk	Only selected cancers and polyps	Yes, up to 10 siblings; also can enter information about step-siblings, first cousins	Yes	
Paper Patient Tools							
ACMG Qx	\\rtifile02\HSERproj2\09815 DeCIDE\008 CDS Tools\003 Literature Review\Sample Family history Tools\ACMG Questionnaire.doc	New York State Genetic Services Program	Collects details but in summary; table does not include lines for each family member Appears to be designed for use in conjunction with genetic interview	Can enter any cancers	Yes		
AMA Qx	\\rtifile02\HSERproj2\09815 DeCIDE\008 CDS Tools\003 Literature Review\Sample	American Medical Association	Not cancer-specific; deals with all genetic issues (birth defects, etc.)	Asks for health problems and hospitalizations of patient, health of relatives	Yes		

Exhibit 3. Currently available tools for collecting family history of cancer (continued)

Computer patient tool	URL	Source or developer	Key educational messages/features/limitations	Conditions addressed	Able to enter at least three generations of history?	Meets the ACMG guidelines for collecting family history (http://www.health.state.ny.us/nysdoh/cancer/obcancer/pp27-35.htm)	Based on which guidelines?
	Family history Tools\adult_history.pdf		Designed for use in medical appointment	Collects family structure information on all first- and second-degree relatives, present health of relatives, age and cause of death			
Utah Department of Health Family History Tool Kit	\\rtifile02\HSERproj2\09815 DeCIDE\008 CDS Tools\003 Literature Review\Sample Family history Tools\UofUT family history tool.pdf	Utah Department of Health	User must make a copy of the tool for each family member; no educational component	Collects info on breast and colon cancer, smoking, weight	Not on same sheet		

Exhibit 3. Currently available tools for collecting family history of cancer (continued)

Computer patient tool	Language used to describe risk status	Statistical model used	Creates graphical family tree for user?	Recommends speaking with health care provider about results or other action steps	Informs user of progress towards finishing tool?	Functionality and usability	Online tool	Printable results
Interactive Cancer Family Tree (ICFT)	"Increased, higher." This information may present an increased risk for cancer for you or your family."		Yes, but requires downloading software	Yes. "Only a licensed health care provider, physician, nurse, genetic counselor or other licensed health care professional can accurately interpret the information you have provided and printed from this Web site." "You may wish to review your family history periodically with your physician and/or genetic counselor."	No	Entering information is slow; having to download Macromedia software is time consuming and confusing; pop-ups are sometimes hard to see	Yes	Yes
MyGenerations	"Increased, average, higher" and average 5-year risk percentage for BRCA given in results	Gail model	Yes, along with personalized cancer risk assessment	Yes, and one option is to have it sent to a NorthShore doctor, gives action steps for screening each type of cancer regardless of risk in results	Yes, percentage complete shown on each screen	Fast input due to Web-based form	Yes	Yes, tree and risk assessment report

Exhibit 3. Currently available tools for collecting family history of cancer (continued)

Computer patient tool	Language used to describe risk status	Statistical model used	Creates graphical family tree for user?	Recommends speaking with health care provider about results or other action steps	Informs user of progress towards finishing tool?	Functionality and usability	Online tool	Printable results
Family HealthLink	"High, moderate, average"		No, only printable assessment of risk and suggestions	Yes "Please discuss with your doctor."	No		Yes	Yes
Norwich Union Health Tree				Yes		Cannot be updated over time, has drop-down list of selected health conditions, including breast, ovarian, and colon cancer		
My Family Health Portrait	Gives no information on risk, only a summary of family information	N/A	Yes, only tree and listing of relatives and diseases	Yes. "Use this in consultation with your health care professional. It can be a valuable tool for discussion, risk assessment, and medical advice."	Yes	Available in Spanish with links to BWH tool in four other languages	Yes	Yes

Exhibit 3. Currently available tools for collecting family history of cancer (continued)

Computer patient tool	Language used to describe risk status	Statistical model used	Creates graphical family tree for user?	Recommends speaking with health care provider about results or other action steps	Informs user of progress towards finishing tool?	Functionality and usability	Online tool	Printable results
New My Family Health Portrait (launched 1/2009)	Gives no information on risk, only a summary of family information	N/A	Yes.	Yes. "Your family health history can help your health care practitioner provide better care for you. It can help identify whether you have higher risk for some diseases. It can help your health care practitioner recommend actions for reducing your personal risk of disease."	Yes.	Data entry for each family member is a little long and contains fields not needed for BRCA risk calculation. Once family members are entered, user can display members in a table format. This table is also useful for providers to scan.	Yes.	Yes
Myriad Cancer History Guide	Gives no information on risk, only a summary of family information	N/A	No, gives only a summary of information on relatives (age, disease, etc.)	Yes. "The family history summary should be discussed with a doctor, genetic counselor, or other health care provider as part of your cancer risk assessment."	Yes	Point and click entry is very slow; does not save data for update; graphics and font are very small	Yes	Yes

Exhibit 3. Currently available tools for collecting family history of cancer (continued)

Computer patient tool	Language used to describe risk status	Statistical model used	Creates graphical family tree for user?	Recommends speaking with health care provider about results or other action steps	Informs user of progress towards finishing tool?	Functionality and usability	Online tool	Printable results
Paper Patient Tools								
ACMG Qx			No	No	No	Very short and general	No	No
AMA Qx			No	Yes	No	General	No	No
Utah Department of Health Family History Tool Kit			No	No, designed to be kept for each member of the family	No	Short	No	No

Exhibit 3. Currently available tools for collecting family history of cancer (continued)

Computer Patient Tool	Hard Copy Only	Data can be saved and updated	Readability (FK score)	Plain Language Compliant	508 Compliant	Length/Time needed to complete	User help available?	Security/Can user remain anonymous?
Interactive Cancer Family Tree (ICFT)	No	No	Grade 11.4 on homepage	Partially. User friendly layout, information presented is manageable and personalized for the user. Pop-up results screen uses complicated terminology and lacks white space.		Short	Not within tool	Yes.
MyGenerations	No	Yes, with user ID/password	Grade 11.8 on homepage	Partially. Font is small and hard to read, message is clear, but some (non-medical) words used are complex		Short	Not within tool	Yes, uses only a username and ID chosen by user. User who is also a patient of NorthShore has the option to include contact info.

Exhibit 3. Currently available tools for collecting family history of cancer (continued)

Computer Patient Tool	Hard Copy Only	Data can be saved and updated	Readability (FK score)	Plain Language Compliant	508 Compliant	Length/Time needed to complete	User help available?	Security/Can user remain anonymous?
Family HealthLink	No	No	Grade 12.2 on homepage	Partially. User friendly layout, amount of information presented is manageable, but terminology used is complex (CHD is referenced without explanation or definition)		Short	Not within tool	
Norwich Union Health Tree		No	Grade 15.9 on home page					
My Family Health Portrait	Paper-only version available	Yes, but must be downloaded to home computer	Grade 15.2 on home page	Yes. User-friendly layout, information presented is manageable and personalized for the user.	Accessible via screen readers and other accessibility tools; post-2001 info is 508-compliant	Short	Yes	Yes, site mentions that data is not stored

Exhibit 3. Currently available tools for collecting family history of cancer (continued)

Computer Patient Tool	Hard Copy Only	Data can be saved and updated	Readability (FK score)	Plain Language Compliant	508 Compliant	Length/Time needed to complete	User help available?	Security/Can user remain anonymous?
New My Family Health Portrait (launched 1/2009)	On-line version only	Yes, but must be downloaded to home computer; Users who save family history data using the older version (prior to 1/2009) must recreate their family history to use the new tool	Not indicated	Yes	Yes	Site indicates 15-20 minutes.	Yes. Users can contact the application support desk at that National Cancer Institute's Center for Biomedical Informatics and Information Technology (CBIIT) by email or phone.	Yes, site mentions that data is not stored.
Myriad Cancer History Guide	Paper worksheet available	Yes, but must be downloaded to home computer	Grade 14.7 on home page	Partially. Font is small and hard to read; message focuses on security and is complex; extremely long and complex disclaimer that must be agreed to in order to proceed		Small type, hard to follow, makes tool take longer	Not within tool	Explains security of personal data, and user must agree to very long legal disclaimer

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Exhibit 3. Currently available tools for collecting family history of cancer (continued)

Computer Patient Tool	Language used to describe risk status	Statistical model used	Creates graphical family tree for user?	Recommends speaking with health care provider about results or other action steps	Informs user of progress towards finishing tool?	Functionality and usability	Online Tool	Printable results
Paper Patient Tools								
ACMG Qx	Paper-only	Saved in hard copy	Grade 7.7			Short		No
AMA Qx	Paper-only	Saved in hard copy				Long (5 pages)		No
Utah Department of Health Family History Tool Kit	Paper-only	Saved in hard copy				Short (1 page for each family member)		

Norwich Union Health Tree, Aviva, London, England

This tool is no longer available online. It was provided by Aviva, an insurance group based in London, England. It asks the user to input family history for all cancers, but does not collect information on the age at diagnosis or the vital status of relatives. It does not allow the user to save information.

New My Family Health Portrait, U.S. Department of Health and Human Services

In January 2009, the Surgeon General's Office released a new version of My Family Health Portrait. This tool collects family history of all cancers, as well as other major diseases using drop-down menus. Users can add other conditions as well. The tool asks for the age of living and deceased relatives. The new My Family Health Portrait collects information beyond that which is needed for screening for risk of BRCA mutations (e.g., race, height, weight). All essential data fields are included except for whether the users'/family members' breast cancer was bilateral and if so, the age of onset for second breast. Data can be saved and updated later, but it must be downloaded to the user's home computer. This tool provides a crude graphical family history, but does not provide any information about risk.

Myriad Cancer History Guide, Myriad Genetic Laboratories

This tool is provided by Myriad Genetic Laboratories, a genetic testing company that is the sole worldwide source for BRCA mutation analysis. It collects information on only select cancers, but the user can add additional types of cancer. The user can also add additional relatives. The font is small and generally hard to read. Myriad Cancer History Guide is not extremely user-friendly and is difficult to navigate. It also requires the user to have a fairly high level of health literacy. The tool provides a worksheet for gathering data, but it could function as a stand-alone tool. Data can be saved and updated later, but it must be downloaded to the user's home computer. Myriad Cancer History Guide follows ACMG guidelines for collecting family history. It provides a summary of family history of cancer, but does not provide a risk assessment. As the company directly profits from increased testing, screening results have the potential to be biased.

2.3.2 Paper Tools

There are three paper tools available for collecting family cancer history. The first, ACMG Qx, which is provided by the New York State Genetic Services Program, allows users to include any cancers and appears to be designed for use in conjunction with a genetic interview. It is very short and general. The second, AMA Qx is provided by the American Medical Association. It is not cancer-specific, but deals with all genetic issues (e.g., birth defects). It was designed for patients to bring to an appointment with a physician. AMA Qx collects family history information on all first- and second-degree relatives, the present health of relatives, the age of relatives, and the cause of death. This tool is fairly lengthy (five pages) and time-consuming to complete. The third paper tool is actually a kit called The Utah Department of Health's Family History Tool Kit. It requires the user to make a copy of the tool for each family member, but does not include an educational component. The tool collects information on breast cancer, colon cancer, and a variety of other diseases, and it also asks about risk factors, such as smoking, exercise, and weight.

2.4 Incorporating Input from Technical Expert Panel

We recruited a TEP to advise us on the development of each set of clinical decision tools. We sought input from the TEP in three stages:

1. Prior to beginning the full literature review, we summarized the information obtained from the relevant evidence-based reviews, the remaining gaps in information needed to develop the tools, and our suggested search terms to fill the identified gaps. We sent this summary to the TEP and our consultants and asked them to review the summary and comment on any information they felt was incorrect, unidentified gaps in information, and the suggested search terms. These comments were incorporated into the literature search and into the full literature review.
2. We sent the draft literature review to the TEP members and asked them to review sections in which they had expertise and to provide written comments.
3. We scheduled a conference call with the TEP to discuss the literature review and to provide input on specific questions.

The TEP remarked that providers needed to understand the needs for the tools, how to interpret and discuss the results of the tools, and the use the information in patient care. The TEP recommended we conduct patient and provider focus groups to gather information relevant to the features, design, and content of the tool; however, they were not included in the scope of work for this project. Instead, we will need to rely on input we gather from interviews with providers, as discussed in Section 2.1 and from usability testing postdevelopment (see Section 3.5).

The TEP described potential barriers to CDS implementation in primary care practices and privacy and security issues, especially with regard to incorporation into EMR systems. These issues are discussed in more detail below.

The TEP felt that the BRCA tools needed to explain to the providers the goals and function of the tools and the reasons for BRCA testing. The TEP felt the tools would need to explicitly inform the provider of when a patient had a cancer family history that put her at risk; how to interpret the information, especially the risk estimates; and how to use the information for patient care. The TEP and the client identified a need for more discussion of the benefits and risks of available preventive measures for women with hereditary breast cancer. The TEP also felt that it was important to address situations where women may have a family history consistent with hereditary breast cancer, yet the affected family members may not have a BRCA mutation. Another concern was how to advise women whose family history was not consistent with hereditary breast and ovarian cancer, but included more cases of cancer in the family than would be expected. This is complicated by the lack of clinical guidelines for followup for women whose risk appears to be increased based on family history, but whose family history is not consistent with a known hereditary cancer syndrome. The lack of clear follow-up action in this situation can be a barrier to tool implementation. Providers can fear liability when information is collected on sensitive issues but there is no clear action or recommendation to be made, and can feel they have failed the patient if the family history risks recorded in a patient's record have not been addressed.

The primary barriers to implementing the tools into primary care practices were felt to be the lack of adequate time to collect family history, difficulty in communicating risk information, and privacy and liability issues. Collecting an adequate family history for hereditary cancer risk assessment takes about 30 minutes, far more time than is available in a primary care visit, suggesting it will probably be necessary to collect the information outside of the visit. Providers

will need help not only in understanding risk information themselves, but also in communicating that information to their patients. The TEP recommends that the tool developers need to remember that people's understanding of risk and preferred message of risk communication differ. Providers may need resources to help them assess the patient's level of understanding—communications needs to be two-directional. The tool may need to have built-in prompts for providers to check the patient's understanding, sometimes referred to as the “teach back” method. Finally, the messages to the patient will differ based on risk status. The TEP recommends that the tool provide a template suggesting how providers present risk information to their patients. The template could be tailored by the clinician during the visit based upon the individual patient and circumstances.

Another consideration is how to share information between the patient and provider. The TEP felt communication would be more thorough if patients and providers could exchange some information before the visit. Patients could be prompted to complete their family history, and the provider could review it prior to the appointment. This would require electronic sharing and storage of information, which raises patient confidentiality and privacy issues and is logistically challenging.

The TEP input on the feasibility of building the BRCA tools to allow incorporation into existing electronic medical records (EMRs) confirmed that the tools will probably need to be developed as a stand-alone tool that is cross-walked to any existing standards to allow for integration into other systems as possible. EMRs are becoming more widespread, but many providers are still not using them. The systems in use are not very sophisticated, and there are no defined standards for EMRs. Slow connections would also pose a problem for accessing electronic records during a patient visit. (A delay of more than 15 to 30 seconds would deter usage of the system.)

3. Tool Content and Development

In this section, we describe the goals of the BRCA1/2 tool, the proposed tool contents, and the tool development and testing process. When developing the tool, we will take into careful consideration the guidance offered by the International Patient Decision Aid Standards (IPDAS) Collaboration, such as their Patient Decision Aid Checklist for Users (see Appendix A).

3.1 Objectives

Tool Steps/Objectives
Provide patients with a user-friendly computerized tool to record detailed cancer family history data.
Empirically assess patients' risk of having a clinically significant BRCA1 or BRCA2 mutation using cancer family history data and an algorithm accurate for a primary care population.
Educate patients about hereditary breast and ovarian cancer, its risks, genetic counseling/testing, ^b and cancer surveillance practices.
Educate patients about how to talk to their doctor about their risk for BRCA mutations.
Support patients' exploration of their values and preferences for involvement in decisionmaking about genetic risk assessment, counseling, and testing.
Present providers with patients' risk assessment results and guidelines for referring patients to a genetic counselor.
Offer providers guidance on educating patients about their risk and choice of next steps (e.g., seeing a genetic counselor, regular cancer screenings).
Facilitate patient-provider communication about patients' values and preference for involvement in decisionmaking about genetic risk assessment, counseling, and testing.

The goal of the BRCA1/2 tool is to facilitate appropriate referral of women for genetic counseling based on their individual risk level, as calculated by family history and other relevant data. The long-term objective is to have a tool that is available to and adopted by the clinician for use in real-time decisionmaking at the point of care and results in routine screening for BRCA mutations in primary care. The tools must adhere to all current relevant U.S. Department of Health and Human Services (HHS) requirements, such as compliance with Section 508 of the Americans with Disabilities Act to allow access to disabled persons. The tools should be flexible to allow easy incorporation of new clinical or software knowledge; easy to maintain; capable of working on different IT platforms, systems, and architecture; adaptable to allow different user interfaces and outputs; and easy to modify.

Overall, the tool will educate women about familial breast cancer, its risks, and genetic counseling/testing.^c The tool will encourage women to share their family cancer history and risk with their providers and to encourage them to explore their own values and preferences regarding genetic testing. The tool seeks to equip clinicians with the knowledge and skills to effectively and efficiently screen primary care patients and refer appropriately to genetic testing based on risk levels. Eventually, the hope is to promote and facilitate physicians' adoption of a new practice in primary care: screening for BRCA1/2.

We are developing a theoretically based, interactive, computer-based tool that engages both the patient and provider in a series of steps (see text box above).

Below we describe our current thinking regarding the patient and provider portions of the tool.

Patient portion of the tool. A woman will enter cancer family history data into the tool at home, allowing her to consult family members and other sources as needed. The tool will ask the user to enter data about her cancer family history for three generations and provide additional demographic (e.g., ancestry) and selected health status information. Once the data are as complete as possible, the tool will calculate her risk for a genetic mutation (e.g., average risk,

^b The tool assumes that the genetic counselor will provide high risk patients in-depth education about genetic testing and the availability of clinical interventions to reduce the risk of breast or ovarian cancer among BRCA mutation carriers.

^c The tool assumes that the genetic counselor will provide high risk patients in-depth education about genetic testing and the availability of clinical interventions to reduce the risk of breast or ovarian cancer among BRCA mutation carriers.

high risk). The tool will incorporate a modified version of the algorithm BRCAPRO for risk assessment. BRCAPRO is a Mendelian risk model. Mendelian models calculate the probability a person carries a BRCA1 or BRCA2 mutation by representing the mode of inheritance of BRCA mutations and the correlation between phenotype (cancer status) and genotype (mutation status) as mathematical relationships. The tool will estimate the probability a person carries a mutation as a percentage between 0 and 100. The value at which a woman will be classified as belonging to a particular risk category (average vs. high) will be determined by an analysis of retrospective data by the BRCAPRO algorithm. Risk categories will be determined and verified through accuracy testing (see Section 3.6) and consultation with Dr. Giovanni Parmigiani from Johns Hopkins University, the developer of BRCAPRO and a consultant to this project.

The tool will direct her to educational information targeted at her risk level (see Exhibit 4).

Exhibit 4. Preliminary content of brief patient educational information, by risk status

High risk	Medium/low risk
Definitions of terms (e.g., familial risk)	Definitions of terms (e.g., familial risk)
Information on what proportion of hereditary breast and ovarian cancer is associated with a BRCA1/2 mutation	Reminder that risk status is based on current cancer family history information and risk could change if/when history changes
Interpretation and explanation of risk score for having mutation	Information on what proportion of hereditary breast and ovarian cancer is associated with a BRCA1/2 mutation
Naming and describing the test to identify a genetic mutation	Interpretation and explanation of risk score for having mutation
Options other than testing (e.g., interventions to detect cancer early) and their pros and cons	Interventions to detect cancer early and their pros and cons
Responses to frequently asked questions	Responses to frequently asked questions
A summary of possible interventions for women with a positive family history whose affected relatives do not have a mutation in BRCA1 or BRCA2	Importance of sharing family history information throughout the family
Importance of sharing family history information throughout the family	

After completing the cancer family history, there will be an option to print out a summary that contains the users’ family history information and pedigree, risk category, and recommended next steps, which will include talking to their doctor about the results and suggestions about how to start conversations with providers and family members. To assist with communication between patients and providers, patients will be able to print out a list of key questions and concerns appropriate to their risk category that they can bring with them to their appointment, as well as guidance for what to expect when talking with their physician.

To further support patients (and physicians) in the process of informed decisionmaking, women who are assessed by the tool as being at high risk will be given additional information about genetic counseling and testing, and what to expect during this process. This will provide information that patients should consider when making a decision about whether to talk to a genetic counselor and pursue genetic testing. For average-risk women, the tool will provide screening guidelines for each age group.

The desired outcome is that women print out the tool results and bring them to an upcoming visit with their primary care provider. We are interested in studying factors associated with whether or not patients print out the summary and whether the patients and providers discuss the risk result, which is a primary outcome of the tool.

Provider portion of the tool. Based on recommendations from the TEP, the provider section of the tool will include an educational module that contains the following information:

- an overview of hereditary breast and ovarian cancer,
- reasons to screen primary care patients,
- data on what proportion of hereditary breast and ovarian cancer is associated with a BRCA1/2 mutation,
- prevalence of BRCA mutations,
- interpretation and explanation of risk scores and suggestions for how to explain them to patients,
- a summary of the preventive and follow-up options and their benefits and risks,
- a summary of possible interventions for women with a positive family history whose affected relatives do not have a mutation in BRCA1 or BRCA2, and
- links to resources to locate genetic counselors and insurance coverage for genetic counseling.

In addition to this educational module, which will offer continuing medical education (CME) credits to providers, providers will be able to use the tool to review a patient's cancer family history and risk score prior to or during the appointment. At the visit, the patient and provider would make any corrections or other modifications to the information the patient entered and reassess the risk level if necessary. The tool will also provide reminders to the provider to actively engage the patient in a discussion, regardless of whether or not genetic counseling is recommended, and, if counseling is recommended, to discuss why and the process for undertaking the testing. To facilitate this discussion, the tool will offer providers appropriate, targeted messages to give to patients and will prompt providers to check patients' understanding (e.g., with the teach back method).

The specific message contents for the tools are described in greater detail in Section 3.2.

3.2 Theoretical Framework

A theory is a set of interrelated concepts, definitions, and propositions that presents a *systematic* view of events or situations by specifying relations among variables in order to *explain* and *predict* events or situations.³ One criticism of the existing body of research on decision aids is that it is largely atheoretical.^{4,5} The benefits of a theoretical model are that it (1) explains a priori the underlying assumptions of the tool; (2) helps to define the research questions and hypotheses; (3) supports the selection of tool elements and concepts that promote the desired behavior; and (4) supports replication of the intervention in other studies.⁶ Bowen and colleagues⁶ concluded that “advances in the field of informed decisionmaking (IDM) interventions would be facilitated by application and specification of theoretical frameworks, used in the design of the intervention and in the measurement of outcomes. Important methodological concerns, such as the need for consistency in conceptual definitions of IDM outcomes, standardization of measures, and design of interventions that target the primary mediating factors of the decisionmaking process, could be addressed, in part, through utilization of a common conceptual base.”

There are numerous theories in the fields of health behavior and social psychology and the decision sciences that could be used to develop the CDS tools for this project. Based on a review of existing theories, we will apply concepts from the Health Belief Model (HBM),⁷ as well as concepts from other behavioral theories appropriate to this intervention (e.g., perceived efficacy of the intervention from the Theory of Planned Behavior), to guide the patient portion of the tool. The HBM proposes that “people will take action to prevent, to screen for, or to control

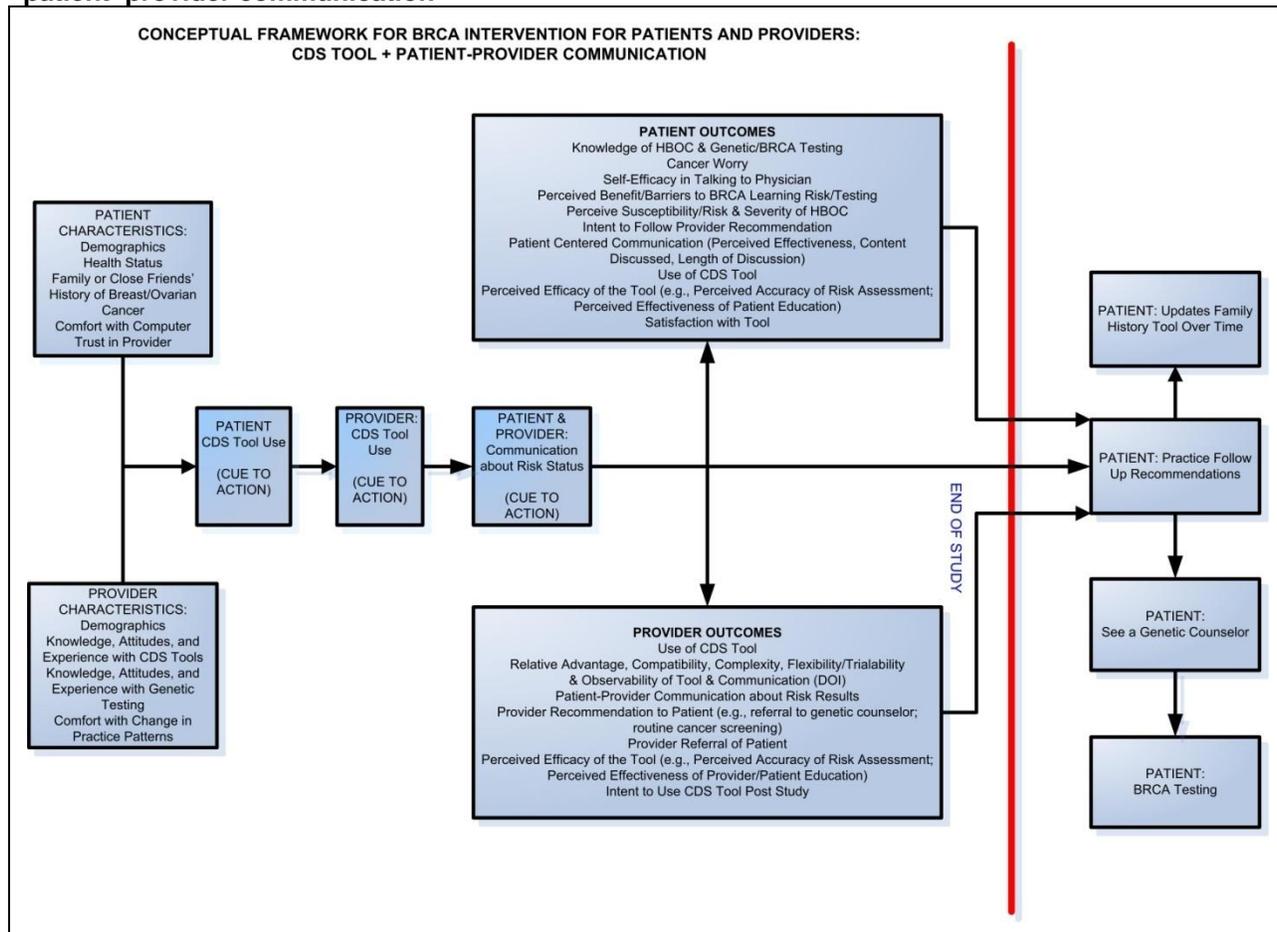
ill-health conditions if they regard themselves as susceptible to the condition, if they believe it would have potentially serious consequences, if they believe that a course of action available to them would be beneficial in reducing either their susceptibility to the severity of the condition, and if they believe that the anticipated barriers to (or costs of) taking the action are outweighed by its benefits.”⁸ Rimer⁴ has suggested that it may be especially timely to consider the HBM as a model for studying responses to genetic susceptibility testing in light of recent scientific advances, and several HBM scales have been developed for use in cancer screening studies.⁹

In applying the HBM to BRCA1/2 screening, if a woman believes that by getting screened, she will gain information about her likelihood of having a genetic mutation that predisposes her to breast cancer, and that the barriers (financial, psychological) are less of an issue relative to the perceived benefit of the information, the HBM suggests that she would choose to get screened (see Exhibit 5).

Our conceptual framework assumes that both patient and provider factors are relevant and are accounted for. For example, each patient will have her own unique set of demographic and health status-related factors that she brings to the situation, and each patient and provider pair have a unique influence on the experience in terms of their tool use and related communication (which both serve as a cues to action). In addition to the traditional HBM influences (e.g., perceived susceptibility and severity), our framework factors in attributes of the tool as an intervention, most significantly patient/provider communication about the tool, including the relative advantage of using it and its compatibility, complexity, flexibility. We also consider some elements from the definition of informed decisionmaking in our framework (e.g., patient and provider knowledge, recognition of a decision to be made.)

Self-efficacy was later added as a key element to the HBM and is a key element of our conceptual framework. Self-efficacy is a strong predictor of behaviors, especially of those that require significant skills to perform. In this situation, self-efficacy is specific to a woman’s ability to communicate with her clinician about her tool results, family cancer history, risk level, and perspectives about genetic testing. Self-efficacy for participating in her medical encounter is a critical element of patient-centered communication,¹⁰ which we are proposing. Self-efficacy also serves as a mediator to the intention to follow the clinician’s testing recommendation and, ultimately, for those at high risk, the woman’s decision about whether or not to see a genetic counselor and to be screened.

Exhibit 5. Conceptual framework for BRCA intervention for patients and providers: CDS tool + patient-provider communication



In considering the utilization of this tool, particularly by providers, we have added constructs from the Diffusion of Innovation (DOI) theory, which describes the process through which an innovation spreads via communication channels over time among the members of a social system.¹¹ An innovation is an idea, practice, service, or other object that is perceived as new by an individual or other unit of adoption.¹² For our study, the “innovation” would be our core intervention of the CDS tool plus the patient-provider communication. The system to which the CDS tool would eventually be disseminated is the health care system in which we are testing (e.g., Providence Health and Baylor Health Care System).

Potential users who are considering adopting an innovation go through what is known as the innovation-decision process. There are five stages of this process:

1. knowledge of the innovation,
2. forming an attitude toward the innovation,
3. deciding to adopt or reject the innovation,
4. implementation of the innovation, and
5. confirmation of the decision

A basic assumption underlying this theory is that adoption and rates of adoption are determined by the unique characteristics of the adopter and the scientific attributions of the innovation.¹² For this study, individual characteristics of patients and providers that we believe would influence use of the CDS tool and patient-provider communication are represented in Exhibit 5, our conceptual framework for the intervention. Exhibit 6 lists and defines constructs from the DOI model that we have incorporated into our conceptual model.

Exhibit 6. Diffusion of Innovation Model Constructs: Attributes of the Innovation/Intervention

Construct	Definition
Relative advantage of the innovation	The level at which an innovation is perceived as better than the idea it attempts to replace
Compatibility of the innovation	The level at which an innovation is viewed as being consistent with the existing values, past experiences, and needs of the potential adopters
Complexity of the Innovation	The level at which an innovation is viewed as difficult to use and understand
Trialability or flexibility of the innovation	The level at which an innovation can be experimented with on a limited or “trial” basis
Observability of the innovation	The level at which the results of an innovation can be seen by others

All of these factors (HBM, IDM, and DOI) feed into whether and to what extent the tool is used during the clinical encounter, the provider’s recommendation, and the patient’s intention to seek genetic counseling. While we are ultimately interested in actual behavior related to receipt of genetic counseling services and subsequent actions (e.g., genetic screening), our study ends at the intention stage.

3.3 Outcome Measures

Based on our conceptual framework, we propose that the patient- and provider-level outcomes in Exhibit 7 would ideally be measured using a pre-post study design that is described in Section 4. As such, we would have measures before and after exposure to the tool from both patients and providers and could measure potential change over time.

In addition to these outcomes (many of which will be measured pre-post), we will assess patients’ and providers’ reactions to the tools, including whether they found them easy or hard to use, whether or not they found them helpful, and the extent to which they felt the tools facilitated obtaining and presenting accurate family history information. Given respondent burden, however, we may not be able to fully measure all of these outcomes.

The short field period for this study precludes us from gathering the longer-term outcomes that are presented in Exhibit 7 as being beyond the end of our study. For example, outcomes that are key to determining the effectiveness of the tool include seeing a genetic counselor and receiving a BRCA test for high-risk women. For women who are not at high risk, desirable outcomes include continued use of the family history tool (e.g., updating cancer history as it changes within the family) and following cancer screening recommendations.

IPDAS has established a set of standards to measure the quality of decision aids.¹³ These criteria focus on three areas: content, process, and effectiveness. We will use these criteria (see Appendix A) to ascertain the quality of the CDS tool we develop for this project.

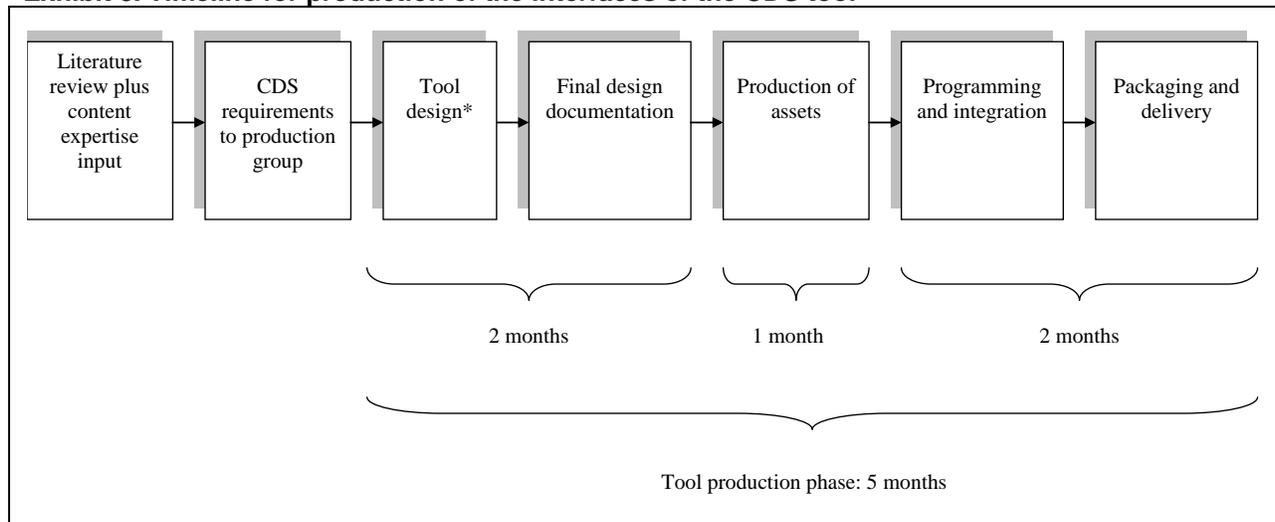
Exhibit 7. Possible Patient and Provider Outcomes to be Measured

Patient Outcomes	Provider Outcomes
Use of the tool	Use of the tool
Knowledge of the tool's purpose	Relative advantage of the tool
Knowledge of hereditary breast and ovarian cancer	Perceived complexity of the tool
Knowledge of BRCA testing	Perceived flexibility/trialability of the tool
Worry about cancer	Observability of using the tool
Perceived risk/susceptibility of breast cancer	Perceived efficacy of the tool in providing an accurate risk assessment
Perceived severity of breast cancer	Perceived efficacy of the tool in educating patient
Perceived benefits of learning risk	Perceived efficacy of the tool in providing information support for provider
Perceived barriers/costs of learning risk	Perceived efficacy of the tool in supporting patient-provider communication
Attitude toward gathering family history, receiving risk assessment result, and genetic testing for BRCA1/2	Patient-provider communication about risk results
Recognition that for high risk women, there is a decision to be made about seeking genetic counseling and screening	Referral of patient to genetic counselor
Patient-centered communication*	Alignment of provider's referral with the tool's recommendation (or reason for deviation)
Self-efficacy in communicating with provider about family history and risk	Follow-up recommendations for patient
Decision to gather family history	Intention to use tool in everyday practice post-study
Decision to learn risk of BRCA mutations	
Risk status	
Delivery of tool output to physician	
Completeness of family history information	
Comprehension of risk assessment result	
Self-efficacy in following provider's recommendation	
Intention to (a) follow provider's recommendation to see a genetic counselor; (b) get screened; (c) update family history information; (d) participate in breast cancer screening practices	
Satisfaction with CDS tool	

3.4 Design and Functionality

In this section, we describe our plans for addressing the design and functionality of the CDS tool, including the workflow from the literature review to delivering the Web-based version for the evaluation. Development and production of the CDS tool will proceed in a sequence of phases, with iterative feedback from the research team and potential users. Exhibit 8 depicts the workflow and timeline for producing the patient and provider interfaces of the CDS tool.

Exhibit 8. Timeline for production of the interfaces of the CDS tool



*Includes review/revise cycles and feedback from content experts

3.4. 1 Design Requirements for Tool Interfaces

Following the needs assessment, we will complete a detailed description of the design requirements for the CDS tool. We have adopted a Web-based strategy for the tool, which is desirable, since it will maximize flexibility in data collection, data storage, refinement, review with a health care provider, and data security. A Web-based tool will allow for an open environment where users can select resources based on their specific needs (e.g., a module about genetic risk).

The design requirements will serve as the detailed instructions for the production team in developing the tool. The design requirements will include the aims and objectives of the CDS tool and specific statements about required outcomes for the tool—in this case, obtaining an accurate family history and making appropriate management decisions based on the patients’ degree of risk for BRCA1/2 genetic mutations.

Identifying the key learner content for the design requirements is a time-intensive step but also is essential before the programming step can be launched. We will develop definitions for all data elements included in the family history assessment (e.g., what it means to be a “blood relative,” what is ovarian cancer). Key messages for each user group (patients and providers) will also be developed following the conceptual framework for the BRCA clinical decision tool (see Exhibit 5).

Exhibit 9 provides an example for key messages for use in the patient interface. The content is linked to the constructs in the conceptual framework, and, where applicable, primary sources for the information will be listed. The sources will be included in the final design documentation for the family history program.

The design requirements document also describes the plan for importing data provided by the user for calculation of the risk level based on the selected risk assessment algorithm.

Exhibit 9. Sample content areas and message themes for users of the family history tool

Concept	Suggested Content for Users	Source
Perceived susceptibility/severity	Severity: messages about breast cancer mortality (e.g., annual deaths, rank among other cancers) Perceived susceptibility: message comes after patient's completion of tool, integrated with risk score/level	To be included
Self-efficacy in talking with physician	Describing the importance of communicating with provider Provision of questions for patient to ask provider about family history and risk for BRCA mutations	To be included
Knowledge	Information on breast cancer, genetics, and genetic counseling An estimated 10% of all breast cancers are hereditary What does high risk mean? (define) What are genes? (define) "What is a genetic counselor? (define) Address misconception that there is one universal test for all cancers Counseling is specific to breast cancer genes	To be included
Attitudes toward genetic testing/ BRCA1/2	Assuaging fears Address misconception that family history of cancer means the patient is doomed to have cancer Even if there is a pattern of breast or ovarian cancer in the patient's family, cancer is not inevitable This does not mean the patient has cancer Even if there is a pattern of breast or ovarian cancer in the patient's family, it does not mean the patient has cancer Referral does not mean the patient has cancer Referral is for counseling vs. treatment The patient has not been diagnosed with any specific disease at this time Remember, not everyone needs to be tested	To be included

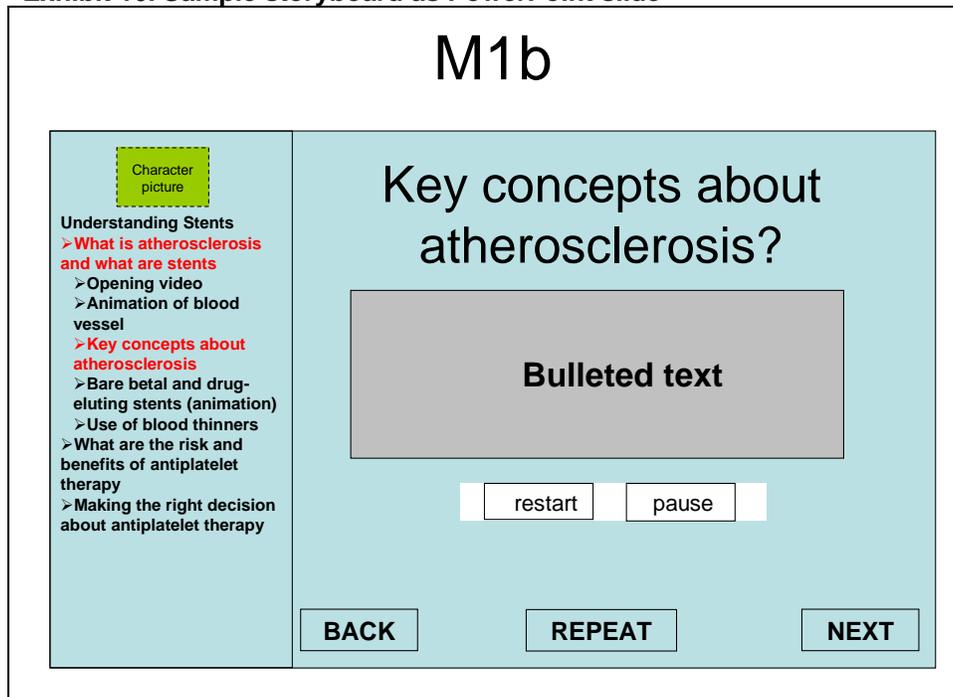
3.4.2 Interface Design

The production phase will begin with a conceptual flowchart of the tool's key elements and their interrelationships. The conceptual flowchart will be reviewed by the research team for comprehensiveness and accuracy. From there, we will identify the modules to be included in both the patient and provider sections of the tool and the inputs/outputs for each module.

The storyboard step involves creating screen sequences showing content, layout, data inputs, and other elements. Storyboards will be created using PowerPoint to facilitate feedback from the research team and other content experts. Revisions to the program will be considered at this point, and input from potential users via informal usability testing will be sought. A sample storyboard from a program on drug-eluting stents is given in Exhibit 10. The approach is to give the user a visual depiction of a program module or screen.

Following approval of the storyboards, a list of program assets will be developed. Assets could possibly include the video segments to be filmed, graphic images and illustrations, buttons, on-screen text, and voiceover narration. A reference document is compiled during the process to serve as a catalog of all program elements.

Exhibit 10. Sample storyboard as PowerPoint slide



3.4.3 Final Interface Design Documentation

A final design document will be assembled and will include the reference materials, flowchart, and list of assets. It will serve as the blueprint for the program.

3.4.4 Production of Assets

The next phase involves the preparation of the program assets. We will work with our production contractor to film any video segments needed, draft the graphic images and illustrations, and write the final narration. There will be limited opportunities for input from the research team at this point, but we will distribute graphic images and video segments for feedback. Where time allows, modifications will be considered.

3.4.5 Programming and Integration

To program and integrate the various components and assets into a seamless, functional product, we will apply RTI's System Development Life Cycle (SDLC). Each phase consists of established entry and exit criteria, defined activities, and verification procedures. Standard operating procedures for the SDLC will contain scripts that summarize the purpose, entry and exit criteria, and process for each step. These scripts will ensure consistent implementation of software development processes and provide a roadmap and a benchmark for progress through the development activities. The SDLC consists of the following phases: concept, requirements, design, implementation, release, and operation and maintenance.

During the concept phase, we will define system needs for patients and providers. We will develop scenarios to help determine how the users will interact with the system, commonly referred to as "use cases." The product from this phase will be a user needs document. It is expected that this document will be updated throughout the other phases.

In the requirements phase, we will identify all requirements that the software system must meet. For example, the IT Feasibility Assessment will help to formulate the constraints within which the tool must operate while identifying early barriers to integration. We will make sure that all pertinent security requirements are met. Three documents will be produced from this phase: the system requirements specification, the draft user's manual, and the initial system test plan. Requirements will cover all aspects of the system, including functionality, usability, security, and reliability. The draft user's manual and system test plan documents will be updated as necessary during subsequent phases of the process. The requirements will cover the issues of data privacy and security, data transfer between systems and the protocols to be used (i.e., HL7 or CCR), Section 508 compliance, and other details that define system structure and limitations.

The design phase consists of two distinct subphases: high-level design and detailed design. In the high-level design phase, key activities will include structural design, development strategy, and system design documentation. The system will be broken down into high-level components, and each component will be described in context of the whole system. During the detailed design phase, RTI will produce design specifications and documentation on each system component. This will include core components of the system such as the security module, the logic engine to evaluate the tool's algorithms, the family history data collection, data output, and, if possible, EMR integration. The system specifications will serve as input to these steps.

During the implementation phase, the system will be built according to the specifications from the previous phases. This will include writing code, performing code reviews, performing tests, and selecting components for integration. Testing is a key activity of the implementation phase. Unit testing will be performed at a structural and a functional level to identify any problems with system components. Integration testing will occur near the end of this phase to ensure that all system components function together properly. In addition, pre-acceptance testing will be performed based on the system test plan to ensure that the completed system meets the specifications.

In the release phase, the system and all associated products will be deployed to the production environment and versioned. Activities will include installation and configuration of the system in the operational environment, installation testing and qualification, training of the system's users, and formal acceptance testing by the users.

The operation and maintenance phase will begin once the system is in use during the prestudy pilot test and evaluation. This phase assesses the performance of the system while in use. Defect detection and change control procedures will enable the system to mature and improve over time.

3.5 Usability Testing: Second Technical Expert Panel Comprised of Intended Users

Easy navigation and operation are critical to the CDS tool's success, and we strongly recommend having dedicated periods of usability testing prior to tool implementation at the clinical sites. The goal of the usability testing will be to determine whether patients and clinicians, without prior training, can effectively use the tool as intended.

In particular, we intend to test primary care physicians' and patients':

- comfort with the tool interface,
- ability to provide requested information,
- ability to incorporate the tool—or tool output—into a clinical discussion, and

- ability to interpret and act on tool output and recommendations.

We will conduct usability testing in two different phases. First, we will assess the usability of each version of the draft tool throughout the tool development process. We will conduct cognitive testing of the various components of the tool with patients and primary care physicians to ensure the components are understandable and easy to navigate. Local physicians and patients at Baylor College of Medicine will participate in the cognitive testing sessions.

Second, we will host a dedicated usability testing session with a second TEP, which will consist of five individuals—three women without cancer and two nonacademic primary care physicians. TEP members will be located in North Carolina, and we will recruit them through existing professional relationships with area hospitals and area health education centers (e.g., University of North Carolina hospitals). We plan to pay TEP members a small honorarium (\$100 for patients; \$200 for physicians) and provide refreshments in exchange for their service.

The usability testing session will last approximately 2 to 3 hours, and we will assess the tool's usability through two exercises. First, TEP members will review the fully functioning tool and participate in interviewer-guided cognitive testing. During testing, participants will enter mock data, navigate the tool interface, and review the tool recommendations. Interviewers will observe the participants and ask probing questions to assess their comfort with the tool.

For the second exercise, TEP members will participate in a role-play activity and use the tool during a mock medical visit. We will observe this role play to see if patients and providers can provide/review the requested family history data and how they integrate the tool and its recommendations into their discussion. After the role play, interviewers will ask follow-up questions to learn more about participants' comfort with the tool and identify barriers to clinical adoption.

3.6 Accuracy Testing for BRCA Risk Algorithm

The literature review identified several tools to identify women at high risk who should be referred for genetic counseling but did not clearly identify which risk assessment tool would best identify women in a primary care population. After discussion with AHRQ, we decided to plan on incorporating BRCAPRO into our CDS tools. Three considerations guided this decision: (1) The literature indicates that computer-based algorithms are better at identifying high risk women than clinical guidelines. (2) BRCAPRO was developed in a U.S. population and would be expected to require less modification than risk algorithms developed in Europe. (3) One of the developers of BRCAPRO serves as a consultant to this project and is willing to modify the risk algorithm to maximize its performance in primary care.

We will assess the performance of BRCAPRO using the following criteria:

1. What is the sensitivity of BRCAPRO in identifying women with a BRCA mutation as high risk when women with a probability of 0.05 and above are classified as high risk? How many women in the general population are identified as high risk?
2. Among families known to have a BRCA mutation, what proportion of family members are correctly identified by risk status?
3. Among families who have tested negative for a BRCA mutation, what proportion of family members are identified as low risk for carrying a BRCA mutation?

Methods. We will use existing datasets to assess these questions. We have identified two possible datasets for testing: the 2005 California Health Interview Survey (CHIS) and the Breast

Cancer Family Registry (BCFR). The CHIS has data on the respondent's personal history of breast cancer and cancer family history data. These data will be used to determine how many women in the general population are classified as high risk for a given cutpoint. The BCFR has data on cancer family history and genetic test results. These data will be used to determine how well BRCAPRO classifies members of high risk families with respect to their BRCA1 or BRCA2 mutation status when using population estimates of mutation prevalence and a range of cutpoints.

We will use the following methods to compare the predictive value of BRCAPRO at each cutpoint:

Generalized R-square statistic. The generalized R-square statistic R^2 measures predictive power as a function of the likelihood ratio test, $R^2=1-(L_0/L_1)^{2/n}$.

Classification table. The classification table tabulates the risk class and compares the predicted classification to the actual classification. Cases are allocated to risk classes using the predicted probability and specified cutpoint. Specificity and sensitivity will be computed as follows:

Sensitivity = (true positives)/(total positives)

Specificity = (true negatives)/(total negative).

The receiver operating characteristic (ROC). The ROC chart is a graphical display of predictive accuracy. The chart displays the sensitivity and specificity, where sensitivity is charted as the horizontal axis and 1- specificity is charted as the vertical axis. If the ROC curve rises quickly and the area under the curve (measured by c statistic) is large, the tool has high predictive power. If the ROC curve rises slowly and the area under the curve is small, the predictive power is low.

The probability cutpoint to be incorporated in the clinical decision tool will be chosen based on its predictive value, with input from AHRQ and members of the TEP.

4. Pilot Implementation and Evaluation

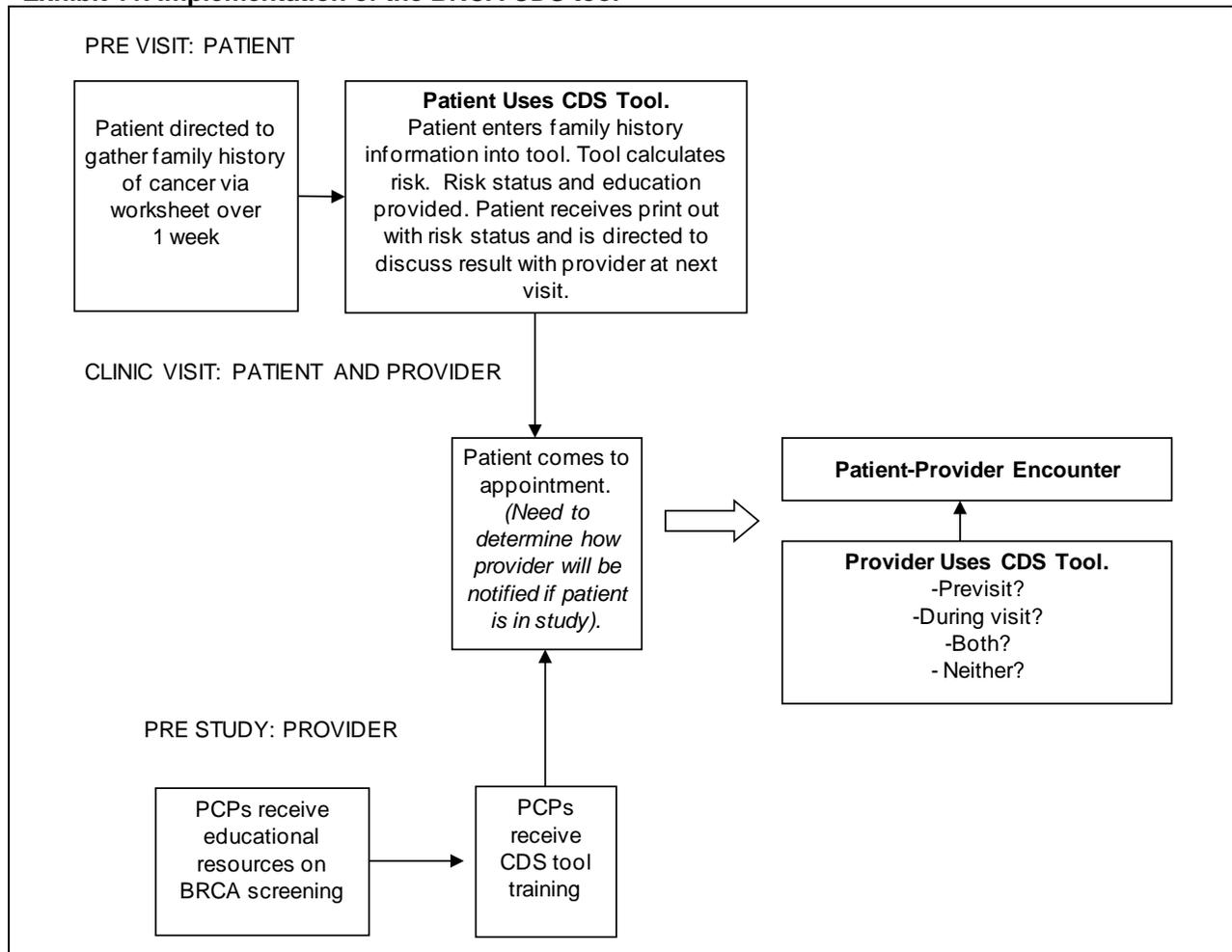
As part of this project, we are charged with assessing the impact of the BRCA1/2 tool. We have designed an implementation and evaluation approach that matches the project's budgetary limitations. Although we recognize that larger scale approaches will be needed in the future, once the tools have been refined, the proposed approach is intended to provide early yet time-sensitive information that can be used to design more rigorous studies hereafter.

4.1 Implementing the Tools in Pilot Sites

Providence Health and Baylor Health Care System (our subcontractors on this project) will each provide two primary care clinics, in which the Integrated Patient-Provider BRCA CDS tool will be implemented. Implementing the tool in all four sites will allow us to assess the factors that influence the degree to which patients and providers use the tool as intended within different practice settings. This assessment will be described in detail in Section 4.2.

As described in Section 3, the CDS tool will have two interfaces: one for the patient and one for the provider. Exhibit 11 depicts a likely approach for how patients and providers will use the tool.

Exhibit 11. Implementation of the BRCA CDS tool



Step 1: Patient Use of CDS Tool. Patients will be given instructions and a worksheet to gather their family history of cancer over 1 week prior to a scheduled appointment. The worksheet will contain all of the fields required to complete data entry for the patient cancer family history section of the tool and will be organized similarly to the data entry screens on the tool. Once these data have been entered for all family members, participants will be asked if they would like to learn their risk for having a BRCA mutation based on the cancer family history information they entered. If the patient says yes, she will be instructed to hit the appropriate control on the tool, which will trigger the calculation of the risk using the adjusted BRCAPRO algorithm (see Section 3.1). The participant will receive her risk classification and be directed to the appropriate educational module (e.g., high risk or medium/low risk). At the conclusion of the module, the patient will be directed to print out a summary to bring to her physician. This summary will contain her risk classification, her pedigree, appropriate educational messages, and specific action items, including questions to ask the physician. The tool will also include a safety net of resources for patients to turn to if they experience immediate anxiety as a result of collecting their family history and learning their risk level. Specific strategies may vary from clinic to clinic, but patients will be able to contact someone right away, if necessary.

Step 2: Provider Use of the CDS Tool. Prior to the launch of the study, physicians will be directed to a CME course about BRCA screening and trained on the purpose and use of the CDS tool. CME credit will be offered to providers. Once this education and training has been completed, providers will then be able to use the tool to aid them in screening study participants for risk of BRCA mutations.

Prior to a patient's appointment, the physician will be alerted that the patient is a study participant and be reminded to use the CDS tool. The provider can review the study participant's family history and risk status, either prior to or during the scheduled appointment. The provider will be able to fill in gaps or make corrections to the family history data. The tool will provide information and appropriate messages the provider should give to the patient based on her risk status. The tool will offer the provider suggestions about how to check the patient's knowledge via teach back or some other method. Providers can also use the tool to develop a printed instruction sheet tailored for each patient that gives additional educational messages and next steps. For high-risk patients, the printout will include contact information for genetic counselors. For medium/low risk patients, the printout will include messages about updating the cancer family history and information on breast cancer screening.

4.2 Evaluating Tools in Pilot Sites

Our preliminary pilot evaluation will focus on three objectives:

1. Assess the degree to which the CDS tool is used as designed in four clinical settings and explore the characteristics of the tool that influence adoption.
2. Pilot evaluation procedures, instruments, and processes to inform the development of a larger outcome evaluation postcontract.
3. Use the data from this pilot outcome evaluation to examine potential effects of the CDS tool on both patient and provider outcomes.

To achieve these three objectives we will evaluate the implementation and outcomes of the CDS tool^d.

4.2.1. Implementation Evaluation

Implementation evaluation focuses on assessing the degree to which an intervention has been implemented as planned, which is also referred to as fidelity.¹⁴ Many evaluations use the "black box" approach, which measures participants only before and after the intervention. This approach assumes that the intervention was delivered with fidelity; however, that is typically not the case. According to Rossi and Freeman,¹⁵ a large number of interventions that fail to demonstrate significant changes in outcomes are really failures in delivery rather than in the intervention itself. They describe three types of implementation failures: (1) no intervention, or not enough, is delivered; (2) the wrong intervention is delivered; and (3) the intervention is not standardized and varies across intervention sites or populations. Carroll et al.,¹⁴ state that "primary research into interventions and their outcomes should involve an evaluation of implementation fidelity if the true effect of the intervention is to be discerned."

Implementation is "a process, not an event."¹⁶ To conduct an implementation evaluation, core intervention components need to be identified and operationalized. Although both patients

^d Prior to this evaluation, we will secure approval through the following RTI's IRB as well as the IRBs at each of our clinical sites. In addition, we will complete and submit the needed applications for OMB clearance as advised by AHRQ.

and providers receive training and educational materials to prepare them to use the CDS tool, we consider the core intervention components to be the following: (1) use of the tool by patients; (2) use of the tool by providers; and (3) patient-provider discussion of the risk classification and next steps. All three of these core intervention components could be either adopted or rejected by the intended user groups. It is important that our evaluation be able to assess which components of the intervention are adopted, which are not adopted, and why.

Assessment of the Implementation of the Core Intervention Components

Use of the CDS tool by each patient enrolled in the study will be assessed through an examination of the family history data the patient entered. Features of the tool used by the patient will be documented. Providers' use of the tool (e.g., modules accessed, time in each module) with each study participant will be documented and associated with the patient data record.

To assess the content and level of patient-provider communication and the BRCA risk assessment, providers will complete a brief checklist after every encounter with a study participant. The format for this checklist (e.g., online, paper) will be determined after consulting with providers at our clinical sites. Patients will complete a post-visit survey before leaving the clinic. (See Section 4.2.2 and 4.2.3 for more details on data collection procedures and constructs measured in each tool.)

Assessment of Evaluation Procedures, Instruments, and Processes

When considering how to test the tool in a short timeframe with the available resources, we have set the evaluation objectives to be realistic and to inform a future larger scale evaluation. Given that our field period is limited to 8 weeks maximum, it will be challenging to accrue enough patient participants to be able to compare outcomes across clinical settings. Our plan is to implement the CDS tool in all four primary care clinics available to us for this study so that we can conduct a rigorous evaluation of the implementation and adoption of the tools. We have built in a 2-week prestudy pilot period to test out our implementation strategies, thus giving clinics the opportunity to try out the procedures and provide suggestions for improvements. This prestudy pilot will also allow us to test data collection procedures and instruments that will be used during the outcome evaluation and make needed modifications. Testing these procedures in all four clinic sites and gathering outcome data from all participants gives us the greatest opportunity to develop future plans for evaluation, implementation, and dissemination. The TEP suggested that we could visit the four data collection sites to collect process evaluation information and observational data; however, this strategy currently falls outside the scope of work for this project. Instead, information will be collected via Web-based surveys and telephone interviews, as discussed below.

Exhibit 12 presents the core evaluation components for patients and primary care providers. We have developed this assessment strategy so that we will be able to determine how different intervention components affect both adoption and outcomes. We will first describe the data collection points for the patient, followed by a description of the same for providers.

Exhibit 12. Core evaluation components for patients and providers

User	Core Evaluation Components
Patient	Pretest
	Post-test after CDS use
	Post-test after appointment with primary care provider
Provider	Prestudy assessment
	Posteducation assessment
	Postencounter checklist
	Post-study assessment

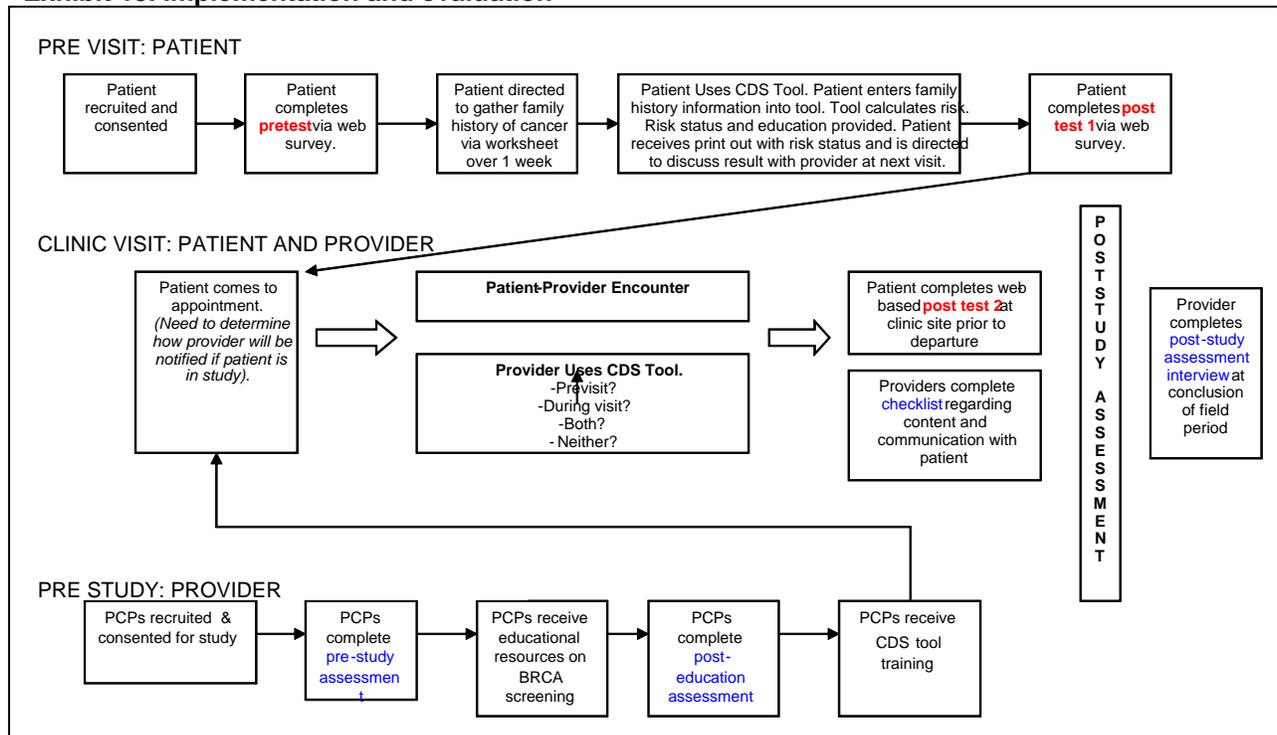
Exhibit 13 presents how the core evaluation components align with our implementation procedures.

4.2.2 Data Collection for Patients

Patients who are eligible to participate include women between the ages of 21 and 60 who (1) will see a primary care physician at one of the clinic sites for a routine well-woman appointment during the field period; (2) do not have a personal history of cancer; and (3) have access to the Internet and a printer at home.

Patients who meet the eligibility criteria for the study will be recruited and consented for the study. All procedures and materials will be submitted to RTI’s Institutional Review Board (IRB) for approval. Eligible patients will then be asked to complete a pretest via a Web-based survey. The pretest will assess the key constructs presented in our conceptual framework. At the conclusion of the Web survey, participants will print out a worksheet to use to gather their cancer family history. Participants will be asked to gather this cancer family history within about 1 week and enter it into the tool prior to their scheduled appointment. After entering the cancer family history data, each participant will receive information about her risk for BRCA mutations, will be directed to the appropriate educational module, will be given her risk status, and will be prompted to discuss her result with her physician at her scheduled appointment. Upon completion of the tool, patients will be prompted to complete a post-test that will focus on their impressions (e.g., helpfulness, utility) and use of the tool.

Exhibit 13. Implementation and evaluation



The patient will then attend her scheduled appointment where the provider will use the tool to updated any family history information, rerun the risk algorithm if needed with support of clinic staff and using the clinic’s computer resources, and receive prompts and guidance on additional information and education appropriate for the patient. It is anticipated that the use of the tool by both patients and provider will prompt an active conversation about risk and next steps.

Prior to departing the clinic, the patient will be asked to complete a postintervention Web survey that will document the patient–provider interaction from her perspective and recommendations she received from the provider. The survey will also assess changes in targeted outcomes as a result of the physician encounter.

4.2.3 Data Collection for Providers

Study sites will recruit and obtain consent from providers for the study and then ask them to participate in a prestudy assessment administered by RTI researchers via telephone interview or web survey. This structured interview or survey will assess influences on providers’ use of the CDS tool, such as knowledge, attitudes, and experiences with CDS tools, hereditary breast cancer, and BRCA mutations, as well as constructs from the health belief model and informed decisionmaking. After the prestudy assessment, providers will be asked to complete a CME course on genetic testing, including BRCA. Providers will be asked to complete a posteducation assessment via web-survey. Having providers complete a survey at this point will help determine the degree to which the resources affected their relevant knowledge and help us differentiate the effects of the education from the effects of use of the tool.

Providers will also receive training via Webinar on the use of the CDS tool and subsequent evaluation procedures. Should additional resources become available, RTI would be

happy to conduct these trainings in person. After the training, providers will then be ready to see patients over the 8-week field period. To assess whether a patient's BRCA risk assessment was discussed, providers will be asked to complete a short checklist that documents the content of the conversation, if it occurred, and recommendations given to the patient. After the 8-week field period, providers will be asked to be complete a post-study assessment via structured telephone interview or web-survey. Like the prestudy assessment, the post-study interview will assess constructs from the health belief model and informed decisionmaking as well as perceived attributes of the intervention and intent to use the tool to screen patients after the study.

4.2.4 Piloting Evaluation Methods and Tools

One of the objectives of our evaluation is to pilot our evaluation procedures, instruments, and processes to inform the development of a larger outcome evaluation post-contract. For a scaled-up evaluation to be successful, the evaluation procedures need to be as nonburdensome as possible for both patients and providers. We will seek to answer the following questions regarding the implementation of the evaluation:

- How does implementation of the evaluation protocol vary in each clinic? Are patients and providers compliant with the evaluation protocol? Why or why not?
- What are the barriers and facilitators toward implementing the evaluation at each site? What would need to be put in place at each site to support a scaled-up outcome and implementation evaluation?
- Do patients/providers understand the questions on the outcome assessments? Are the data gathered on the surveys or via the structured interviews complete? Are questions working as intended? Are there any questions that are not producing variability in responses? Which ones and why?
- Do patients and providers perceive the data collection to be burdensome? What alternate methods would they prefer?

These questions will be incorporated into post-test 2 for the patient and the post-study interview for the providers.

In addition to obtaining study participants' perspectives on the evaluation methods and tools, we will assess whether our chosen methods are obtaining the data needed for both the implementation and outcome evaluations. Through a review and analysis of the data, we will identify any problematic questions or procedures. Our final report will detail how well the evaluation methods worked in this pilot and recommend specific alterations or additions.

4.3 Outcome Evaluation and Data Analysis

Using a preintervention and postintervention design, we will conduct the outcome evaluation in all four clinics. We anticipate that over 8 weeks, each clinic will be able to accrue up to 40 patients, with the overall accrual goal of 160 patients. The TEP members advised us that this goal was quite ambitious and perhaps unachievable during our pilot period. We anticipate that one to two providers per clinic will participate in the study, so we will have between four and eight providers participating in the study.

Outcomes we will measure are listed in Exhibit 7. Constructs for the outcome evaluation can be found in Exhibit 14 and Exhibit 15, which present, for each construct and user group, the evaluation question to be answered and the instrument that will be used to assess the construct.

Exhibit 14. Outcome evaluation: providers

Construct	Evaluation Question	Data Collection Instrument
Demographics: Type of primary care provider, age, length of time in practice	What are the demographic characteristics of the providers in the study?	Prestudy assessment
Knowledge of CDS tools, hereditary breast cancer, genetic testing, and BRCA screening	How much do providers know about CDS tools, hereditary breast cancer, genetic testing, and BRCA screening?	Prestudy assessment
Attitudes toward CDS tools, hereditary breast cancer, and BRCA screening	What are providers' attitudes toward CDS tools, hereditary breast cancer, genetic testing, and BRCA screening?	Prestudy assessment
Previous use of CDS tools or experience in genetic testing	Have providers used any type of CDS tool in the past? What type of experience do providers have with genetic testing?	Prestudy assessment
Patient-provider communication about risk status	How frequently did providers discuss patients' risk status with them during the clinical encounter? What content and messages were included in that discussion?	Postencounter checklist
Perception of patient-provider interaction	How well does the provider perceive that the patient understood her risk of BRCA mutations?	Postencounter checklist
Intention to use the CDS tool	Do providers intend to use the CDS tool in their practice after the study ends?	Post-study assessment
Use of the tool	Do providers report that they used the tool? How often do they report using the tool? When do they report using the tool (i.e., before or during a patient visit)?	Post-study assessment
Referral and referral alignment	Do providers refer patients who were at high risk for genetic counseling? Why or why not? Do they refer patients who were not high risk? Why? Do providers' referrals match what was suggested by the tool?	Post-study assessment + tool metrics

Constructs for the implementation evaluation can be found in Exhibit 15, which present, for each construct and user group, the evaluation question to be answered and the instrument that will be used to assess the construct. We will use implementation measures gathered from multiple sources (e.g., CDS tool metrics, patient and provider post-tests, postencounter checklist) to develop indexes of implementation of each of the core components of the evaluation. We will combine these indexes of the core components to create an overall index of implementation. We will use this index at the clinic level and, should there be varying levels of implementation, we will use this to compare outcomes between clinics, between providers, and between patients.

Exhibit 15. Outcome evaluation: patients

Construct	Evaluation Question	Data Collection Instrument
Demographics/characteristics: age, race/ethnicity, marital status, children	What are the demographics characteristics of the patients in the study?	Pretest
Length of time with provider	How long has the patient been a patient of the practice?	Pretest
Comfort with computers	Does the patient regularly use a computer? How comfortable is she in using one?	Pretest
Trust in provider	To what degree does the patient trust the provider or practice?	Pretest
Health status	How does the patient perceive her health status?	Pretest
Close friends/family with cancer	Does the patient have any close friends or family members with cancer?	Pretest
Knowledge of CDS tools, hereditary breast cancer, genetic testing, and BRCA screening	How much do patients know about CDS tools, hereditary breast cancer, genetic testing, and BRCA screening?	Pretest and post-test 1
Previous use of CDS tools or experience in genetic testing	Have patients used any type of CDS tool in the past? What type of experience do patients have with genetic testing?	Pretest
Perceived risk of patient seen at clinic	Do patients perceive they are at risk for BRCA mutations?	Pretest and post-test 1
Perceived severity of hereditary breast cancer	How severe do patients feel hereditary breast cancer is?	Pretest and post-test 1
Perceived benefits of risk assessment	Do patients perceive that learning their risk of BRCA mutations would be beneficial to them?	Pretest and post-test 1
Perceived barriers/costs of gathering cancer family history and risk assessment	What do patients perceive to be the barriers to gathering their family's cancer history? What do patients perceive to be the barriers to learning their risk?	
Decision recognition	Do high risk patients recognize that they need to make a decision about whether or not to (1) see a genetic counselor, (2) be tested for BRCA mutations, (3) discuss their risk status with family members?	Post-test 2
Patient-provider communication about risk status	How frequently did providers discuss patients' risk status with them during the clinical encounter? What content and messages were included in that discussion?	Post-test 2
Self-efficacy in communicating with provider	How confident are patients in their ability to ask their provider questions? How confident are patients in their ability to providers to clarify information they don't understand?	Pretest and post-test 1
Perceptions of patient-centered communication	Do patients feel their provider exchanged information with them, answered questions and managed their uncertainty, supported a healing relationship, and made decisions with them?	Post-test 2
Perception of patient-provider interaction	Was the patient satisfied with the information related to BRCA risk and genetic testing discussed in the interaction? How does the patient rate the quality of the interaction? How well does the patient perceive the provider did in helping her understand her risk of BRCA mutations?	Post-test 2
Intention to use the CDS tool	Do patients intend to use the CDS tool after the study if their cancer family history changes?	Post-test 2
Use of the tool	Do patients report they used the tool? Do patients report that their provider used the tool?	Post-test 1 Post-test 2
Decision to gather family history	What proportion of patients decide to gather their family history? What reasons do patients who chose not to gather their family history give?	Post-test 1
Decision to learn risk	What proportion of patients decide to learn their risk of having a BRCA mutation? What reasons do patients who chose not to learn their risk give?	Post-test 1
Delivery of tool output	Do patients bring the printed output from the CDS tool to their provider? Why or why not?	Post-test 2

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Exhibit 15. Outcome evaluation: patients (continued)

Construct	Evaluation Question	Data Collection Instrument
Comprehension of risk result	Do patients understand the result of their risk assessment?	Post-test 1 Post-test 2
Referral	Were patients at high risk referred for genetic counseling? Why or why not? Were patients who were not at high risk referred? Why?	Post-test 2
Intent to follow provider's recommendation	Do patients intend to follow the recommendations concerning screening and referral, if given? Why or why not?	Post-test 2

Exhibit 16. Implementation evaluation: providers

Construct	Evaluation Question	Data Collection Instrument
Relative advantage of the innovation	Is using the CDS tool to gather a patient's family history of cancer better than previous practices (which may be <i>not</i> gathering the family history?) Is using the CDS tool to screen women for risk of having a BRCA mutation better than not screening women at all? How much time does it take for providers to use the tool prior to a patient's visit? Is this time (cost) worth the benefit (screening women or having a patients' family history of cancer available)? Does the CDS stimulate better quality patient-provider communication than that which takes place without using the CDS tool?	Post-study assessment
Compatibility of the innovation	Is use of the tool compatible with providers' current practices and procedures? If not, what could make it more compatible? Or did providers have to alter current practices to use the tools? Were those alterations acceptable?	Post-study assessment
Complexity of the innovation	How easy or difficult do providers and patients find the tool? Are the messages and information presented easily understood? Are they remembered? Are they believed? Are there particular aspects of the tool that providers find problematic or too complex/difficult? How should they be adjusted?	Post-study assessment
Trialability or flexibility of the innovation	How and why does implementation of the CDS tool vary at each site? Do providers use the tool as designed? Do clinics adjust implementation procedures? If so, how and why do they adjust? Does use change over time? Do providers perceive the tool to be flexible? Do providers use the tool prior to the patient's visit, during the patient's visit, or both? Do providers perceive that the tool can be incorporated into practice? Why or why not? What are the barriers to implementation? What would facilitate implementation?	Post-study assessment
Observability of the innovation	Do providers perceive that others in their practice are using the tool? Do they perceive that other providers would believe they should use the tool? Do they discuss their use with others? What do they say? What do their colleagues say? Do providers believe that their physicians are assessing whether or not they are using the tool correctly? Do providers perceive that their peers at their site will know whether or not they are using the tool?	Post-study assessment
Overall satisfaction with the tool	Overall, how satisfied were providers with the tool? What recommendations do they have for improving the tool's functionality or content? What parts of the tool were most and least useful?	Post-study assessment

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Construct	Evaluation Question	Data Collection Instrument
Use of the tool	Did providers use the tool with each patient in the study? Why or why not?	Post-study assessment Post-encounter checklist
Content of tool used	What parts of the tool were most used?	Tool metrics
Efficacy of the tool	Do providers believe that the tool provides accurate risk assessments for their patients? Do providers perceive that the tool effectively educates patients about BRCA risk? Do providers believe that the information support provided in the tool is credible and accurate? Do providers believe that the tool helps them better communicate with their patients about the risk of BRCA mutations?	Post-study assessment
Tool vs. provider recommendations	Did providers refer high risk patients for genetic counseling? Why or why not?	Post-encounter checklist Post-study assessment
Evaluation fidelity	Did providers follow the evaluation protocol? Why or why not?	Post-study assessment
Perceptions of evaluation	What do providers perceive were barriers to participating in the evaluation? Do providers perceive the data collection to be burdensome? What alternate methods or procedures would they prefer? What do providers believe would improve evaluation procedures or instruments? What would be needed for their clinic to participate in a longer and larger evaluation?	Post-study assessment
Effectiveness of data collection tools and procedures	Did providers understand the questions asked on the prestudy and post-study assessment? Were data gathered from them complete?	Post-study assessment

Exhibit 17. Implementation evaluation: patients

Construct	Evaluation Question	Data Collection Instrument
Relative advantage of the innovation	Do patients perceive that using the CDS tool to document and share their family history of cancer with their providers is better than previous practices (which may be <i>not</i> gathering the family history?) Do patients perceive the tool to be effective in learning about BRCA screening and genetic testing compared to other methods they would likely use? How much time does it take for patients to use the tool prior to their visit? Is this time (cost) worth the benefit (screening women or discussing risk with provider)? Does the CDS stimulate better quality patient-provider communication than that which takes place without using the CDS tool?	Post-test 1 (after CDS use) Post-test 2 (after appointment)
Compatibility of the innovation	Is use of the tool compatible with patients' computer use? Were patients able to remember to complete the tool prior to their visit?	Post-test 1 (after CDS use)
Complexity of the innovation	How easy or difficult do patients find the tool? Are the messages and information presented easily understood? Are they remembered? Are they believed? Are there particular aspects of the tool that patients find problematic or too complex/difficult? How should they be adjusted?	Post-test 1 (after CDS use)

Exhibit 17. Implementation evaluation: patients (continued)

Construct	Evaluation Question	Data Collection Instrument
Trialability or flexibility of the innovation	How easy or difficult was it for patients to use the tool prior to the visit? How easy or difficult was it for patients to contact their family members to gather their cancer history? Did patients use the worksheet to record family history prior to entry into the tool? Was the worksheet an effective way to record the information? How easy or difficult was it for patients to enter family cancer history information into the tool? How easy or difficult was it for patients to use the educational modules?	Post-test 1 (after CDS use)
Observability of the innovation	Do patients perceive that their provider will review the cancer family history they record in the tool? What do they perceive to be the consequences if they do not complete this task?	Post-test 1 (after CDS use)
Perception of patient-provider interaction	Was the patient satisfied with the information related to BRCA risk and genetic testing discussed in the interaction? How does the patient rate the quality of the interaction? How effective does the patient perceive the provider to be in providing information about risk of BRCA mutations?	Post-test 1 (after CDS use) Post-test 2 (after appointment)
Overall satisfaction with the tool	Overall, how satisfied were patients with the tool? What recommendations do they have for improving the tool's functionality or content? What parts of the tool were most and least useful?	Post-test 1 (after CDS use) Post-test 2 (after appointment)
Use of the tool	Did patients use the tool as designed? Why or why not?	Post-test 1 (after CDS use)
Content of tool used	What parts of the tool were most used?	Post-test 1 (after CDS use)
Efficacy of the CDS tool	How credible do patients find the information presented in the tool? Do patients believe that their risk assessment result is accurate?	Post-test 2 (after CDS use)
Tool vs. provider recommendations	Were high risk patients referred for genetic counseling? Why or why not?	Post-test 2 (after appointment)
Evaluation fidelity	Did patients follow the evaluation protocol? Why or why not?	Post-test 2 (after appointment)
Perceptions of evaluation	What do patients perceive were barriers to participating in the evaluation? Do patients perceive the data collection to be burdensome? What alternate methods or procedures would they prefer? What do patients believe would improve evaluation procedures or instruments?	Post-test 2 (after appointment)
Effectiveness of data collection tools and procedures	Did patients understand the questions asked on the pre-study and post-study assessment? Were the data gathered from them complete?	Post-test 2 (after appointment)

These measures of implementation will allow us to determine how implementation of the intervention affects outcomes. The timing of our data collection allows us to examine the individual impact of different intervention components. For example, our design for patients (pretest to post-test 1) allows us to examine the effects of completing the patient portion of the CDS tool on selected outcomes independent of the patient-provider interaction. The degree to which implementation of all intervention components affects patient outcomes will be examined by comparing outcome measures from pretest to post-test 2.

For providers, our design allows us to examine the effects of receiving educational resources on BRCA screening (prestudy assessment to posteducation assessment) independent of their knowledge and use of the CDS tool or their interaction with patients who have used the tool. The degree to which using the tool with study patients affected provider outcomes will be examined by comparing outcome measures from the prestudy assessment to outcome measures from the post-study assessment. We will also determine whether attributes of the innovation and constructs from the health belief model moderate the use of the tool by providers and provider outcomes.

5. Project Timeline and Next Steps

5.1 Project Timeline

This project began July 28, 2008, and we delivered to AHRQ a preliminary work plan for the project in early September 2008. Since then, we have had discussions internally at RTI and with the AHRQ Project Officer about the vision and plans for the CDS tools. In our most recent discussion with the AHRQ Project Officer, we concluded that given what we have learned to date, developing one BRCA CDS tool that incorporates interfaces for both patients and providers is the most promising strategy.

As our plans for this project evolve, we are faced with the challenge of completing the tools on time to meet our project timeline while ensuring that we incorporate the necessary inputs (e.g., results from the literature review; advice from TEP members, experts, our clinical partners, and users; and detailed requirements gathering) to develop the best tool and evaluation of the tool possible with the allocated resources. To meet this challenge, we suggest a revised end date for the BRCA project of January 29, 2010 (7 weeks later than is currently planned). Based on the evolution of this project to date, we also suggest alternative due dates for some of the deliverables. The proposed revised project timeline is presented in Exhibit 18. The remainder of this section describes our rationale for these suggested changes.

Requirements-Gathering Process. As the project has unfolded, we have recognized the importance of having one task inform the next (e.g., the literature review needs to inform the tool development). We identified gaps in the literature regarding providers' baseline behaviors and educational needs regarding BRCA screening; thus, have added a more rigorous needs assessment of providers to help inform the content and design of the tool. Using the results from the literature review and input from the TEP has also been essential in developing the questions for our IT specialist interviews. These assessments took place in December, 2008. Completing these assessments and obtaining this feedback are essential steps in our requirements-gathering process and will help ensure that we are developing a tool that is usable by patients and providers and adaptable to varying IT platforms used in primary care clinics. Our goal is to have this requirements-gathering process completed by January 31, 2009. Production of the tool can begin soon thereafter.

Tool Production. Given its complexity and dual interfaces, we estimate production to take a minimum of 5 months, with the first version of the tool being delivered to AHRQ on June 1, 2009—approximately 2 months later than in our original work plan. This later delivery date will allow us to use the BRCA PRO to complete the accuracy testing prior to the delivery of the first version of the tool, rather than after as originally planned. Extending the timeline by 2 months at

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this stage has the added benefit of giving us the time to receive approval to use data from NCI's Breast Cancer Family Registry for the accuracy testing; this approval process takes approximately 4 months.

We will subject the first version of the tool to usability testing with members of our second TEP (providers and patients). Based on these results, we will produce and deliver a second version of the tool to AHRQ on June 29, 2009. We will use this second version to evaluate its implementation and outcomes in the primary care clinics with which we have partnered. The third and final version of the tool will incorporate results from the implementation and outcome evaluation of the tool in the clinics. We will deliver this final version to AHRQ at the conclusion of the contract.

Tool Production. Given its complexity and dual interfaces, we estimate production to take a minimum of 5 months, with the first version of the tool being delivered to AHRQ on June 1, 2009—approximately 2 months later than in our original work plan. This later delivery date will allow us to use the BRCAPRO to complete the accuracy testing prior to the delivery of the first version of the tool, rather than after as originally planned. Extending the timeline by 2 months at this stage has the added benefit of giving us the time to receive approval to use data from NCI's Breast Cancer Family Registry for the accuracy testing; this approval process takes approximately 4 months.

We will subject the first version of the tool to usability testing with members of our second TEP (providers and patients). Based on these results, we will produce and deliver a second version of the tool to AHRQ on June 29, 2009. We will use this second version to evaluate its implementation and outcomes in the primary care clinics with which we have partnered. The third and final version of the tool will incorporate results from the implementation and outcome evaluation of the tool in the clinics. We will deliver this final version to AHRQ at the conclusion of the contract.

Exhibit 18. Project timeline

Task	Start Date	Due Date	Task Completed?	New Deliverable Date Proposed
Task 1—Literature Review and TEP				
Kickoff call and notes	8/5/2008	8/11/2008	<input type="checkbox"/>	
Abstract		8/25/2008	<input type="checkbox"/>	
Conference calls and summaries (due 1 week after calls)		monthly		
Invoices (15th day of the month)		monthly		
Peer review and TEP list	8/5/2008	8/25/2008	<input type="checkbox"/>	
Work plan #1	8/5/2008	9/2/2008	<input type="checkbox"/>	
Literature Review				
Search and retrieval	8/6/2008	9/26/2008	<input type="checkbox"/>	
Draft literature review portions of report	9/19/2009	10/13/2009	<input type="checkbox"/>	
TEP review of draft report		10/17/2008	<input type="checkbox"/>	
Incorporate reviewers comments	10/18/2008	12/18/2008		

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Exhibit 18. Project timeline (continued)

Task	Start Date	Due Date	Task Completed?	New Deliverable Date Proposed
Final literature review report to AHRQ (including the Disposition of Reviewer Comments Report)	12/19/2008	1/20/2009		
Task 2: Develop BRCA Tool				
Task 2 and 3 Work Plan				
Proposed plan Task 2 and 3 to AHRQ	11/17/2008	12/1/2009	<input type="checkbox"/>	
Send to TEP/Peer review for feedback	12/2/2008	12/15/2008		
TEP conference call to review work plan	12/10/2008	12/10/2008		
Final plan Phase 2 and 3 work plans to AHRQ	12/16/2008	2/2/2009		
Feasibility Assessment				
Create interview guide	11/1/2008	12/1/2008		
Schedule and conduct IT interviews	12/2/2008	12/15/2008		
Feasibility brief—including as an appendix for phases 2 and 3 final work plan	12/16/2008	2/2/2009		<input type="checkbox"/> (earlier date than original)
Physician Needs Assessment				
Create interview guide	11/1/2008	12/1/2008		
Schedule and conduct primary care physician interviews	12/2/2008	12/15/2008		
Needs assessment brief—including as an appendix for phases 2 and 3 work plan	12/16/2008	12/31/2009		
Accuracy Testing—Retrospective and Hypothetical Data				
Select retrospective dataset	10/1/2008	12/1/2008		
Develop hypothetical dataset	1/1/2009	1/31/2009		
Dataset secure (4 months for NCI dataset)	12/1/2008	3/31/2009		
Write program	1/1/2009	1/31/2009		
Run accuracy testing	4/1/2009	4/15/2009		
Consult with Dr. Parmigiani	4/16/2009	4/17/2009		
Adjust algorithm	4/20/2009	4/30/2009		
DEVELOP TOOL				
CDS Requirements				
Aims and objectives, required outcomes, key learner content, data collection and IT needs, and Section 508 compliance	10/1/2008	1/1/2009		
Tool Production (includes iterative testing during production phase)				

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Exhibit 18. Project timeline (continued)

Task	Start Date	Due Date	Task Completed?	New Deliverable Date Proposed
Tool design and final design documentation (flow diagrams, story boards, etc.)	1/5/2009	3/2/2009		
Engage selective TEP members/consultants as needed	1/5/2009	4/1/2009		
Produce assets (video, text, narration, graphic design)	3/2/2009	4/1/2009		
Program and integrate assets	4/1/2009	5/15/2009		
Incorporate final algorithm based on accuracy testing	5/18/2009	5/29/2009		
Delivery of First Version of Tool	6/1/2009	6/1/2009		<input type="checkbox"/>
2nd TEP/Usability Testing				
Post-development usability testing	6/1/2009	6/12/2009		
Tool revisions (as necessary)	6/15/2009	6/26/2009		
Delivery Second Version of Tool	6/29/2009	6/29/2009		<input type="checkbox"/>
Tool Development Report				
Tool development draft report to AHRQ	6/1/2009	7/13/2009		
Peer review of tool development report	7/13/2009	7/31/2009		
Finalize and deliver tool development report to AHRQ	8/2/2009	8/28/2009*		<input type="checkbox"/>
TASK 3 TOOL EVALUATION				
Design Instruments				
Finalize study outcomes	12/1/2008	12/15/2008		
Develop patient instruments and procedures	12/15/2008	1/30/2009		
Develop physician instruments and procedures	12/15/2009	1/30/2009		
locate provider education materials	1/2/2009	1/30/2009		
design recruitment tracking system	2/1/2009	2/28/2009		
Design outcome and implementation data collection system	5/1/2009	5/31/2009		
IRB Approval				
RTI IRB		—		
Develop RTI IRB application	1/5/2009	1/30/2009		
Submit IRB application to RTI IRB	2/1/2009	2/28/2009		<input type="checkbox"/>
Evaluation site IRBs				
Develop, submit, and review IRB applications	3/1/2009	4/30/2009		
OMB Approval				

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Exhibit 18. Project timeline (continued)

Task	Start Date	Due Date	Task Completed?	New Deliverable Date Proposed
Develop one-page study description for OMB liaison (NEED TEP REVIEW OF DESIGN FIRST)	12/10/2008	12/22/2008		<input type="checkbox"/> (additional deliverable)
Develop and submit clinical exemption	1/2/2009	3/31/2009		<input type="checkbox"/> (additional deliverable)
Develop and submit package under AHRQ's customer satisfaction OMB	1/2/2009	3/31/2009		<input type="checkbox"/> (additional deliverable)
Develop full OMB application for scaled-up evaluation post-contract				
Supporting statement / justification	2/2/2009	3/31/2009		
60-day notice	2/6/2009	2/6/2009		
30-day notice	3/10/2009	3/10/2009		
Draft OMB package to AHRQ for review	3/13/2009	3/20/2009		
Finalize OMB package	3/23/2009	3/31/2009		
OMB submission to AHRQ	3/31/2009	3/31/2009		<input type="checkbox"/>
Secure OMB approval (9 months)	4/1/2009	12/31/2009		
Evaluation at Sites				
Initiate sites (materials, study process, timeline)	6/29/2009	7/10/2009		
Recruit patients (2 weeks prior to pilot study launch)	7/13/2009	7/24/2009		
Conduct pilot implementation (2 weeks)	7/27/2009	8/7/2009		
Identify issues and recommendations	8/10/2009	8/14/2009		
Tool and procedure tweaking (if needed)	8/17/2009	8/28/2009		
Progress report: pilot implementation	8/31/2009	9/18/2009		<input type="checkbox"/>
BEGIN EVALUATION				
Recruit patients (2 weeks prior to study launch)	8/17/2009	8/31/2009		
Collect data (6 weeks)	8/31/2009	10/16/2009		
Analysis and Reporting				
Organize/clean data	10/26/2009	11/13/2009		
Analyze results: implementation	11/16/2009	11/20/2009		
Analyze results: outcome	11/23/2009	11/27/2009		
Write draft report on development and evaluation of CDS tools	11/30/2009	12/31/2009		<input type="checkbox"/>
AHRQ and peer review of draft report	1/4/2009	1/15/2010		
Incorporate reviewers' comments into report	1/18/2009	1/29/2010		

Exhibit 18. Project timeline (continued)

Task	Start Date	Due Date	Task Completed?	New Deliverable Date Proposed
Final report on development and evaluation of CDS tool to AHRQ	1/29/2009	1/29/2010		<input type="checkbox"/>
Tool Dissemination				
Tool dissemination strategies	12/1/2009	1/15/2010		
Final tools (third version), technical documents, and instructions to AHRQ	11/30/2009	1/29/2010		<input type="checkbox"/>

*Deliverable from Baylor to RTI: will be folded into Final Report on Development and Evaluation of CDS tools.

Evaluation Clearances. In addition to the suggested changes to the timeline for the tool, we also suggest changes to the deliverables associated with the evaluation. Originally, the IRB submission package was due on December 1, 2008, and the OMB package was due 1 week later, December 8, 2008. However, since developing our first work plan, we have received preliminary advice from the AHRQ OMB representative to pursue a clinical care exemption for the patient portion of the evaluation and clearance through AHRQ’s customer satisfaction OMB umbrella clearance. This is a critical option because the IRB and OMB packages that we will submit for approval require final versions of the instruments and evaluation design. However, the final versions of the instruments and evaluation design are driven by the conceptual framework, which had not been shared with AHRQ or the CDS TEP until the development of this work plan. Once we receive feedback from AHRQ and the TEP, we can finalize the framework, design, and outcomes, and then develop the data collection instruments. Once these instruments are developed, we will have all the elements needed to draft the IRB package (revised deliverable date is February 28, 2009). After we receive comments from AHRQ and the TEP on this work plan, we will draft a one-page description of the evaluation for the AHRQ OMB representative (proposed due date is December 22, 2009). We will use her feedback to develop the clinical care exemption and customer satisfaction clearance for OMB by March 31, 2009, to leave sufficient time for approval prior to the evaluation.

As negotiated with the AHRQ Project Officer, we plan to develop and submit a full OMB package for a scaled-up evaluation that could be completed in a future contract. We also propose March 31, 2009, as the submission date for this larger package. Assuming that clearance may take 9 months, it is likely that AHRQ would have approval prior to the end of our contract.

Evaluation at Clinic Sites. Since we are proposing that the second version of the tool be used in the clinical evaluation, and since it will be ready June 29, 2009, we would begin the 2-week pilot evaluation thereafter. For this prestudy evaluation, sites would spend 2 weeks recruiting patients prior to the pilot evaluation period, which would begin July 27, 2009, and end August 7, 2009. Tools and procedures would be adjusted based on this prestudy pilot. For the evaluation study, sites would begin recruiting patients from August 17 through August 31, 2009. The field period for the evaluation would be from August 31 through October 16, 2009. All deliverable dates for associated reports have been adjusted accordingly.

5.2 Next Steps

This draft work plan was reviewed by TEP members in December 2008, and RTI hosted a conference call to discuss TEP members' feedback on this work plan. We have used the feedback to develop this final version of the work plan.

It would be beneficial to obtain additional input into the user requirements for the tool from a larger number of providers and patients than we originally budgeted for. Doing so would be beneficial and greatly improve our ability to develop a tool that will be useful and useable to providers from a variety of clinical settings serving diverse patient populations. Should AHRQ be interested in adding this step to the work plan and further extending the timeline, the RTI team is more than willing to perform this additional work if resources are available.

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Appendix A. Patient Decision Aid Checklist for Users



International Patient Decision Aid Standards (IPDAS)
Collaboration

IPDAS 2005: Criteria for Judging the Quality of Patient Decision Aids

Steering Committee: A O'Connor (CA) & G Elwyn (UK) (co-leaders) with A Barratt (AU), M Barry (US), A Coulter (UK), M Holmes-Rovner (US), N Moumjid (FR), H Llewellyn-Thomas (US), M O'Kane (US), R Thomson (UK), D Stacey (CA), T Whelan (CA) **Methods Group:** G Elwyn (leader, UK) with S Bernstein (US), P Shekelle (US), R Thomson (UK), R Volk (US) **Stakeholder Leader:** A Coulter (UK) **Quality Criteria Panels:** A O'Connor (CA) & H Llewellyn-Thomas (US) (editors) with J Austoker (UK), A Barratt (AU), M Barry (US), H Bekker (UK), J Belkora (US), C Braddock (US), P Butow (AU), E Chan (US), A Charvet (Switz), A Clarke (UK), J Davison (CA), J Dolan (US), A Edwards (UK), V Entwistle (UK), A Fagerlin (US), D Feldman-Stewart (CA), J Fowler (US), D Frosch (US), P Hewitson (UK), M Holmes-Rovner (US), T Hope (UK), MJ Jacobsen (CA), A Kennedy (Switz), S Knight (US), M Kupperman (US), B Ling (US), T Marteau (UK), K McCaffery (AU), N Moumjid (FR), A Mulley (US), M O'Connor (US), E Ozanne (US), M Pignone (US), A Raffle (UK), C Ruland (NO), L Schwartz (US), K Sepucha (US), S Sheridan (US), S Stableford (US), D Stacey (CA), D Stilwell (US), V Tait (CA), D Timmermans (NL), L Trevena (AU), T Whelan (CA), C Wills (US), S Woloshin (US), S Ziebland (UK)

What are patient decision aids and why are they needed?

Patient decision aids are tools to help people participate in their health decisions in ways they prefer. They are used when there is more than one medically reasonable option to diagnose or treat a health problem. Each of the options has good and bad features that people value differently. Even when two people are in the same situation, what is important for one person may be different for another person. Therefore, there is no clear answer that applies to everyone. The best choice involves matching which features matter most to a person with the option that has these features. To make a good decision, you need an expert on the facts (e.g. a health practitioner) and an expert on which features matter most (e.g. the patient) and a way to share their views with each other in ways they prefer.

Patient decision aids aim to do three things to prepare a person for decision making. They provide facts about a person's condition, the options and their features. They help people to clarify their values (the features that matter most to them). They help people to share their values with their health care practitioner and others, so a course of action can be planned that matches their values. Patient decision aids do not advise people to choose one option over another. They do not replace counseling from a health care practitioner. Instead, they prepare people to discuss the options with their health care practitioner.

An international group of researchers, known as the 'Cochrane Review Team of Patient Decision Aids' is compiling decision aids and summarizing the results of research trials. The latest review of 34 studies shows that patients and practitioners who use patient decision aids make better decisions. Patients participate more, know more, and have more realistic expectations of what might happen. They are more likely to receive an option with features they most value (O'Connor et al., *Cochrane Library*, 2003).

The **International Patient Decision Aid Standards (IPDAS)** Collaboration is a group of researchers, practitioners and stakeholders from around the world. The goal is to establish an internationally approved set of criteria to determine the quality of patient decision aids. These criteria will be helpful to a wide variety of individuals and organizations that use and/or develop patient decision aids.

Why are standards needed?

There are over 500 patient decision aids available or being developed by many different individuals and groups around the world. However, people have difficulty knowing whether or not a decision aid is a source of reliable health information that can help in decision making.

How were the standards obtained?

There was a 2-stage evidence-informed Delphi consensus process

- Participants included 122 people from 14 countries and 4 stakeholder groups [researchers/developers; health professionals/ patient/consumers; policy makers/health plan administrators]
- A voting document was developed from a series of background papers on 12 quality domains. [The experts who wrote these papers are listed above]. Before voting on the importance of each criterion in judging the quality of a patient decision aid, voters reviewed: definition of decision aids; definition of criterion; theoretical link between criterion and decision quality; and empirical evidence supporting or not supporting its use in decision aids. Evidence was derived from fundamental studies and a Cochrane Collaboration systematic review of randomized trials of patient decision aids.

The standards are summarized in a users' checklist on the next page.

For more information and to obtain copies of the IPDAS documents visit our website at

www.ipdas.ohri.ca

Table 3. IPDAS Patient Decision Aid Checklist for Users

I. Content: Does the patient decision aid ...	
Provide information about options in sufficient detail for decision making?	
<ul style="list-style-type: none"> <input type="checkbox"/> describe the health condition 3.1 <input type="checkbox"/> list the options 3.2 <input type="checkbox"/> list the option of doing nothing 3.3 <input type="checkbox"/> describe the natural course without options 3.4 <input type="checkbox"/> describe procedures 3.5 <input type="checkbox"/> describe positive features [benefits] 3.6 <input type="checkbox"/> describe negative features of options [harms / side effects / disadvantages] 3.7 <input type="checkbox"/> include chances of positive / negative outcomes 3.8 	<p>Additional items for tests</p> <ul style="list-style-type: none"> <input type="checkbox"/> describe what test is designed to measure 3.9 <input type="checkbox"/> include chances of true positive, true negative, false positive, false negative test results 3.10 <input type="checkbox"/> describe possible next steps based on test result 3.11 <input type="checkbox"/> include chances the disease is found with / without screening 3.12 <input type="checkbox"/> describe detection / treatment that would never have caused problems if one was not screened 3.13
Present probabilities of outcomes in an unbiased and understandable way?	
<ul style="list-style-type: none"> <input type="checkbox"/> use event rates specifying the population and time period 3.14 <input type="checkbox"/> compare outcome probabilities using the same denominator, time period, scale 3.15 3.16 3.17 <input type="checkbox"/> describe uncertainty around probabilities 3.18 <input type="checkbox"/> use visual diagrams 3.19 <input type="checkbox"/> use multiple methods to view probabilities [words, numbers, diagrams] 3.20 	<ul style="list-style-type: none"> <input type="checkbox"/> allows the patient to select a way of viewing probabilities [words, numbers, diagrams] 3.21 <input type="checkbox"/> allow patient to view probabilities based on their own situation [e.g. age] 3.22 <input type="checkbox"/> place probabilities in context of other events 3.23 <input type="checkbox"/> use both positive and negative frames [e.g. showing both survival and death rates] 3.24
Include methods for clarifying and expressing patients' values?	
<ul style="list-style-type: none"> <input type="checkbox"/> describe the procedures and outcomes to help patients imagine what it is like to experience their physical, emotional, social effects 4.1 	<ul style="list-style-type: none"> <input type="checkbox"/> ask patients to consider which positive and negative features matter most 4.2 <input type="checkbox"/> suggest ways for patients to share what matters most with others 4.3
Include structured guidance in deliberation and communication?	
<ul style="list-style-type: none"> <input type="checkbox"/> provide steps to make a decision 5.1 <input type="checkbox"/> suggest ways to talk about the decision with a health professional 5.2 	<ul style="list-style-type: none"> <input type="checkbox"/> include tools [worksheet, question list] to discuss options with others 5.3
II. Development Process: Does the patient decision aid ...	
Present information in a balanced manner?	
<ul style="list-style-type: none"> <input type="checkbox"/> able to compare positive / negative features of options 6.1 	<ul style="list-style-type: none"> <input type="checkbox"/> shows negative / positive features with equal detail [fonts, order, display of statistics] 6.2
Have a systematic development process?	
<ul style="list-style-type: none"> <input type="checkbox"/> includes developers' credentials / qualifications 7.1 <input type="checkbox"/> finds out what users [patients, practitioners] need to discuss options 7.2 7.3 7.4 <input type="checkbox"/> has peer review by patient / professional experts not involved in development and field testing 7.5 7.6 <input type="checkbox"/> is field tested with users [patients facing the decision; practitioners presenting options] 7.7 7.8 7.9 	<p>The field tests with users [patients, practitioners] show the patient decision aid is:</p> <ul style="list-style-type: none"> <input type="checkbox"/> acceptable 7.10 7.11 <input type="checkbox"/> balanced for undecided patients 7.12 <input type="checkbox"/> understood by those with limited reading skills 7.13
Use up to date scientific evidence that is cited in a reference section or technical document?	
<ul style="list-style-type: none"> <input type="checkbox"/> provides references to evidence used 8.1 <input type="checkbox"/> report steps to find, appraise, summarise evidence 8.2 8.3 <input type="checkbox"/> report date of last update 8.4 <input type="checkbox"/> report how often patient decision aid is updated 8.5 	<ul style="list-style-type: none"> <input type="checkbox"/> describe quality of scientific evidence [including lack of evidence] 8.6 <input type="checkbox"/> uses evidence from studies of patients similar to those of target audience 8.7
Disclose conflicts of interest?	
<ul style="list-style-type: none"> <input type="checkbox"/> report source of funding to develop and distribute the patient decision aid 9.1 9.2 	<ul style="list-style-type: none"> <input type="checkbox"/> report whether authors or their affiliations stand to gain or lose by choices patients make after using the patient decision aid 9.3 9.4
Use plain language?	
<ul style="list-style-type: none"> <input type="checkbox"/> is written at a level that can be understood by the majority of patients in the target group 10.1 <input type="checkbox"/> is written at a grade 8 equivalent level or less according to readability score [SMOG or FRY] 10.2 	<ul style="list-style-type: none"> <input type="checkbox"/> provides ways to help patients understand information other than reading [audio, video, in-person discussion] 10.3

Table 3. IPDAS Patient Decision Aid Checklist for Users

- Meet additional criteria if the patient decision aid is Internet based
- provide a step-by-step way to move through the web pages 8.1
 - allow patients to search for key words 8.2
 - provide feedback on personal health information that is entered into the patient decision aid 8.2
 - provides security for personal health information entered into the decision aid 8.4
 - make it easy for patients to return to the decision aid after linking to other web pages 8.5
 - permit printing as a single document 8.6
- Meet additional criteria if stories are used in the patient decision aid
- use stories that represent a range of positive and negative experiences 9.1
 - reports if there was a financial or other reason why patients decided to share their story 9.2
 - state in an accessible document that the patient gave informed consent to use their stories 9.3

III. Effectiveness: Does the patient decision aid ensure decision making is informed and values based?

- Decision processes leading to decision quality. The patient decision aid helps patients to ...
- recognise a decision needs to be made 13.1
 - know options and their features 13.2, 13.3
 - understand that values affect decision 13.4
 - be clear about option features that matter most 13.5
 - discuss values with their practitioner 13.6
 - become involved in preferred ways 13.7
- Decision quality. The patient decision aid ...
- improves the match between the chosen option and the features that matter most to the informed patient 13.8

Note: numbers behind items correspond to endorsed criteria in the [IPDAS second round voting document](#).

September 21, 2009

Work Plan for BRCA Clinical Decision Support Tools: GEP

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**Contract No. HHS290-2005-0036-I
RTI Project No. 0209815.008.003**

**Work Plan for BRCA Clinical Decision
Support Tools: GEP**

1. Introduction

In July 2008, the Agency for Health Research and Quality (AHRQ) contracted with RTI International to develop a clinical decision support tool to aid oncologists and breast cancer patients in making decisions about when to order and how to using the findings from gene expression profile (GEP) tests. To inform the development of this tool, we conducted a series of formative research activities including:

1. Reviewing the literature to identify patient and clinician needs
2. Constituting a technical expert panel (TEP) and obtaining their advice
3. Reviewing existing on-line educational tools on GEP testing and adjuvant chemotherapy
4. Reviewing existing educational materials on GEP testing and adjuvant chemotherapy
5. Conducting an assessment of the IT needs of two clinical sites.

Findings from each of these activities have been used to develop an outline of a Web-based tool for patients.

1.1 Literature Review

RTI conducted a literature review which focused on the effectiveness and design characteristics of clinical decision support tools and also sought to answer the following key questions:

1. What GEP tests are currently available? What are the testing parameters for each test? How is the test interpreted?
2. How well do gene expression profiling tests predict outcomes?
3. What other characteristics have been and should be considered in treatment decisions?
4. What educational information needs need to be included in the tool?

Results from this literature indicated that Oncotype DX is the test most commonly used in the United States and that studies have demonstrated some evidence that *Oncotype DX RS* can predict the likelihood of response after preoperative chemotherapy in women who are ER positive and lymph node negative.

While we found published research on the effectiveness of the test, at the time we conducted our literature review in the Fall of 2008, we found little research on the following:

- The type of clinicians who order the test (e.g., oncologists, pathologists, surgeons) and how the results are shared within the health care team.
- How widespread the use of GEP tests is. We also did not find any information about regional differences in use of the test.
- For whom clinicians order the test. Are they ordering it for those patients who have the clinical indicators warranting the test or are they ordering for those who fall outside those indicators?
- The specific types of clinician practices (e.g., academic cancer centers vs. community cancer centers) which are more likely to order the test.
- Clinician's and patient's knowledge and attitudes toward use of the test.
- The educational needs of patients and clinicians.
- When and how test results are shared with the patient.

- How easy or difficult it is for clinicians and patients to understand the results of the test.
- How test results influenced treatment decisionmaking for both clinicians and patients.

1.2 Incorporating Input from Technical Expert Panel

We recruited a technical expert panel (TEP) to advise us on the development of the GEP clinical decision tool (see Appendix A for list of members).

We sought input from the TEP in three stages.

1. Prior to beginning the full literature review, we summarized the information obtained from the relevant evidence-based reviews, the remaining gaps in information needed to develop the tools, and our suggested search terms to fill the identified gaps. We sent this summary to the TEP and our consultants and asked them to review the summary and comment on any information they felt was incorrect, unidentified gaps in information, and the suggested search terms. These comments were incorporated into the literature search and into the full literature review.
2. We sent the draft literature review to the TEP members and asked them to review sections in which they had expertise and to provide written comments.
3. We scheduled a conference call with the TEP to discuss the literature review and to provide input on specific questions. These reviewers commented on the literature review and recognized that the lack of published literature left us in great need of learning more about patients and providers knowledge of, attitudes toward, and behaviors regarding GEP testing. They suggested we conduct formative research with both patients and providers and also suggested that we convene a second TEP made up solely of practitioners in oncology. Specifically, they suggested we recruit oncologists from non-academic centers, surgeons, and pathologist. Appendix B lists the members of this second TEP. Reports from discussions with both the first and second TEPs can be found in Appendix C. Below, we summarize key points from these reports.

Key points from TEPs

- Doctors did not perceive the need for a tool to help interpret the results of the GEP test.
- Concern was expressed that the genetic testing field is expanding so rapidly that a tool that focuses exclusively on one test, such as the GEP, would be quickly obsolete.
- The time between GEP testing and results could be a window for patient education, though not all agreed.
- The main need repeatedly identified was to have a tool that could help patients understand risk.
- TEP members also suggested that a tool that helped to educate patients about the factors that are considered when ordering a GEP test (e.g., ER+ status) as not all breast cancer patients are candidates for testing
- Doctors reported that patients do not understand how little treatment reduces their risk of recurrence; that is, patients overestimate the benefit of treatment.
- Doctors and patients view the GEP test as reliable and valid. Caveats and uncertainties about test seem to not often be presented to patients.

1.3 Formative Research Findings from Genomic Health

Given the large gaps in the published research, we contacted Genomic Health to see if they would be willing to share any information they had on test orders or patient and clinician educational needs regarding the test. In August 2009, their lead for patient education. She shared findings from individual in-depth interview Genomic Health conducted in 2008 and 2009 with 75 patients who received Oncotype DX and 50 newly diagnosed cancer patients.

Key findings from market research performed in Q1 2009 with 75 patients who *received Oncotype DX*:

- Most patients learn about diagnosis and treatment options from their physician, but more than half of the patients go to the web to find additional information.
- In terms of factors that influence treatment decisions, the most commonly cited were potential for cure, risk of recurrence and the doctor's opinion.
- More than three-quarters of the respondents, particularly older women, acknowledge that they thought that chemotherapy might not be necessary for them.
- Only a minority of patients recall their physician or nurse providing materials to describe Oncotype DX results after receiving the test; most often mentioning the printed test results. This is an area that needs to be developed as 50 percent of patients said that an explanation of what the results of Oncotype DX mean would be helpful.
- Regardless of their Recurrence Score, almost all of the respondents believe that the Oncotype DX test made them feel more confident about their treatment decisions.

Key findings from market research performed in Q1 2008 with 50 newly diagnosed breast cancer patients (some received Oncotype DX but not all):

- A significant majority of patients used the Internet to access information about breast cancer following diagnosis.
- Nearly half of the patients indicate that they were familiar with the concept of risk of recurrence when first diagnosed.
- Despite relatively low awareness of recurrence risk testing, approximately three-quarters of the patients indicate that the risk of recurrence has influenced their treatment planning.
- Most respondents believe that radiation and chemotherapy will benefit early-stage breast cancer patients; there is less familiarity with the benefits of hormonal therapy. Patients who received Oncotype DX are significantly more likely to agree that few patients benefit from chemo.

As the majority of patients turn to the Internet to find educational information, Genomic Health's formative research findings support the development of a web-based educational tool for patients. Patients wanted more explanation about the results of their Oncotype DX test. Fear of having a recurrence seemed to be influential in patients' treatment decisionmaking. Having the test result seemed to increase patients' confidence in their treatment decision and increase patients' understanding about the costs/benefits of chemotherapy for early stage breast cancer.

1.4 New Studies Identified Since the Literature Review

Lo et al. (2009) conducted a prospective multicenter study of the impact of the 21-gene recurrence score assay on medical oncologists and patient adjuvant breast cancer treatment

selection. Seventeen medical oncologists at one community and three academic practices participated in this study. Each medical oncologist offered enrollment to eligible women (those who had breast cancer, were lymph-node negative, and ER+). Medical oncologists complete pre- and post-RS assay questionnaires their treatment recommendation and their confidence in this recommendation. The 89 patients who participated completed pre- and post-RS assay questionnaires that assessed treatment choice, quality of life measures, anxiety, and decisional conflict. Tests results for these 89 women were as follows: 42.7 percent were low risk ($RS < 18$), 47.2 percent were intermediate risk ($18 \leq RS \leq 30$), and 10.1 percent were high risk ($RS \geq 31$). Medical oncologists changed the treatment recommendation in 31.5 percent of cases after considering the results of the RS assay. The largest change was from a recommendation of chemotherapy plus hormone therapy to hormone therapy only (22.5 percent of cases). Medical oncologists' confidence in their treatment recommendation increased from pre to post test. In addition, 97 percent of medical oncologists said they would order the test again and 83 percent said that the result of the RS assay influenced their treatment decision. Twenty-seven percent of patients changed their adjuvant treatment decision based on results of the RS assay and 95 percent said they were glad they took the RS assay. Results from the RS assay were associated with less adjuvant chemotherapy administration.

Richman et al. (in press) surveyed 77 women who had early-stage breast cancer and who were ER+ with 0-3 lymph nodes and whose medical records indicated they had previously received Oncotype DX. The mailed questionnaire assessed knowledge of genomic recurrence risk testing. Survey findings indicated that knowledge of genomic recurrence risk testing was low. While most women (88 percent) understood that the test results could be used to help make decisions about adjuvant chemotherapy, few (22 percent) understood that the test's estimate of the chance of metastasis assumes the patient is receiving hormone therapy. Women who had higher levels of education, higher levels of health literacy, had received both verbal and printed information about the test had higher levels of knowledge. Women who reported having an active role in their treatment decisions also had higher levels of knowledge.

Using this same dataset, Tzeng (2009) analyzed how women received and understood recurrence risk information based on the GEP test result. They supplemented the surveys by reviewing women's medical records to validate their test results. Most women accurately recalled their risk results (71 percent) and felt they understood much of what they were told about it (67 percent). About one quarter of women experienced test-related distress. Women's perceived recurrence risk was associated with their actual genomic-based recurrence risk, having had a previous cancer diagnosis, and worry about recurrence. Only 11 percent of women had heard about the Oncotype DX test before their diagnosis, though almost all (97 percent) remember receiving some type of information from their oncologist. The majority remember receiving printed materials and verbal information (83 percent). Most women discussed their test result with their oncologist (93 percent). Receiving print materials was associated with higher levels of perceived understanding. Twenty-six percent of women felt anxious or worried about getting the test result. Almost all women (96 percent) said that if they had to decide whether or not to get the test again, they would and that having the test gave them a better understanding of their treatment options' chance of success (95 percent).

Review of Computerized Educational Tools and Decision AIDS Related to GEP Testing and Adjuvant Chemotherapy

As the majority of breast cancer patients and consumer turn to the Internet to find health information, we identified and reviewed web-based educational tools and decision aids related to decision-making about GEP testing and adjuvant therapy, some of their pros and cons, and how they can inform the development of the tool for this project. Appendix D shows details the results of this review. There are currently no provider tools used for GEP decisionmaking and most tools, whether patient or provider, are used for making decisions regarding adjuvant therapy rather than GEP testing.

There is only one online tool that helps patients determine if a GEP test is appropriate for them (available at: www.mytreatmentdecision.com) is from the manufacturer, Genomic Health. This tool has women answer a series of question to assess whether or not they are candidates for testing. This tool also includes narratives about how women have used GEP to make decisions with their doctors about treatment. It also includes tips to help patients discuss GEP testing with their providers and covers topics many topics raised by our TEP (e.g., insurance coverage, identifying who is and isn't eligible for the test).

The other three online tools for patients were designed to help them make decisions about adjuvant therapy. These tools assume patients have detailed knowledge of their cancer diagnosis and tumor characteristics, and only one tool informs the user of the information needed before beginning to use the tool. This same tool is also the only tool that includes a video (of an RN from Johns Hopkins Breast Center who is also a breast cancer survivor) to walk the user through the questions.

All four patient tools request information about the cancer diagnosis and then provide recommendations and other customized information about treatment options based on the information entered. These tools do not ask patients about their preferences and values related to treatment options. Therefore, any consideration of patient preferences and values in decisionmaking has to be initiated by the provider, as it is not considered by these tools.

Most patient tools are designed to be used in conjunction with providers. They encourage patients to discuss recommendations with providers and to collect information about disease characteristics from providers. However, there is only one online decision-making tool for adjuvant therapy aimed specifically at providers (available at: <http://www.adjuvantonline.com/online.jsp>.) It was not designed to be an introduction to adjuvant therapy, but to be used by providers who already have some familiarity with the adjuvant treatment of cancer. This tool includes a discussion of the different types of therapy, possible outcomes with and without therapy, and side effects of therapies. While our TEP members indicated that this tool is widely used by oncologists, it currently does not incorporate the results of GEP testing into the decision aid.

None of these tools are designed for use by both the patient and provider. There are currently no existing computerized tools to aid providers in GEP decisionmaking. Many rely on existing clinical guidelines for adjuvant therapy to make recommendations regarding a woman's use of GEP testing.

1.5 Review of Educational Resources

In order to determine if existing resources available for patients or providers were comprehensive in their discussion of GEP testing and adjuvant chemotherapy decisionmaking, we conducted a brief environmental scan on the Internet to identify materials from major cancer advocacy or education organizations. It is unlikely that this review has identified all available resources; however, we provide it as a resource that could be used if and when the GEP decision aid is developed.

For patients, there are a variety of educational resources available (mainly in the form of Web sites, brochures, and videos) on adjuvant therapy and general cancer treatment options. Appendix E presents nine resources for patients that are readily available on the Internet. Most resources aimed at patients do not include a discussion of GEP testing or provide any information to aid in decisions about whether GEP testing may be appropriate for patients. One resource discussed the different factors that are considered in a GEP test, without directly discussing GEP testing. Most resources allot more space to a discussion of side effects of treatment options than they do to a discussion of benefits and risks. Few resources direct patients to decision aids for adjuvant therapy decisionmaking.

Fewer educational resources on adjuvant chemotherapy are readily available on the Internet for physicians. Our search only turned up two, an online CME course and an informational article. However, both of these resources include an indepth discussion of genetic expression as a factor in making decisions about adjuvant therapy. As educational resources, they do not include as much discussion of shared decisionmaking as the adjuvant therapy clinical decisionmaking tools likely do.

1.6 Conceptualization of a Tool

In developing our ideas for a tool, we reviewed all the research findings related to GEP testing described in our literature review as well as findings from additional studies found more recently, including findings from market research conducted by Genomic Health. We also reviewed existing online tools and educational materials that focused on GEP testing and decisionmaking about adjuvant chemotherapy. We found few Web-based tools that focused on GEP testing and few tools and materials provide a detailed explanation of GEP testing and how results can be used in treatment decisionmaking. The educational resources we identified did not provide a thorough explanation about what type of patients are candidates for testing, what other factors should be considered when deciding on whether or not to be tested, and the implications of test results and how they can be used in treatment decisionmaking. In trying to develop a plan to develop a tool that would best aid the testing and treatment decisionmaking process between patients and clinicians, we also carefully considered the input provided by our TEP members.

1.7 Description of the Tool

The goal of the GEP tool is to help patients understand prognostic test results, such as that provided by GEP testing and Adjuvant! (from adjuvantonline.com), in order to make informed decisions about treatment. As it is highly likely that new prognostic tests will become available, we would develop the tool with the idea that additional prognostic information could be added. In addition, focusing the tool on increasing patients' understanding risk,

communication skills, and ability to make informed decision would make it easy to adapt for other genetic tests or diseases.

1.8 Objectives of the Tool

We have identified the following objectives for the tool:

1. To increase patients' understanding of:
 - Breast cancer and general treatment options
 - The use of GEP testing in treatment decisionmaking
 - Why it's used
 - How the test is conducted
 - For whom it's appropriate and for whom it's not
 - How long it takes it takes to get results
 - The following concepts:
 - recurrence score
 - average rate of distant recurrence
 - survival rate
 - risk
 - benefit
 - uncertainty
 - Their own test results and prognosis
 - The likelihood of experiencing benefits from chemotherapy
 - The likelihood of experiencing side effects or other risks from chemotherapy
2. To increase patients' skills in:
 - Communicating their questions, concerns, beliefs, and feelings to their doctors and other medical care providers
 - Making an informed decision about their cancer treatment

1.9 Educational Modules

To address these objectives, the tool will be organized around eight different modules. Each module will be designed to stand on its own and the tool would be designed so that new modules could be readily added.

1. **Breast cancer basics.** To help women understand the disease, this module will present women basic information about breast cancer: what it is and how it develops. Terms typically used by the medical team will be define and explained.
2. **Informed decisionmaking.** This module will present the concept of informed decisionmaking and help the user develop questions to ask her clinician. A video or script of how a patient can ask questions, communicate concerns and feelings, and share personal values and beliefs will be included.
3. **Understanding risk (general).** This module will help define the concept of risk and explain how risk estimate are developed and how to interpret them in relationship to other risks we face in everyday life. An outline for this module can be found in Appendix F.

4. Tests to help inform treatment decisions.

Gene Expression Profile Testing

Oncotype DX

1. What is it?
2. Who can be tested?
3. What does the test result look like? Score.
4. What does the test result mean? Low, Intermediate, High
5. How can I use the test result to help me make a treatment decision?

Other tests

Treatment options. This module will present different treatment options for early stage breast cancer and describe their risks and benefits. Nonmedical options, including no treatment will be included.

Your treatment decision. This module will contain a variety of different exercises and quizzes to help women clarify the following: gaps in knowledge including risks, benefits, alternatives, and uncertainties; values/quality of life; attitudes toward testing, treatment, and side effects; confidence in test results; and preferred role in medical decisionmaking.

1.10 Resources for Providers

In addition to the patient tool, we suggest developing a brief checklist for clinicians, perhaps one that could be included on a personal digital assistant that has the criteria used to decide whether or not a woman is a candidate for testing. Given our findings from the IT Feasibility Assessment (see Appendix G), it may be more viable to connect providers to resources through a PDA than through a computerized tool that would be housed at the clinic.

TEP members also supported the development of a resource for providers to help learn how to explain risk information to patients. To meet this need, we have drafted a brief outline of an educational module for providers which would teach them how to help patients understand their risk (see Appendix H).

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Appendix B. Literature Review

January 20, 2009

**Computer-based Clinical Decision Support Tools for
Gene-based Tests Used in Breast Cancer:
Literature Review**

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**Computer-based Clinical Decision Support Tools for
Gene-based Tests Used in Breast Cancer:
Literature Review**

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Structured Abstract

Background. Increased use of electronic health records and electronic medical records, dissemination of clinical evidence and health-related information on the Web, and use of computers by clinicians and patients allow the creation of electronic tools that can deliver evidence-based information at the point of care to guide clinical decisionmaking.

Objectives. This project, *Computer-based Clinical Decision Support (CDS) Tools for Gene-based Tests Used in Breast Cancer*, addresses those needs by developing CDS tools to aid decisionmaking in two contexts: (1) the use of family history information in the primary care setting to identify women at risk of familial breast cancer and refer them for genetic counseling (BRCA CDS), and (2) the use of gene expression profiling (GEP) in the oncology setting to guide adjuvant treatment decisions for women with breast cancer (GEP CDS).

Methods. To inform the design and development of these CDS tools, we reviewed the literature to identify and provide the information required for developing risk algorithms, user interfaces, and educational messages. We drew as much information from review articles as possible and supplemented these articles with additional literature as needed.

Results. The literature review demonstrated that CDS tools can improve practitioner performance and identified the tool characteristics and development steps necessary to ensure that the tools would be effective. While patient decision aids have been found to be effective, there is little information available that identifies which components and processes affect targeted outcomes. The review of the BRCA1/2 literature review also identified several tools to help collect cancer family histories as well as tools to estimate a woman's risk of having the gene for hereditary breast and ovarian cancer. A few major issues remain and will need to be resolved through other means: the ability to collect data on surgeries associated with cancer risk reduction; the definition of high-risk women to be incorporated into the tools, and the type of decisionmaking to be supported by the tools.

Although there are several gene expression profiling tests in development, only three (Oncotype DX,[®] Breast Cancer Gene Expression Ratio Test, and MammaPrint[®]) are commercially available. Although not without limitations, the existing literature provides reasonable evidence of the independent prognostic and predictive value of Oncotype DX[®], which is also the test most commonly used in the United States. Guidelines and tools to aid decisionmaking on adjuvant therapy that incorporate Oncotype DX[®] results exist, but the literature contains insufficient information to evaluate or improve upon these tools. Given these findings, the tool most needed by physicians may be one that focuses on educating physicians about GEP testing and the guidelines surrounding its use and assisting them with interpreting the GEP test results. We could not determine from the literature how GEP testing is used in current oncology practice (or how it is likely to be used in the near future), the educational needs of patients and providers around GEP testing, or the best way to present this information so that it can be understood by patients and their providers. Other methods will need to be used to obtain this information.

Conclusions. The development of these tools presents an exciting opportunity to improve women's health and experience in the area of breast cancer, but also presents challenges. Our plan for meeting these challenges is discussed in the tool development work plan.

Introduction

The Effective Health Care (EHC) Program of the Agency for Healthcare Research and Quality (AHRQ) holds to the principle that clinicians and patients should have the best available evidence upon which to make choices in healthcare items and services. The Developing Evidence to Inform Decisions about Effectiveness (DEcIDE) Network develops scientific evidence and new analytic tools to assist health care providers, patients, and policy makers make informed decisions about health care services. Rapid research that provides valid results for health care decisionmaking is a hallmark of the DEcIDE program. The primary aim of this project is to develop two clinical decision support (CDS) tools for gene-based tests in breast cancer. The goal of the first tool is to support providers in screening patients for BRCA1 or BRCA2 mutations in a primary care setting. The second tool will help oncologists to determine which patients would benefit from gene expression profile (GEP) testing, i.e., to identify those who are most likely to have a recurrence of their cancer. In addition, this GEP tool will help providers use the GEP test results, patient preferences, and other clinical factors to help the patient make a decision about adjuvant chemotherapy. To inform the design and development of these CDS tools, we present a literature review focused on the information required to develop the risk algorithms, user interfaces, and educational messages. In addition, the review identifies the specific data needed for the risk algorithms and the best way to present risk information to promote patient-provider communication.

This literature report is organized into five chapters. Chapter 1 provides an overview of the project and describes the CDS tools to be developed. Chapter 2 summarizes the characteristics of successful CDS tools, Chapter 3 discusses the literature on the BRCA1 and BRCA2 (abbreviated as BRCA 1/2) CDS tools, Chapter 4 describes the literature on the GEP CDS tools, and Chapter 5 discusses the implications of our findings for tool development and evaluation design. Within each chapter are subsections that include background on the topic; methods used for the literature review; our findings; and any conclusions about the design, development, content, or evaluation of the tools.

Chapter 1. Project Overview

Increased use of electronic health records and electronic medical records, increased dissemination of clinical evidence and health-related information on the Web, and increased use of computers by clinicians and patients allow for the creation of electronic tools that can deliver evidence-based information at the point of care to guide clinical decisionmaking. The Department of Health and Human Services (DHHS) Secretary's Advisory Committee on Genetics, Health, and Society recently recommended measures to improve communication and decision support for genetic tests:¹

To better understand the usefulness of genetic tests, DHHS should create and fund a public-private partnership to evaluate the clinical utility of genetic tests, develop a research agenda to address gaps in knowledge, conduct public health surveillance to assess the health impact of genetic testing, and help advance the appropriate use of electronic health records as a resource for assessing clinical utility and quality of health care.

To meet the educational needs of health professionals, public health workers, patients, and consumers, HHS should support efforts to identify education or training deficiencies

in each of these groups and support research and development of effective clinical decision support systems. In addition, FDA [Food and Drug Administration] should prepare a guidance document articulating the scope of its regulation of clinical decision support systems. (p. iv)

This project, *Computer-based Clinical Decision Support (CDS) Tools for Gene-based Tests Used in Breast Cancer*, addresses those needs by developing CDS tools to aid decisionmaking in two contexts: (1) the use of family history information in the primary care setting to identify women at risk of familial breast cancer and refer them for genetic counseling (BRCA CDS), and (2) the use of gene expression profiling in the oncology setting to guide adjuvant treatment decisions for women with breast cancer (GEP CDS). The following tools will be developed by this project:

- A BRCA CDS tool for patients. This tool will provide patients with information on familial breast and ovarian cancer, BRCA mutations, and how cancer family history can be used to determine who is at risk for having a mutation. The tool will help patients collect and record their family's history of cancer. Patients can learn their risk, based on the recorded family history, of carrying a BRCA1 or BRCA2 mutation and obtain educational information targeted to their risk status. The tool will encourage women to share their family history and risk status with their doctors and help them prepare for this discussion.
- A BRCA CDS tool for primary care providers. This tool will allow providers to review the patient's family cancer history, update any information, and recalculate the patient's risk if necessary. The tool will contain information for health care providers on risk calculation and results, genetic testing, patient education, and referrals to genetic counselors. Providers will be able to use the tool to develop a printed instruction sheet, tailored for each patient, that gives additional educational messages and next steps. For high-risk patients, the printout will include contact information for genetic counselors. For average-risk patients, the printout will include messages about updating the cancer family history and information on breast cancer screening.
- A provider GEP CDS tool. This tool will provide oncologists with information on clinical guidelines regarding the use of GEP test results to guide their recommendations for adjuvant therapy for breast cancer. It will also include information to aid in the interpretation of GEP test results and educational information that they could share with patients.

Chapter 2. Effectiveness and Design Characteristics of Clinical Decision Support Tools

2.1 Background

CDS, defined in the broadest sense, provides clinicians, staff, patients, or other individuals with knowledge and person-specific information, intelligently filtered or presented at appropriate times, to enhance health and health care.² Implicit in this definition is the notion that tools can be directed at providers and patients, that they can be electronic or nonelectronic, and, that they deliver either patient-specific recommendations or context-relevant educational materials, such as guidelines. Other definitions in use include limitations that the tool be directed

toward providers only and that only patient-specific recommendation constitute the system output, as in the following definition used in two large systematic reviews of clinical decision support systems (CDSS).^{3,4} In this research, the authors state, “We defined a CDSS as any electronic or nonelectronic system designed to aid directly in clinical decisionmaking, in which characteristics of individual patients are used to generate patient-specific assessments or recommendations that are then presented to clinicians for consideration.” A third systematic review focused its study on computerized CDS tools—information systems designed to improve clinical decisionmaking—and limited inclusion in their review to CDS tools that provided patient-specific advice reviewed by a healthcare practitioners before any clinical actions were taken.⁵ For purposes of this review, we will adopt the broadest definition of CDS, recognizing that our specific project focus will include only computerized tools for provider decisionmaking.

Most CDS tools rely on patient information either manually entered by providers, patients, or staff or queries of electronic systems such as electronic medical records (EMRs) or electronic health records (EHRs). Patient characteristics are then matched against a computerized knowledge base, and software algorithms are used to generate patient-specific recommendations. These recommendations are then delivered to the clinician via EMRs or EHRs, pagers, handheld devices, or printouts placed in patient charts.⁵ Most CDS tools have been developed for management of specific disease conditions, or for adherence to clinical preventive service guidelines.

Some decision aids are based on conceptual frameworks that incorporate rational decision-making models.⁶ Patient decision aids are designed to support rather than replace patient-provider interaction/communication and are used most often for preference-sensitive health decisions or decisions where the benefit-harm ratio is uncertain.⁷ Most decision aids are for single-event choices (e.g., type of surgery, type of screening procedure).⁷

Decision support tools have been developed in a variety of formats, including pamphlets, interactive media, video, checklists, decision boards, personal computers, audio tapes, and audio-guided workbooks.^{8,9} Elwyn et al.⁹ state that patient decision aids “help patients to personalize this information, to understand that they can be involved in choosing among the various options, to appreciate the scientific uncertainties inherent in that choice, to clarify the personal value or desirability of potential benefits relative to potential harms, to communicate their values to their practitioners, and to gain skills in the steps of collaborative decisionmaking.”

As EHRs become more widespread, CDS tools would ideally capture information from health records and link it to evidence-based guidelines to allow the presentation of tailored information and recommendations at the point of care.¹⁰ Such tools would allow the rapid dissemination of evidence-based recommendations into clinical practice, a process that currently may require years.¹¹ The ability to disseminate evidence-based knowledge quickly is important in all areas of clinical practice, but it is particularly crucial in rapidly evolving fields such as genetic testing. In addition, decision support tools for patients hold promise for promoting patient-provider communication and shared decisionmaking.

2.2 Methods

We began the literature review on CDS tools by identifying key questions to address the development and evaluation of these tools (Table 1). We reviewed and abstracted the systematic review of cancer-related decision tools by Whelen et al.¹² and recent review articles on CDS tools to answer as many of these questions as possible. We identified search strategies to update the information from the review and fill any information gaps (Appendix A). We searched

PubMed using the identified search strategies. For each search, we reviewed the article titles and abstracts and eliminated any that were clearly not relevant. We requested 90 articles for review and abstracted 21.

Table 1. Key questions about the design, performance, and evaluation of CDS tools

Number	Key Question
1	Are CDS tools effective, and how has their effectiveness been assessed? 1a. Are CDS tools for breast cancer treatment effective, and how have they been assessed?
2	What features and functions of a clinical decision tool affect the likelihood that it will be incorporated into routine clinical practice, affect clinic workflow, or affect patient use?

CDS=computer-based clinical decision support.

2.3 Results

There is substantial evidence that CDS tools are effective.⁹ Studies have assessed decision aids to determine their effect on the following outcomes:

- acceptance, use, and satisfaction;^{13,14}
- knowledge;^{9,15}
- accurate risk perceptions;
- decisionmaking,^{13,16} decision quality, decision conflict,⁹ and value congruence with the chosen option;
- process measure, such as the timing of tool use;¹⁷
- level of involvement in healthcare decisions;⁹
- psychological outcomes, such as breast cancer worry and anxiety; and
- health outcomes.¹⁸

Using the definitions discussed in the introduction, CDS tools can be divided into two groups—clinician-directed decision tools and patient-directed decision tools. For purposes of evaluating their effectiveness, we present results for each type of tool separately.

2.3.1 Clinician-Directed Tools

Overall, the literature evaluating outcomes related to CDS tools is limited—no large evidence base exists. The results of the evaluations are mixed, with some studies showing benefits but many failing to demonstrate an effect on either practitioner performance or patient outcomes. This could be the result of many different factors, including study design. In general, study design in this area has improved over time, with poorer quality noted in earlier studies.⁵ Additionally, studies that have examined provider adherence to disease- management protocols have had challenges due to a lack of evidence about the effectiveness of standard (not CDS tools-supported) disease- management programs. Many evaluations of CDS tools have focused on a specific disease condition or risk status and have measured adherence to disease management or preventive services guidelines and recommendations. Two large systematic reviews of the effectiveness of CDS tools have been conducted in recent years.^{4,5} Both have shown CDS tools to improve practitioner performance overall.

Garg's research focused on randomized and nonrandomized controlled trials that evaluated the effectiveness of a CDS tool compared with care provided without a CDS tool on practitioner performance or patient outcomes. They searched MEDLINE, EMBASE, the Cochrane Library, Inspec, and ISI databases and identified 100 studies that tested the effect of diagnostic systems, reminder systems, disease management systems, and prescribing systems

meeting their inclusion criteria. Overall, the CDS tools improved practitioner performance in 64 percent of the studies assessing this outcome (N = 97). Of the various CDS tool types, reminder systems had the greatest effect on practitioner performance, demonstrating improvements 76 percent of the time. Prescribing systems improved performance 66 percent of the time, disease management systems improved performance 62 percent of the time, and diagnostic systems improved performance only 40 percent of the time. When evaluating trials that measured patient outcomes (N = 52), only 13 percent reported improvements. Factors contributing to CDS tools' success included automatic prompts for users rather than systems requiring user activation (success in 73 percent of trials vs. 47 percent; $P = .02$) and studies in which the authors also developed the CDS tool software rather than studies in which the authors were not the developers (74 percent success vs. 28 percent, respectively; $P = .001$).

Kawamoto's research used stricter inclusion criteria, allowing only randomized trials to be evaluated but also allowing nonelectronic systems to be included. Literature searches via MEDLINE, CINAHL, and the Cochrane Controlled Trials Register were used to identify initial trials, and reference lists and relevant reviews of these initial articles were used to identify further trials for inclusion. Overall, CDS tools were found to significantly improve clinical practice in 68 percent of trials examined (N = 70). More than half of the trials examined were of computerized systems, with the two most common being systems that printed patient-specific advice for placement in the patient paper chart or record (34 percent), and CDS tools associated with computerized provider order entry systems (16 percent). While Kawamoto's research showed an overall positive impact on clinical practice, the greatest contribution of this research is the identification of specific CDS tool features that were most likely to improve clinical practice. Using multiple logistic regression techniques, Kawamoto identified four features as independent predictors of improved clinical practice:

- Automatic provision of decision support as part of clinical workflow ($P < .001$)
- Provisions of recommendations vs. just assessments ($P = .019$)
- Provision of decision support at the time and location of decisionmaking ($P = .026$)
- Computer-based decision support ($P = .029$)

Of the 32 systems possessing all four features, 94 percent significantly improved clinical practice. Additional evidence through direct experimental justification was found for the following features: providing periodic performance feedback, sharing recommendations with patients, and requesting documentation of reasons for not following recommendations.

Another study¹⁹ sought to determine how best to deliver CDS tools. For purposes of this research, a CDS tool was defined as "passive and active referential information as well as reminders, alerts, and guidelines." Using the criteria for defining a CDS tool described in the Background section of this review, these systems would be provider directed, electronic systems that provide not only patient-specific recommendations, but context relevant educational material as well. Using their own institution—consisting of a large, tertiary care institution and a large integrated delivery system, the researchers identified the following "Ten Commandments" for effective CDS tools:

1. *Speed Is Everything*—the speed of an information system is the characteristic users value most.
2. *Anticipate Needs and Deliver in Real Time*—clinicians are increasingly pressured by time, and an information system must anticipate their needs and bring information at the appropriate time.

3. *Fit into the User's Workflow*—understanding clinician workflow especially in the outpatient setting is critical.
4. *Little Things Can Make a Big Difference*—usability testing can dramatically improve user system acceptance and use.
5. *Recognize That Physicians Will Strongly Resist Stopping*—presenting physicians with recommendations not to do something without presenting an alternative to do something else will typically result in multiple system overrides.
6. *Changing Direction Is Easier than Stopping*—the computer is a very powerful tool for getting physicians to change behaviors.
7. *Simple Interventions Work Best*—guidelines must fit onto a single screen if physicians are to be expected to use them.
8. *Ask for Additional Information Only When You Really Need It*—the likelihood of success in implementing a computerized guideline is inversely related to the number of extra data elements needed.
9. *Monitor Impact, Get Feedback, and Respond*—tracking the impact of CDS tools early and often can yield important midcourse corrections.
10. *Manage and Maintain Your Knowledge-based Systems*—successful delivery of CDS tools requires maintenance of the knowledge within the system and management of individual pieces of the system over time. (pp. 524–528)

2.3.2 Patient-Directed Tools

Trials have found that decision aids are better than standard counseling at improving patients' knowledge and giving them realistic expectations about the results of treatments and other procedures.^{9,15} In addition, they have been shown to improve patient involvement in healthcare decisions, agreement between values and choices, and decisional conflict.^{9,15} Patient decision tools have been found to affect the adoption of options (e.g., use of one treatment method over another) and procedures (e.g., colon cancer screening).

The 2003 Cochrane Collaboration systematic review identified 200 patient decision aids, 38 of which had been evaluated in a randomized trial (30 were in trials at the time of the review).⁸ The review concluded that patients who used decision aids were more knowledgeable, had more realistic expectations, had lower decisional conflict related to feeling informed, and had increased levels of active decisionmaking compared with those in usual care. Yet patients who used decision aids did not fare better or worse than those in usual care in terms of their satisfaction with decisionmaking, anxiety, and health outcomes, and the effect of decision tools on actual therapeutic choices was variable.⁸ The review found that there were no unanticipated iatrogenic outcomes⁷ and that patients were satisfied with the tools and found them to be helpful.

In 2005, the International Patient Decision Aids Standards (IPDAS) Collaborative used an evidence-informed Delphi process completed by researchers, practitioners, and stakeholders from around the world to develop criteria for judging the quality of patient decision aids. These criteria focus on content, development, and effectiveness (Appendix B). O'Connor et al.⁶ conducted a systematic meta-analysis to determine if patient decision aids met the effectiveness criteria of the collaborative and found that 38 (69 percent) of the 55 randomized trials that met the study criteria used at least one measure that mapped onto an IPDAS effectiveness criterion. They concluded that patient decision aids improve decision quality; however, the effect size was variable across studies.

While patient decision aids have been found to be effective, there is little information available that identifies which components and processes affect targeted outcomes.⁹ Questions remain about the effectiveness of elements such as interactive vs. noninteractive values clarification and patient testimonials or stories.⁸

2.3.3 Key Question 1a. Are CDS Tools for Breast Cancer Treatment Effective, and How Have They Been Assessed?

A number of studies have examined whether CDS tools for breast cancer treatment are effective (see Table 2 for study summaries). Whelan et al.¹² developed an evidence report on the impact of cancer-related decision aids and found 61 unique studies. Of these studies, 18 were randomized controlled trials and 5 were nonrandomized controlled trials. The majority of the tools (14/22) were developed to aid decisions about breast cancer treatment. The most frequent outcomes measured were patients' decisions, knowledge, anxiety, depression, satisfaction, and acceptability of the decision aid. The decision aids increased knowledge and patient involvement in decisionmaking among the randomized controlled trial studies, but they did not affect anxiety and depression. Whelan et al.¹² indicated that, overall, the studies were of low methodological quality.

The Cochrane review on patient aids was recently updated. Stacey et al. report that the update found 23 randomized trials of cancer-related decision aids, including 6 for breast cancer genetic testing and 4 for breast cancer treatment.²⁰ Patient aids increased patient knowledge and resulted in decisions that agreed with patient values. People who used cancer decision aids that included descriptions of outcomes and probabilities were 1.5 times more likely to have accurate risk perceptions than those who did not receive this information and were 50 percent less likely to assume a passive decision-making role.²⁰

Table 2. Summaries of studies examining the effect of CDS on breast cancer treatment

Authors	Type of Tool (Control)	Goal of Tool	Specific Features	Study Design	Effectiveness
Whelan et al., 2002 ¹²	Various	Treatment	Various	Mixed	Increased knowledge; patient involvement
Stacey et al., 2008 ^{20*}	Various	Genetic testing; Treatment	Various	Mixed	Increased knowledge; improved patient decisionmaking
Siminoff et al., 2006 ¹⁶	Computer program (pamphlet)	Adjuvant therapy	Estimates outcome with/without treatments	RCT	Influence on treatment decision; ease of understanding tool; understand patients' preferences (physicians); provided useful information (physicians)
Green et al., 2004 ²¹	Computer program (standard genetic counseling)	Genetic testing	Education about breast cancer , heredity; benefits and limitations of genetic testing	RCT	Increased knowledge (low-risk group); [standard genetic counseling showed benefit in anxiety reduction and accurate risk perceptions]
Epstein et al., 2006 ¹³	Web-based computer program (Tumor Board recommendation)	Adjuvant therapy	Separate risk/benefit; compare treatments given clinical context; present balanced information on treatment	User survey	Influence on treatment decision
Wilson et al., 2005 ¹⁴	Computer program (referral guidelines)	Genetic testing	Risk assessment module; education about cancer genetics; Web links; email contact with Cancer Genetics Service	RCT	None demonstrated
Apkon et al., 2005 ¹⁸	Computer program (usual care)	Quality of care	24 quality process measure recommendations for diagnosis or treatment	RCT	None demonstrated overall

*Review articles

RCT=randomized controlled trial.

Siminoff et al.¹⁶ found that patients using a computer-based decision aid on the probability of outcomes with and without adjuvant therapy reported that it influenced their decisionmaking (86 percent) and was easy to understand (95 percent). Computer-based education about hereditary breast cancer has been effective in research settings in increasing patient knowledge and allowing healthcare providers more time to discuss personal risk and decisionmaking.²¹

A clinical decision tool designed to aid physicians in deciding on recommended adjuvant treatment for breast cancer patients led to modification of treatment recommendations in 13 percent of cases.¹³ In most cases, the change resulted because the estimated benefit of treatment was lower than physicians initially believed. The program impacted decisionmaking because it

- clearly separated disease prognosis from therapeutic benefit, focusing attention about therapy decisions on the benefit of the intervention;
- distinguished between reduction in relapse and reduction in mortality, leading to a deeper analysis of the goals, costs, and benefits of treatment;
- provided estimated benefits for different therapeutic regimens, facilitating selection of treatment protocols; and

- quantified therapeutic benefits of modest size, encouraging consideration of the benefit in relation to adverse effects and costs.¹³

Results have been less encouraging in routine clinical practice, however. A trial of a computerized tool to aid British general practitioners in referral decisions about hereditary breast cancer found it was not effective: less than half of the clinicians in the intervention practices were aware that the software existed and only 22 percent had used it.²² A large randomized trial of a decision- support tool that used structured questions to link patient complaints to a database of recommended care and was to be incorporated into the U.S. Department of Defense health information network found no difference in health outcomes between the control and intervention arms.¹⁸

2.3.4 Key Question 2. What Features and Functions of a Clinical Decision Tool Affect the Likelihood It Will Be Incorporated into Routine Clinical Practice, Affect Clinic Workflow, or Affect Patient Use?

A pilot study of implementation of CDS tools within an electronic medical record found that, in order for clinicians to use the Smart Form, it had to be as good as or better than the tools they were using and provide added value: either time-saving features or tools to improve patient care while remaining time neutral. Also, the pilot study found improved usability required many small changes identified by iterative testing and refinement.¹⁰ A study of Canadian physicians' responses to three decision aids found that, although 85 percent of physicians said the tool was well-developed and presented the needed information in an understandable, balanced, and unbiased manner, only 54 percent said that they intended to implement it into their practice, and less than one-third of those actually used it.²³ Intention to implement the decision tool was affected by physicians' comfort with offering it to their patients and perception of the ease of integrating the tool into the workflow, and the topic of the tool. The paper did not provide information on the barriers to implementation among physicians who intended to implement the tools. Another study, however, found that the involvement of physicians who would use an antibiotic prescription decision tool in the tool's design resulted in immediate uptake and ongoing use.²⁴

We found little information in the literature on the aspects of a clinical decision tool that affect how well it integrates into clinic workflow. The one study we found that addressed this issue found that the physicians were less likely to attend to CDS alerts when they were behind schedule, and 84 percent were at least 20 minutes behind schedule at least some of the time.²⁵

Holmes-Rovner et al.⁷ said that "the lack of uptake by clinicians appears to be a major obstacle to decision aids achieving an impact on clinical practice"; this finding indicates that more research should be done to examine when decision aids are used in the clinical encounter and whether a reimbursement climate in healthcare that provides payment for counseling and use of decision tools as well as disease management and followthrough on decisions made would affect use rates (p. 605). Provider training on the decision tool was also identified as a need.⁷

Other researchers provided relevant commentary about factors that could affect use of CDS tools in clinical practice. For example, a 2007 review found that the literature on CDS implementation in the United States was highly weighted toward academic medical centers and that the literature did not include physician or settings common in the United States.²⁶ In addition, given the new and emerging information both on BRCA and GEP testing and cancer treatment, Barnato et al.⁸ indicate that it will be critical for decision aids to be easily updated.

Glaser et al.¹¹ indicate that the use of CDS tools by providers “is hampered by the uncertainty of how vendor-based electronic health record system can integrate these tools into their individual systems” (p. 9).

We found few studies that examined factors affecting patient use of breast cancer–related CDS tools. Rapport et al. conducted focus groups with women to evaluate three decision aids around genetic testing for breast cancer and found that women were intimidated by the statistics and charts included in a paper-based decision tool.²⁷ The women also did not like the negative wording of the messages, which they felt were alarmist. Finally, they wanted a paper-based tool to be kept small but to include additional resources to which they could turn for more information if desired. For CD-ROM–based tools, there were mixed opinions about the value of videos, still photographs, and patient stories. Those who liked videos felt that they held the viewers’ attention, whereas those who did not found them distracting and had little interest in the personal stories.

Chapter 3. Literature Review for BRCA1 and BRCA2 Screening Decision Tools

3.1 Background

Hereditary breast and ovarian cancer syndrome (HBOC) is a familial form of breast and/or ovarian cancer that is inherited as an autosomal dominant condition. In over 90 percent of families who present with both breast and ovarian cancer, and 40 percent of those who present with breast cancer alone, the syndrome is due to a mutation in the BRCA1 or BRCA2 gene. Women who have a mutation in these genes have up to an 85 percent lifetime risk of breast cancer. The tumors of BRCA1 mutation carriers are more likely to be high-grade, estrogen-receptor negative, and fatal than those of women without a family history of cancer and are less likely to be associated with survival.¹ Genetic testing for HBOC has been available for several years, and studies have shown that prophylactic measures are effective. For these reasons, the United States Preventive Services Task Force (USPSTF) recommended in 2005 that physicians refer women who have a family history consistent with HBOC for genetic counseling and possible testing.²⁸ The implementation of this recommendation is hampered by the time required to collect detailed family histories and the resulting incomplete family histories in medical records, and physicians’ difficulties in interpreting family histories and explaining genetic tests.

AHRQ requested the development of clinical decision tools for patients and providers because they felt it would increase compliance with the USPSTF recommendations. RTI’s goals for each of the BRCA1/2 CDS tools to be developed are listed in Table 3. We conducted a targeted literature review to gather the information needed for to develop the tools.

Table 3. Goals of the BRCA1/2 CDS tools

Patient Tool	Provider Tool
Collect detailed cancer family history data	Collect breast and ovarian family history data from patient
Assess the patient’s risk of having hereditary breast and ovarian cancer (BRCA1 or BRCA2 mutation) given her family history	Provide an assessment risk of patient having a BRCA 1 or 2 mutation given family history
Educate the patient about familial breast cancer, its risks, genetic counseling and genetic testing, and the availability of interventions to reduce the risk of breast or ovarian cancer among BRCA mutation carriers	Provide recommendations on referral for breast cancer genetic counseling and testing
Educate the patient about the need to talk to her doctor about genetic counseling and the importance of considering her values and preferences for involvement in deciding about genetic counseling and testing	Provide educational information needed by providers to effectively educate patients about cancer family history, risk assessment, and results and to refer them for genetic counseling Provide providers with access to educational materials and messages about familial breast cancer and resources for genetic counseling, genetic testing, and referral in order to educate the patient
Improve patient–provider communication about familial breast cancer risk and genetic testing	Improve patient-provider communication about familial breast cancer risk and genetic testing
Incorporate use of the tool into routine primary care	Incorporate use of the tool into routine primary care

BRCA=breast cancer

3.2 Methods

We began the literature review for the BRCA CDS tools by identifying the key questions that needed to be answered to develop and evaluate the tools (Table 4). We then abstracted three recent evidence-based reviews to answer as many of these questions as possible.²⁹⁻³¹ We identified the remaining information gaps and targeted our search to fill those gaps (see Appendix A). We searched PubMed using the identified search strategies. We looked for information on current practice, identification and referral of patients at high risk of HBOC, and for research that described the effect of CDS tools for breast cancer and genetic testing on patient-provider communication. We also reviewed the literature on three topics relevant to BRCA1/2 screening: (1) the prevalence of BRCA mutations and estimated cancer risk in those with mutations, (2) the benefits of pre-cancer identification, and (3) the harms of pre-cancer ascertainment.

To maximize efficiency, we extracted information from review articles when possible. For each search, we reviewed the article titles and abstracts and eliminated any that were clearly not relevant. We supplemented the initial search with papers identified from reference lists and additional sources as needed. We collected additional information on family history and risk assessment tools from Web sites referenced in the journal articles reviewed or identified in the evidence reports.

Table 4. Key questions regarding the design and evaluation of the BRCA CDS tools

Question 1. What family history is needed to classify the likelihood a woman carries a BRCA1/2 mutation? 1a. Can patients report the needed family history of information? 1b. What are the current practices regarding family history collection and pre-cancer identification of BRCA mutation carriers? 1c. What tools exist to improve family history collection, and how well do they perform?
Question 2. How do we calculate a woman's risk for carrying a BRCA1/2 mutation given her family history? 2a. What are the screening guidelines from national professional organizations? 2b. What risk assessment tools exist for BRCA mutations? 2c. Which measures are used to assess how the risk assessment tools perform?
Question 3. What information about breast cancer and familial risks should be included in the patient education module of the tool, and how should the information be presented? 3a. What do women know about HBOC genetics? 3b. What is a <i>woman's understanding of the information provided by the BRCA test and her overall perception of cancer risk</i> ? 3c. What are the issues related to the testing process and results? 3d. Are there alternatives to genetic testing?
Question 4. What educational materials on BRCA1/2 testing have been developed?
Question 5. What information needs to be included in the followup recommendations for physicians?
Question 6. How good is current communication between patients and providers about genetic risks for breast cancer?
Question 7. What health and psychological outcomes of genetic testing for BRCA1/2 mutations have been assessed?
Question 8. How satisfied are patients and providers with patient decisions about BRCA1/2 testing?

BRCA=breast cancer.

3.3 Results

3.3.1 Genetics and Management of HBOC

Prevalence of BRCA mutations and cancer risk among mutation carriers. Based on an extensive review conducted by Nelson et al.,²⁹ over 20 percent of women who develop breast cancer will have a first- or second-degree relative with the disease, and 5 percent to 10 percent will have a family history consistent with hereditary breast cancer. Mutations in two genes, BRCA1 and BRCA2, account for 30 percent to 50 percent of hereditary breast cancer. Among families registered in a population-based Breast Cancer Family Registry sites, BRCA1 mutations were identified in 4.0 percent of tested families and BRCA1 mutations were identified in 3.7 percent of families.³² Both BRCA1 and BRCA2 mutations were segregating in six families. The sensitivity of testing varied across sites, so some families may have had unidentified mutations.

The prevalence of BRCA mutations in the general U.S. population is estimated to be between 1 in 800 (0.1 percent) and 1 in 300 (0.3 percent).³³ Stratified by family history risk, the prevalence is estimated to be 0 percent and 0.24 percent among low-risk women, 0.24 percent to 3.4 percent among moderate-risk women, and 8.7 percent or higher among high-risk women.²⁹ Among people of Ashkenazi Jewish ancestry, the prevalence of clinically significant mutations in BRCA1 is estimated to be 0.8 percent and in BRCA2, 1.1 percent, for a total prevalence of 1.9 percent in either gene.²⁹

In the general population, the estimated risk of breast cancer by age 75 is 9 percent, and the lifetime risk is 12.5 percent.³⁴ Estimates of cancer risk among women with BRCA1/2 mutations vary greatly (Table 5). The estimated risk is lowest when it is calculated using the

mutation prevalence among breast cancer cases and the estimated risk of breast cancer in the general population.²⁹ Lifetime risk estimates are higher from studies of families with known mutations, such as the study of a large kindred in Utah with a BRCA1 mutation.³⁵ The study found 27 percent to 34 percent of carriers developed either breast or ovarian cancer by age 40 and 53 percent to 80 percent did so by age 70, depending on the statistical estimation method used. A meta-analysis of studies from population-based samples or those that adjusted for sample ascertainment calculated estimated penetrance rates of BRCA1 mutations similar to those estimated in the Utah kindred.³⁶ For BRCA2 mutation carriers, breast cancer risk to age 70 years was 49 percent (95 percent CI, 40 percent to 57 percent) and their ovarian cancer risk was 18 percent (95 percent CI, 13 percent to 23percent).³⁶

Table 5. Risk of breast or ovarian cancer among BRCA1 and BRCA2 mutation carriers

Risk by age (years)	Breast Cancer					Ovarian Cancer			
	40	50	70	75	Lifetime	40	50	70	75
General population ³⁷	0.5%	2%	7%	9%	12%	0.07%	0.2%	0.7%	0.9%
BRCA1/2 carriers									
From mutation rates in breast cancer patients ²⁹	5%–8%		20%–35%			3%–13%		15%–21%	
Utah kindred ³⁵	11%–18%		30%–53%			7%–20%		17%–47%	
Meta-analysis ³⁶									
BRCA1	57%					40%			
BRCA2	49%					18%			
Male carriers									
BRCA1 ³⁸	1%								
BRCA2 ²⁹	5%–10%								

BRCA=breast cancer

Gronwald et al. reported that the risk of breast cancer among first-degree relatives of BRCA1 mutation carriers was lower among women whose affected relative had been diagnosed with ovarian cancer compared to those diagnosed with breast cancer.³⁹ A few recent studies have also found a twofold increase in the risk of breast cancer among noncarrier family members of women with BRCA1 or BRCA2 mutations.⁴⁰ These studies suggest that genetic or environmental factors may influence the phenotypic expression in BRCA1 and BRCA2 families. These factors have not yet been identified, however.

3.3.2 Key Question 1. What Family History Is Needed to Classify the Likelihood a Woman Carries a BRCA1/2 Mutation, and How Do We Best Collect It?

Guidelines for BRCA mutation screening based on cancer family history have been formulated by several professional organizations, including:

- the American College of Medical Genetics (ACMG),⁴¹
- USPSTF,²⁸
- the National Comprehensive Cancer Network (NCCN),⁴²
- the National Institute for Clinical Excellence (NICE),⁴³
- the National Breast and Ovarian Cancer Centre (NBOCC),⁴⁴ and
- the Wales Cancer Genetic Service (WCGS).

Although each organization's guidelines differ somewhat, they each require some or all of the following information: the number of first- and second-degree relatives with breast or ovarian cancer, the age at diagnosis for each relative with cancer, whether any family members had bilateral breast cancer or both breast and ovarian cancer, and if any male relatives had breast cancer. Most organizations recommend, at a minimum, collecting a three-generational history of breast and ovarian cancer for both the maternal and paternal lines that includes age at diagnosis for each cancer and the presence or absence of Ashkenazi Jewish ancestry.^{29,30,41} This minimal family history may not identify high-risk women who have few female relatives who lived past age 45 years.⁴⁵ Risk assessments will be improved if information is gathered for all cancer diagnoses in as many first-, second-, and third-degree relatives (parents, children, siblings, grandparents, aunts, uncles, great-grandparents, nieces, nephews, and first cousins) as possible.⁴² Information on all types of cancer is needed because BRCA mutations can be associated with cancers other than breast or ovarian, including prostate cancer,²⁹ pancreatic cancer,⁴⁶ and sarcomas.⁴⁷

Key Question 1a. Can patients report the needed family history information? One concern about using family history as a screening tool is uncertainty about patients' ability to correctly report their cancer family history. A recent evidence report found that family members could report their cancer family history reasonably accurately in settings that used structured interviews or questionnaires to collect the information.³⁰ The sensitivity of breast cancer reporting was 89 percent to 90 percent and of ovarian cancer reporting was 67 percent to 83 percent. The specificity of reporting was 91 percent to 99 percent for all cancers, 95 percent to 98 percent, for breast cancer, and 96 percent to 99 percent for ovarian cancer. The accuracy of family history reporting was affected by the following:

- vital status of the relative—reporting was more accurate for living relatives;³⁰
- type of cancer;
- patient's race—black patients were less knowledgeable about paternal relatives than white patients;
- breast cancer laterality—unilateral cancer was reported better than bilateral cancer, but this observation was explained in part by the fact that the relatives who had bilateral cancer were more likely to have died;
- recruitment source—patients who were recruited from clinics reported more accurately than those recruited from the general population;
- degree of kinship—reporting was more accurate for first-degree relatives than for second- or third-degree relatives; and
- insurance status—patients with health insurance reported more accurately than those who did not have health insurance.³⁰

Formative research conducted by Centers for Disease Control and Prevention (CDC) for the development of Family Healthware, a family history screening tool for common diseases, found that knowledge about individual relatives can differ greatly depending on the relative's vital status and age of death, the difference in age between the patient and the relative, and the genetic or emotional closeness of the relationship.⁴⁸

The accuracy of family history reporting was not affected by the patient's age, sex, education level, marital status, or family size. There is some indication that women report more maternal than paternal relatives with breast cancer, but it is unclear if this is caused by biased

reporting, a greater likelihood for expression in the maternal line, or more opportunity for expression in the maternal line, which is guaranteed to have at least one female relative.⁴⁹ Women can also report their own history of breast or ovarian cancer accurately. Dominguez et al. found that the sensitivity of self-reports of breast cancer was 92 percent and that the sensitivity of self-reports of ovarian cancer was 83 percent.⁴⁷

Key Question 1b. What are current practices regarding family history collection and pre-cancer identification of BRCA mutation carriers? Family history is not consistently requested or documented in medical records, and when present, the cancer family history information in primary care medical records is inadequate for valid screening.⁵⁰⁻⁵⁴ Although 90 percent of primary care physicians in one study reported that they asked about cancer in first-degree relatives, only 56 percent asked about second-degree relatives, and only 40 percent asked the age of diagnosis.⁵¹ Only 58 percent of women participating in a mammography registry, however, reported that a physician had asked about their family history of breast cancer.⁵⁰ Physicians were more likely to take a cancer family history for patients who were younger, worried about breast cancer, or who had a well care visit.⁵⁰ In another study, for only 43 percent of patients who had a cancer family history was that history documented in the medical record, and only 40 percent of these records included the age of diagnosis.⁵² At one cancer center, 89 percent of women with breast cancer had some family history reported, but only 42 percent of the histories included three generations.⁵³ Volk et al. found that asking patients for family history information outside of the clinic setting could provide valuable information: less than 10 percent of positive family histories of osteoporosis, glaucoma, or colon cancer were identified through patient survey, and less than 20 percent of positive family histories of diabetes, breast cancer, or coronary artery disease were documented in the patients' medical record.⁵⁴ However, only 15 percent of patients solicited to participate actually returned a family history. When assessing the cancer risk of patients, the information on family history increased the risk of breast cancer of 33 percent of patients, and of other conditions for 40 percent to 95 percent of patients.⁵⁴ Although messages were sent to physicians through the electronic health record notifying them of the patient's increased risk and recommending specific followup actions, most of the recommended actions were taken less than 50 percent of the time. None of the patients for whom genetic counseling or testing were recommended had a referral documented in their chart.

In 2001, 60 percent of primary care physicians surveyed reported that they had discussed genetic screening related to breast cancer with their patients.⁵⁵ Several surveys conducted between 1999 and 2003 found that 30 percent to 50 percent of physicians had referred patients for genetic counseling or testing for cancer susceptibility.⁵⁵⁻⁵⁸ Among physicians who had referred patients for genetic services, most referred only one or two patients in a year.⁵⁷ Urban and suburban physicians were more likely to refer patients for genetic counseling and testing than rural physicians.⁵⁸

The most common reason that physicians referred patients for genetic services was a family history of cancer.⁵⁸ Referral was promoted by patients' interest, a need for evaluation for genetic testing or access to genetic expertise, receipt of advertising, and affiliation with an integrated health system.^{56,58} Patient interest in genetic testing was the strongest motivator for physicians to order a genetic test.^{55,57,59,60} The majority of physicians also expressed an interest in receiving continuing medical education credits for training in genetic risk assessment and genetic testing for cancer susceptibility.^{55,57,59,60}

Commonly cited barriers to the use of genetic services were cost,⁵⁵ lack of insurance coverage,⁵⁵ concern about insurance discrimination,⁵⁵ too great a distance to the services,⁵⁸ unawareness of service availability,⁵⁸ absence of effective interventions,⁵⁸ and patient disinterest.⁵⁸ Some barriers to genetic testing may be more perceived than actual. Most health insurance plans now cover genetic counseling and testing.⁶¹ In addition, although many physicians, like their patients, fear that genetic testing will result in discrimination by insurers,^{55,59,62} no case of insurer discrimination against a BRCA1/2 mutation carrier had been reported as of 2007.⁶³ The Genetic Information Nondiscrimination Act of 2008 further protects BRCA1/2 mutation carriers against insurance discrimination.⁶⁴

Another barrier to the use of genetic testing for cancer susceptibility is the uncertainty physicians feel about their ability to evaluate the appropriateness of testing or interpret test results for themselves, and where to refer patients for these services. Only 40 percent of primary care physicians and 58 percent of tertiary-care physicians surveyed in 1999 felt qualified to recommend genetic testing to their patients.⁵⁹ Studies that test physicians' knowledge of genetics indicate that many do not have the knowledge needed to appropriately refer patients or interpret test results.^{65,66} Among physicians surveyed by Sandhaus et al. regarding a hypothetical test report for BRCA1/2 mutations, all correctly interpreted the report as indicating the patient had a deleterious mutation, but only 70 percent could correctly answer questions about the risk in the patient's first-degree relatives, and only 51 percent could answer all the questions about the report correctly.⁶⁶ The study also found that the ability of physicians to answer the questions correctly was strongly related to their understanding of cumulative risk, and that graphical presentation of results appear to improve their understanding.⁶⁶ Coulson et al. addressed the difficulties that doctors have understanding risk and communicating it to their patients by developing their tool using argumentation, which uses qualitative arguments to support the risk assessment rather than numeric probabilities.⁶⁷

Physicians interviewed in 1998 reported they did not know what to do with a positive result for a cancer susceptibility test.⁶² The study authors concluded that the uncertainty among primary care physicians about the clinical utility and validity of genetic testing was the leading barrier to incorporating genetic testing into practice.⁶² Cho⁶⁸ found that physicians who were early adopters of genetic testing for BRCA1/2 mutations had more knowledge of genetics and access to counseling services.⁶⁸

Key Question 1c. What tools exist to improve family history collection, and how well do they perform? Most assessments of family history tools have compared the information collected from the tool to that collected by trained healthcare professionals (e.g., genetic counselors or genetic nurses).³⁰ Some tools also measured test-retest reliability.⁶⁹ The review conducted by Qureshi et al. identified 22 paper- or computer-based tools for collecting cancer family history. Eleven of these tools were available online at the time of the review conducted by Qureshi et al., but only eight could still be found online in September 2008. We reviewed the tools available online to determine if they collected sufficient information to implement the BRCA mutation screening of the professional organizations referenced above.^{28,41-43,70} Three of the identified tools collected sufficient information for screening (Table 6):

- My Generations from Evanston Northwestern Hospital (available at: <http://www.northshore.org/clinicalservices/medicalgenetics/mygenerations/default.aspx?id=4>),

- Interactive Cancer Family Tree from University of Nebraska Medical Center (available at: <http://app1.unmc.edu/gencancer/>), and
- Cancer History Guide from Myriad Genetics (available at: <http://www.myriadtests.com/cancerhistory.htm>)

Table 6. Use of selected risk factors associated with hereditary breast and ovarian cancer in family history screening guidelines and percentage of women identified as high risk by each protocol (Modified from Palomaki et al.⁷¹)

Factor(s) needed for classification as high risk	ACMG	NBOCC	WCGS	NICE	NCCN	USPSTF
No. relatives with breast cancer at any age*	>3	>3	>3	>3	>3	>3
Bilateral breast cancer alone	Yes	+ 1 other case	If 1st degree	If <50 y at diagnosis	+ 1 other case	If 1st degree
Male with breast cancer	Yes	+ 1 other case	Yes	+ 1 other case	+ 1 other case	Yes
Age defining “early-onset” breast cancer	<45 y	<40 y	<40 y	<40 y	<40 y	No
Breast and ovarian cancer in one relative	No	+ 1 other case	If 1st degree	No	Yes	Yes
Consider Ashkenazi Jewish heritage	Yes	Yes	No	No	Yes	Yes
Consider identified family mutations	Yes	Yes	No	No	Yes	Yes
Consider personal history of breast or ovarian cancer	Yes	No	No	No	Yes	No
Consider other cancers	No	Yes	No	Yes	Increase suspicion	No
Percentage who screened positive in primary care	5.9%	5.6%	5.0%	4.4%	7.8%	7.5%

ACMG=American College of Medical Genetics; NBOCC=National Breast and Ovarian Cancer Centre; NCCN=National Comprehensive Cancer Network; NICE=National Institute for Clinical Excellence; USPSTF=United States Preventive Services Task Force; WCGS=Wales Cancer Genetic Service.

*Each side of family should be assessed independently (not required by USPSTF).

We also identified two additional family history tools through conversations with AHRQ and interested parties. One of these is the CDC Family Healthware tool discussed above.⁴⁸ The other is the updated version of the Health and Human Services Family Health Portrait, which has not yet been released or described in the literature (Weikart, personal communication).

3.3.3 Key Question 2. How Do We Calculate a Woman’s Risk for Carrying a BRCA1/2 Mutation Given Her Family History?

Key Question 2a. What are the screening guidelines from national professional organizations? As noted above, many professional organizations have published guidelines for identifying women who are at risk of HBOC. The USPSTF estimates that approximately 2 percent of adult women in the U.S. general population would have a family history consistent with their guidelines for referral.²⁸ One study found, however, that most current guidelines identify 4 percent to 8 percent of women in primary care settings as high risk (Table 6).⁷² We did not find studies that assessed how well any of the guidelines correctly identified women with a BRCA1/2 mutation as high risk. A study comparing the application of all six sets of guidelines to a primary care population found fair to poor agreement between most protocols.⁷¹ We found no information on which guidelines are more commonly used by physicians in routine clinical practice. We searched for guidelines that identified patients at high risk of hereditary cancer without regard to a particular syndrome. Hampel et al. attempted to provide such guidelines, but their criteria were still quite complex.⁷³

Key Question 2b. What risk assessment tools for BRCA mutations exist? There are two types of risk assessment models for breast cancer: those that predict breast cancer risk and those that predict the risk of carrying a BRCA mutation.⁷⁴ Breast cancer risk assessment models include some measure of family history but also include reproductive history and other factors that are not relevant to our study. We will focus on the BRCA mutation risk assessment models that use family history information to calculate the risk a BRCA mutation is segregating in the family.

Paper and computer risk assessment tools have been developed to aid in identifying women at high risk of a BRCA mutation (Table 7).²⁹ Since the review by Nelson et al. in 2005, new tools have been developed, and old tools have been modified. Based on the information we have found, all the risk assessment tools have been evaluated in high-risk populations, either breast cancer patients or families with multiple cases of breast cancer.²⁹ Sensitivity and specificity among a primary care population would be expected to be much different than among high-risk or oncology populations.

Three recent studies have compared models for assessing the risk of carrying a BRCA 1/2 mutation among families seen in a cancer genetic clinic. The sensitivity and specificity of the models vary for different study populations and parameters.⁸⁰⁻⁸² Antoniou et al. found that only BOADICEA, which was developed by the authors, accurately predicted the presence of a mutation and was also the best discriminator (Table 8).⁸⁰ Roudgari et al. found that the sensitivity and specificity of each model varied by family structure and characteristics.⁸¹ For the completed sample, COS had the highest sensitivity and BOADICEA had the highest specificity (Table 8). Parmigiani et al. found that test performance varied by population.⁸² They presented sensitivity and specificity values using a risk threshold (the lowest risk level considered as high risk) of 10 percent, although they recommended against the use of this value in clinical practice because a substantial proportion of women with a BRCA1/2 mutation will be missed. We were unable to find any study that evaluated the performance of these models in a primary care setting, but we would expect the performance of the tools to differ in that setting. In a recent evaluation of several risk assessment tools, predictions were less accurate from women at lower risk than those at higher risk.⁸⁰

As mentioned above, families that have few female family members who survive to the relevant age may not be identified by a risk assessment based on family history.⁴⁵ The occurrence of bilateral prophylactic mastectomy or bilateral salpingo-oophorectomy as a prophylactic measure or incidental to a hysterectomy may also result in underestimating the mutation risk.^{83,84} The strongest effects on risk estimates occur if the relevant family member was a first-degree family member⁸⁴ or was long-lived after the intervention.⁸³

Table 7. Risk assessment models for predicting BRCA1/2 mutations or genetic risk of breast cancer

Tools	Model
FHAT ²⁹ Risk threshold: 22%	Points are assigned based on the number and relationship to proband of third-degree or closer relatives diagnosed with breast, ovarian, colon, or prostate cancer, the age at diagnosis, and the number and type of primary cancers. Patients with scores of ≥ 10 warrant referral.
Claus Model ⁷⁴	Developed for use by clinical oncologists, this model estimates risk of breast cancer based on cancer history in mothers and sisters; it does not take into account ovarian cancer in family. The model was developed with Caucasian women only.
University of Virginia Brochure ⁷⁵	This 4-page brochure is targeted to primary care clinic patients and guides women through a simple risk assessment based on family history. Women are informed that they may be at high risk based on their family history and are encouraged to consult their physician.
GRACE ⁷⁶	This assessment method collects family history data from patients at clinics and uses the Claus model for risk assessment.
BRCAPRO ⁷⁷ Risk threshold: 20%	BRCAPRO is a Bayesian model that considers patients' age, age at diagnosis, Ashkenazi Jewish ancestry, and for all first- and second-degree relatives, the presence of bilateral breast cancer, concurrent breast and ovarian cancer, oophorectomies, and males with breast cancer.
Manchester Risk threshold: 29 10%	Points are assigned based on cancer type (breast, ovarian, pancreatic, or prostate), affected family members, and age at diagnosis. Provide scores for BRCA1 and BRCA2 mutations separately.
GRAIDS ⁷⁸	Developed specifically for primary care using clinical practice guidelines for risk assessment. Patient completes the family history questionnaire prior to the visit. Family history collected by the provider has prompts to record age of proband, age at cancer diagnosis; in addition to gender, age, or age of death, Jewish ethnicity, and cancer history. Applies Claus model of risk using Mendel software. Provides patient-specific management advice and risk level. Developed from RAGS. RAGS uses argumentative logic support for recommendations rather numerical probabilities. ⁶⁷
Couch ⁷⁹	This instrument is limited to families with > 2 cases of breast cancer. Predictors include the number of women diagnosed with breast cancer under age 50, ovarian cancer, concurrent breast and ovarian cancer, male breast cancer, and Ashkenazi Jewish ancestry
Myriad 1 (Shattuck-Eidens) ²⁹	Myriad 1 predicts risk for BRCA1 mutation for women with early-onset breast or ovarian cancer, or with a family history of breast or ovarian cancer. The instrument takes into account bilateral breast cancer, age of diagnosis, and Ashkenazi Jewish ancestry and is not dependent on affected relatives.
BOADICEA ⁸⁰	BOADICEA predicts susceptibility, accounting for other genes as well as BRCA1 and BRCA2.
Case Only Study (COS) ⁸¹	This instrument was developed from BRCAPRO and incorporates country and birth cohort-specific data on incidence. COS can use data about third- and fourth-degree relatives and allows censoring for family members who have undergone prophylactic surgery.
Myriad 2 ²⁹	Myriad 2 predicts risk for both BRCA1 and BRCA2 mutations for women with breast cancer under age 50 or ovarian cancer who have at least one first- or second-degree relative with early breast or ovarian cancer. The instrument considers bilateral breast cancer, concurrent breast and ovarian cancer, and breast cancer under age 40.

BOADICEA= Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm; BRCA=breast cancer; COS=case only study; FHAT=Family History Assessment Tool; GRACE=Genetic Risk Assessment in the Clinical Environment; GRAIDS=Genetic Risk Assessment in Intranet and Decision support; RAGS=Risk Assessment in Genetics.

Table 8. Performance of risk assessment tools

Model	Cut-off, %	Setting/Population	Prediction of BRCA1/2 Mutations			
			Sensitivity, %	Specificity, %	PPV, %	NPV, %
BOADICEA	10	Genetics Clinic/UK ⁵⁵	90.4	39.5	25.8	94.6
BRCAPRO	10	Genetics Clinic/UK ⁵⁵	88.2	43.1	26.5	94.0
BRCAPRO	10	General Population/U.S. ⁸²	42.9	93.4		
BRCAPRO	10	Family history/U.S. ⁵⁷	70.6	67.1		
BRCAPRO	10	High risk/U.S. ⁸²	82.4	52.6		
Manchester	10	Genetics Clinic/UK ⁸⁰	92.3	33.4	24.4	94.9
Myriad	10	Genetics Clinic/UK ⁵⁵	78.9	46.3	25.5	90.4
Myriad	10	General Population/U.S. ⁸²	28.6	86.4		
Myriad	10	Family history/U.S. ⁸²	85.3	68.3		
Myriad	10	High risk/U.S. ⁸²	77.5	47.5		
BOADICEA	20	Genetics Clinic/UK ⁸⁰	80.8	58.5	31.2	92.9
		Genetics Clinic/UK ⁸¹	53.0	78.0	NS	NS
BRCAPRO	20	Genetics Clinic/UK ⁸⁰	81.1	56.7	30.3	92.8
Manchester	20	Genetics Clinic/UK ⁸⁰	87.1	43.4	26.4	93.6
		Genetics Clinic/UK ⁸¹	91.0	43.0	NS	NS
Myriad	20	Genetics Clinic/UK ⁸⁰	51.0	80.5	37.8	87.6
COS	20	Genetics Clinic/UK ⁸¹	92.0	43.0	NS	NS

BOADICEA=Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm ; BRCA=breast cancer; BRCAPRO=__; COS=case only study; NPV=negative predictive value; NS=not significant; PPV=positive predictive value; UK=United Kingdom; US=United States

*General population: all breast cancer cases in Orange County, CA. Representative of a general oncology population. Family history: women either had breast cancer < 35 years or a first-degree relative with breast cancer. High risk: a mix of high-risk populations similar to women seen in cancer genetic clinics.⁸²

Key Question 2c. What outcomes are used to assess how the risk assessment tools perform?

Studies whose participants have been tested for BRCA mutations have assessed the predictive value of risk assessment models by the specificity and sensitivity, the positive predictive value and negative predictive value, and the area under the receiver operating curve.^{29,80,81} In the absence of genetic testing, the predictive value of the risk assignment tools have been evaluated by comparison with expert opinion, either that of a cancer geneticist or of regional guidelines.²⁹

A few risk- assessment tools have been evaluated for usability and acceptability. The GRAIDS tool was evaluated in primary care clinics in the United Kingdom.⁷⁸ The measures evaluated included frequency of software use, the practitioners' attitudes toward the software, the total number of referrals to secondary care for familial cancer, the proportion of referrals that met the regional referral guidelines, and informed decisionmaking (currently being validated).⁷⁸ The evaluation of the patient-oriented GRACE tool assessed the patient's attitude toward the interventions; the perceived benefits of the interventions; participants' perceptions of the credibility, trustworthiness, accuracy, clarity, and helpfulness of the risk information provided; and the participants' satisfaction and risk communication preferences.⁷⁶ The evaluation also examined the participants' pre- and post-intervention perception of their risk and the accuracy of that perception. Finally, the evaluation measured the following psychological outcomes pre- and post-intervention: anxiety and depression, current anxiety, and the frequency and impact of

cancer worry. There was no difference between patients who used GRACE and those who received nurse counseling on any measure except patient attitude. Patients had a more positive attitude towards the nurse counseling intervention.

3.3.4 Key Question 3. What Information about Breast Cancer and Familial Risks Should Be Included in the Tutorial, and How Should the Information Be Presented?

The information provided to women about their familial cancer risk, as assessed through their family history, and about BRCA1/2 mutation testing must be sufficient to correct any misconceptions about the genetics of HBOC, to help patients reach a realistic idea of their risk of having this syndrome and to allow them to make an informed choice about whether they should be tested.⁴¹

A recent study identified four approaches to writing or evaluating materials related to genetic testing: the DISCERN-Genetics tool,⁸⁵ the Erfocentrum Guidelines,⁸⁶ a tool published in the *American Journal of Medical Genetics* by Cho et al., and a leaflet published by the Genetics Interest Group.⁸⁷ The four sources were in agreement that 14 key themes should be included in educational materials about genetic testing developed for the public (Table 9).

Table 9. Key themes required in education materials about genetic testing

Theme	Description
Background and effect	Description of frequency and symptoms of condition; difference between being a carrier and having the condition
Treatment and management	Treatment and management options for the condition, their success, and procedures for referrals and follow-up care
Heredity and risk	Information on how the condition is inherited, why the reader might or might not be at risk, the risk of developing the disorder among people who have the faulty gene, the risk to other family members of having the faulty gene or developing the condition, and the risk someone who carries the faulty gene has of passing it onto their children
Type of test	The purpose of the test
Testing procedure	Description of the procedure for testing, the risk of the procedure, and whether it hurts
Testing accuracy	Acknowledgement of the limitations of the test, including laboratory or human error, false positive and false negative test results, any local variation in results, and an explanation of why a repeat test may be needed
Follow-up to testing	A description of how and when the reader will receive results and who will provide them. A description of followup procedures after each potential test result
Shared decisionmaking	Topics the reader may want to discuss with their family, friends, or health professionals
Psychosocial consequences	The positive and negative emotional and social consequences that might be experienced; a range of emotions may be experienced and is normal; possible that there could be discrimination in employment or health coverage
Consequences for relatives and partner	What an increased risk means to the person being tested and to their family; family members may react differently; misattributed paternity may be discovered
Benefits and risks	Information on benefits such as early diagnosis, disease prevention or treatment, etc., and limitations/risks such as emotional difficulties, strained relationships, difficult decisions, and discrimination
Patients rights	Testing is voluntary, results are confidential, and the patient can choose to whom the results are disclosed
Date and sources	The date of the publication and the sources of the information provided in the document
Additional information and support	Information on services (local preferred), support organizations, other sources of information, and other relevant health professionals

A study conducted in the United Kingdom by Lewis⁸⁷ analyzed educational and informational materials about genetic diseases and genetic testing, including but not limited to materials about BRCA1/2.⁸⁷ They found that these materials often lacked social and

psychological information and tended to focus more on scientific and factual information than experience-based information. Half of the materials they analyzed were missing information about where to go for more information, support services, or patient groups. Shepperd⁸⁵ provides a useful list of criteria for assessing the quality of educational information about genetic testing, including the following: aims are clear, aims are achieved, background of the condition, treatment choices, risk, purpose of the test, testing procedure, test accuracy, after the test, access to test results, shared decisionmaking, discrimination, psychosocial consequences, consequences for others, additional sources of information, sources of information used, date of the information, balance and bias, local information (if applicable), and overall quality.⁸⁵ Wakefield⁸⁸ suggests that decision support tools for genetic testing should be tailored to a patient's coping style, with monitors (who seek out information) benefiting from receiving more materials and details than blunters (who seek distractions to avoid thinking about a threat).⁸⁸ Materials could also be designed to accommodate both styles, by providing links or telling monitors where to go for more information.

Two recent articles describe the development of patient education materials about HBOC and BRCA1/2 testing. Mackay et al. describe a computer-based program developed in the United Kingdom that provides a personalized risk assessment based on the user's family history of breast and ovarian cancer, then presents risk information to the user using the following model:

1. The patient's present situation. An indication of the risk level (e.g., Your answers suggest that there is a slightly increased chance that there is a faulty breast cancer gene in your family).
2. Explanation. The justification of 'your present situation' on the basis of the data inserted and national guidelines.
3. What next? A description of possible options which may be offered.
4. What might change your current situation
5. How confident can you be? Stating that the information package is based on the NICE guideline. Other sources of support are also offered.⁸⁹

Cohn et al. describe the development and evaluation of a simple four-page brochure to educate women about and to help them assess their risk for hereditary breast cancer.⁷⁵ The pilot evaluation of the tool found that many women were already aware of hereditary breast cancer and that many women (82 percent) found the brochure clear and easy to use.

Key Question 3a. What do women know about HBOC genetics? The only assessment we found of women's knowledge of breast cancer genetics was conducted in the United Kingdom between 1996 and 1999.⁹⁰ At that time, 63 percent of women surveyed knew that a woman whose mother had a BRCA1 mutation had a 50 percent chance of passing it to her daughter, but only 26 percent knew the gene could also be passed from father to daughter. The misconception that the gene could only be inherited from the mother was still a concern when the ACMG screening guidelines were published in 2005.⁴¹ Hereditary breast cancer has received considerable press attention in recent years, and public knowledge may have improved.

Providing education about breast cancer genetics prior to counseling can improve efficiency of the counseling session and allow for more individualized attention, including more focus on personal risk and decisionmaking.⁹¹

Key Question 3b. What is a woman’s understanding of the information provided by the BRCA test and her overall perception of cancer risk? Vuckovic⁹² conducted focus groups about participants’ willingness to undergo genetic testing for breast cancer. The research found that women have a lot of misinformation about the inheritance of HBOC, the information provided by a BRCA1/2 test, and how the BRCA testing is conducted.⁹² Many participants believed the test diagnosed breast cancer rather than provided information about the probability of developing breast cancer. Other studies have found that many women with a family history of breast cancer overestimate their risk of cancer or of having a BRCA mutation.⁹³⁻⁹⁵

Women with a family history of breast and gynecologic cancer are highly accepting of genetic testing for these cancers; 85 percent to 90 percent of women reported they would definitely or possibly be tested.^{96,97} Women who are interested in BRCA1/2 testing believe it will help them to make healthcare or medical management decisions^{93,98} and to learn about their cancer risks and whether their children or other relatives may be at risk for cancer.^{92,93} Some reasons women may not have BRCA1/2 testing include concerns about health insurance discrimination, concerns confidentiality or privacy, the desire to avoid the stress and worry that resulting from a positive test, and the fear that friends and family would treat them differently.^{92,93,98} One study found that only 22 percent of study participants who received pretest counseling completed all steps of the testing process, including accepting testing, providing a blood sample, calling for test results, and accepting post-test genetic counseling.⁹⁹ Married women and those at a 10 percent or higher probability of having a mutation were more likely to complete the process.⁹⁹ Whether African American women received pretest counseling that was culturally tailored or standard did not affect BRCA1/2 test result acceptance rates.

Perceptions of cancer risk are likely to derive from more than numerical calculations, however. Women with friends and relatives who have suffered or died from breast cancer are more likely perceive themselves as being at high risk and are more likely to adhere to screening recommendations and adopt risk-reducing strategies, such as surgery or chemoprevention.¹⁰⁰⁻¹⁰³ Women who had a family member who died of cancer perceived it as life-threatening and hopeless, but those who had a family member who survived cancer perceived it as being survivable.¹⁰⁴

Several studies have found that genetic counseling improves the accuracy of patients’ cancer risk perceptions and reduces decisional conflict regarding BRCA1/2 testing.^{95,105} Bowen¹⁰⁶ found that genetic counseling only had a minimal effect on increasing the accuracy of cancer risk perceptions.

Women with a family history of breast cancer are very interested in BRCA1/2 testing, but they may have unrealistic expectations of the test and testing process.¹⁰⁷ Women generally have a poor understanding of the genetic testing process, of the timescale for testing, and the risk calculations. Providing more information about the testing process, timescale, and the calculation of risk may reduce anxiety, result in more accurate expectations of the process, and improve adaptation to risk.¹⁰⁷

The ACMG recommend that women be informed prior to testing that some mutations may not be detectable with the current test and that the BRCA mutation test only needs to be completed once, unless changes to the test make additional genetic changes detectable.⁴¹ Both the National Cancer Institute (NCI) and the ACMG recommend that the three possible test results should be explained prior to testing:^{41,108}

1. The detection of a deleterious mutation. This result would mean the following:
 - The patient has an increased risk of developing breast and/or ovarian cancer.

- The patient's relatives may be at risk of carrying the mutation, and the patient will need to consider informing them of their risk.
 - The patient will need to discuss with her healthcare providers potential detection and prevention strategies.
 - The patient may need psychological support from family, friends, or health professionals to help deal with the test results.
2. The detection of an variant of uncertain significance. This result would mean the following:
 - The interpretation of the result will depend on the presence or absence of the mutation among family members with breast or ovarian cancer.
 - If the mutation is found in all or most affected family members, then the patient is at increased risk of developing breast or ovarian cancer.
 - If the genotype of other family members is not known, then the mutation may or may not be deleterious.
 3. No mutation in the gene could be detected. If the deleterious mutation in the family has previously been identified, this result would mean that the patient did not inherit the deleterious mutation and her risk of developing breast or ovarian cancer is the same as the general population risk. If the genotype of her affected relatives is unknown, the patient does not carry a known deleterious mutation, but she may still be at increased risk based on her family history.

Key Question 3d. Are there alternatives to genetic testing? Women should also be informed of alternatives to testing. Women who choose not to be tested can adopt and maintain intensive surveillance behaviors comparable to those advised for known mutation carriers. Women who are younger than the recommended age for starting surveillance may chose to delay testing. Even if they choose not to be tested, women may choose to store DNA samples for possible future testing in the interest of descendants and other relatives.

3.3.5 Key Question 4. What Educational Materials on BRCA1/2 Testing Have Been Developed?

Educational materials on hereditary breast cancer are available on the Web sites of many professional, government, and advocacy organizations. The National Society of Genetic Counselors Web site has information for providers and patients.¹⁰⁹ The National Cancer Institute Web site has a question and answer page for patients.³⁴ The Web site of the advocacy group for breast cancer families, Facing Our Cancer Empowered (FORCE), includes educational resources for women at risk of HBOC.¹¹⁰ However, Lewis et al. found that few of the 50 examples of patient education materials on genetic testing they evaluated included all 14 key themes recommended for patient education materials.⁸⁷

Key findings from a focus group intended to elicit feedback about decision aids for breast cancer genetic testing were that women were interested in details about additional sources of information; some women preferred video while others preferred photographs, so including both formats will appeal to a range of users; women did not like frightening information; and women did not understand the concept of informed choice.²⁷ The use of decision aids can increase knowledge and answer questions.^{21,111} Decision aids have also been found to decrease perceptions of breast cancer risk in low-risk women.²¹

Coulson et al. found in the development and evaluation of RAGS that a simple interface that could be mastered in a few minutes increased confidence among doctors and patients, encouraged doctor–patient communication, and may have improved data quality.⁶⁷ The pilot was evaluated in a work setting, which resulted in clarifying some needs that were unanticipated. They found that doctors wanted to control when the report appeared on the screen so that they could present it when they were comfortable. The report contains a general overview of what the software does, a short recommendation for follow-up, and the reasons behind the recommendation.⁶⁷

3.3.6 Key Question 5. What Information Needs to Be Included in the Follow-up Recommendations for Physicians?

Primary care providers often lack the knowledge needed to identify and advise patients with HBOC and, in fact, often have the same misconceptions as patients.¹¹² The ACMG screening guidelines state that “to offer testing is to take responsibility (whether oneself or through appropriate referral) for adequate pretest education, the process of informed choice, and post-test counseling.”⁴¹ They go on to say the provider should focus on informed choice (similar to informed decisionmaking) rather than informed consent. The principles of informed choice for BRCA1/2 mutation testing, as stated by ACMG, and the elements of informed consent given by NCI and by American Society of Clinical Oncology (ASCO) are listed in Table 10.^{41,108,113} The elements of informed choice are focused on the context of the testing, while the elements of informed consent are more focused on the specific information to be provided to the patient.

The factors that influence providers to order BRCA testing are those associated with an increased risk of having a mutation: a patient or family history of breast and ovarian cancer, a known BRCA mutation transmitted within the family, age of diagnosis with breast or ovarian cancer, bilateral breast cancer, and Ashkenazi Jewish heritage. Of physicians who sought information or ordered genetic testing for breast cancer susceptibility, 15 percent reported that they had ordered a test for breast cancer susceptibility at the patient’s request in the absence of family history.⁶⁸

Lerman et al. compared a counseling–education (C–E) approach that required patients to consider the personal impact of a positive or negative test result to an education-only approach that only provided information on benefits and limitations and risk of testing.¹¹⁴ The C–E approach increased the patient’s perception of the limitations and risks of testing and decreased the patient’s perceptions of benefits, but it did not change the proportion of patients requesting testing. Review articles and tutorials for physicians, however, tend to focus on the genetics of the disease, whom to refer for genetic testing, and medical management.^{115,116}

Table 10. Elements of informed choice or informed consent for BRCA1/2 mutation testing according to professional and government organizations

	ACMG	NCI	ASCO
Provider offers testing when appropriate but does not recommend for or against it.	*		
Testing should be performed only after counseling and execution of an informed choice document.	*		
Testing should be voluntary.	*		
Anyone being tested to benefit a relative should be encouraged to consider the implications of testing for themselves.	*	*	
Provider elicits and discuss patients expectations, beliefs, goals, and motivation with them.		*	
Provider explains how inheritance of genetic factors may affect cancer susceptibility.		*	*
Provider clarifies person's increased risk status.		*	
Provider discusses potential benefits, risks, and limitations of testing.		*	*
Provider discusses costs and logistics of testing and follow-up.		*	*
Provider discusses possible outcomes of testing (e.g., positive, negative, inconclusive, uninterpretable, true positive, false positive).		*	*
Provider discusses medical options available for those who choose to test, for those who choose not to test, and for those who have positive, negative, or inconclusive results.		*	*
Provider discusses data on efficacy of methods of cancer prevention and early detection.		*	*
Provider discusses possible psychological, social, economic, and family ramifications of testing or not testing.		*	*
Provider encourages consideration of how the person's screening or other behaviors might change depending on the test result.		*	*
Provider discusses alternatives to genetic testing (e.g., tissue banking, risk assessment).		*	*
Provider attains verbal and written informed consent or clarifies the decision to decline testing.		*	
Provider encourages consideration of personal acceptability of screening and risk reduction options.		*	
Provider discusses confidentiality issues.			*

ACMG=American College of Medical Genetics; ASCO=American Society of Clinical Oncology; NCI=National Cancer Institute

3.3.7 Key Question 6. How Good Is Current Communication Between Patients and Providers about Genetic Risks for Breast Cancer?

The communication of risk between providers and patients is problematic.^{94,107,117} Patients' perceptions of risk may not be consistent with providers' perceptions.¹¹⁷ Patients may not understand how the risk was calculated or may not believe the risk.^{94,107} Providing comparative risk estimation may affect how patients interpret risk. In one study, all women were presented with a theoretical scenario in which their risk of breast cancer was 6 percent, and the risk could be cut to 3 percent by taking medication. They were told that the medication could also cause problems and side effects consistent with those of tamoxifen. They were then asked if they would choose to take the medication. Women who were told they were above-average risk were more likely to say they would take the medication and to believe it would reduce cancer risk than women who did not receive comparative data.¹¹⁸

O'Doherty et al.¹¹⁷ make several suggestions on ways to address the problems in risk communication and patient perception (pp. 411–416). Many of their suggestions may not be applicable to educational messages provided through CDS, but others are:

- “Encourage the client to use estimates of risk to assist in decisionmaking rather than as meaningful predictors of future events.”
- “Frame the information in a variety of ways e.g., the chance of developing cancer, the chance of not developing cancer.”
- “Relative risks...should be avoided when conveying information to a client. Provide information in terms of absolute probabilities, specifying the period over which the absolute risk applies.”
- “Encourage the client to reflect on their professed preferences from different perspectives, such as using different framing, or imagining their situation in 10–20 years’ time.”
- “Encourage the client to view decision-making in terms of selecting the most appropriate course of action rather than in terms of correct vs. incorrect.”
- “Use numerical probabilities as the basis for providing risk information, but include verbal qualifiers to set the numerical risk in the context of other life events.”
- “Encourage the client to place the risk of cancer in context by outlining what the diagnosis might actually entail for the client. This requires explicit recognition of the client’s life situation (age, well-being, experience, children, etc).
- Also outline what the diagnosis may not entail. A diagnosis of cancer may not be as catastrophic as the client believes, especially if the cancer is identified at an early stage.”
- “The same principles apply to a discussion about interventions to reduce the risk of an adverse outcome, placing the possible outcomes into the broader context of the client’s life situation.”

3.3.8 Key Question 7. What Health and Psychological Outcomes of Genetic Testing for BRCA1/2 Mutations Have Been Assessed?

Benefits of testing. *Cancer risk reduction interventions and their effectiveness.* A critical reason for identifying women at high risk of HBOC is the availability of interventions, including chemoprevention and prophylactic surgery, that can reduce the risk of breast cancer and of intensive surveillance protocols to identify tumors early.

Intensive screening for cancer. The National Comprehensive Cancer Network⁴² recommends that high-risk women receive training in breast self-exam, begin monthly self-exams at age 18 years, and begin semiannual clinical breast exams at age 25 years. Intensive clinical surveillance, including mammograms and breast MRI screening, should begin at age 25 years or may be individualized based on the earliest age of onset in the patient’s family. Semiannual screening for ovarian cancer by CA-125 testing and transvaginal ultrasound is recommended beginning at age 35 years or 5 to 10 years before the earliest ovarian cancer diagnosis within the family for women who have not undergone risk-reducing salpingo-oophorectomy.⁴²

The studies reviewed by Nelson et al. found the sensitivity of intensive screening for breast cancer detection ranged from 74 percent to 95 percent. Many of these studies of defined risk status by family history rather than mutation status. When analysis was limited to BRCA1/2

mutation carriers, sensitivity dropped and the frequency of interval cancers increased.²⁹ Screening younger women with a family history of breast cancer by breast self-exam, clinical breast exam and mammography increased survival by approximately 75 percent.¹¹⁹ The tumors of screened women were significantly smaller, less likely to be node-positive, and less likely to be invasive than tumors that present symptomatically in similar aged women who are not undergoing intensive screening. The European Familial Breast Cancer Collaborative found that increased cancer screening was moderately effective in detecting tumors in women at risk for familial breast cancer who complied with the recommended screening regime. Examination detected 75 percent of the tumors of screened women were detected by examination, and mammography detected 57 percent. For women under age 59 at diagnosis, 68 percent of their tumors were detected by examination and 45 percent by mammography.¹²⁰ Sardanelli et al. reported sensitivity of 50 percent for clinical breast exams, 59 percent for mammography, 65 percent for ultrasounds, and 94 percent for MRI, with no interval tumors.¹²¹

Ovarian cancer screening has much lower efficacy.¹²² The sensitivity of transvaginal pelvic ultrasound (TPU) alone has been as high as 100 percent in some studies, but the positive predictive value (PPV) was low, only 13 percent. Combining TPU with CA125 screening improved the PPV to 43 percent at the cost of reducing the sensitivity to 43 percent.¹²² Even with screening, most tumors were detected at Stage II or later.¹²² One study reported a sensitivity of 40 percent, and a positive predictive value of 21 percent with pelvic exam alone.¹²²

The willingness of women to adhere to intensive screening protocols varies and appears to be associated with recommendations from their personal physician. A recent systematic review reported that testing increased screening behaviors in carriers, but the effect was smaller than expected.¹²³ Lux et al reported that following a genetic consultation, only 20 percent of high-risk women had utilized all recommended screening methods, and only 1 percent had completely followed the protocol by using all recommended screening methods at the recommended frequency.¹²⁴ Tinley et al. examined the compliance of family members who had a BRCA1/2 mutation or were at 50 percent risk of having a mutation with the cancer screening recommendations provided by cancer geneticists during family information sessions.¹⁰³ These recommendations include monthly breast self-examination, semiannual clinical breast examination, annual mammograms for breast cancer screening, and annual ultrasound and semiannual CA125 screening for ovarian cancer. The personal physicians of 89 percent of patients with a BRCA1/2 mutation also recommended annual mammography. Only 22 percent of patients with a BRCA1/2 mutation and a family history of ovarian cancer had a personal physician who recommended regular ultrasound and CA125 screening. Physician recommendation was highly associated with patient adherence to the screening protocol. Among patients whose personal physicians also recommended annual mammography, 79 percent adhered to recommendations; by contrast, among women whose personal physicians did not make recommendations, only 10 percent complied.¹⁰³ Similarly, 66 percent of patients whose physician recommended ovarian cancer screening followed the recommendation, but only 6 percent of those whose physician did not recommend the screening received the appropriate screening.

Chemoprevention. Selective estrogen receptor (ER) modulators and oral contraceptives have been considered as possible chemoprevention agents. When Nelson et al. reviewed the evidence in 2005, they found limited evidence for a preventive effect on breast cancer by tamoxifen. Four randomized trials had been completed, but none specifically examined the effect in BRCA

mutation carriers. A meta-analysis of these trials found an overall reduction in the risk of breast cancer among women treated with tamoxifen (RR: 0.62; 95 percent CI, 0.46–0.83). None of these trials specifically considered BRCA status in enrollment. One study that conducted genotyping of trial participants found that BRCA2 mutation carriers treated with tamoxifen, in whom 66 percent of tumors were estrogen-receptor positive, were less likely to develop breast cancer (RR: 0.31; 95 percent CI, 0.22–0.45).²⁹ A recent review of the effectiveness of preventive interventions for HBOC families found only one study examining the effect of tamoxifen treatment on contralateral breast cancer.¹²⁵ A significant effect was found only for BRCA1 carriers, which is somewhat counterintuitive. The review's authors concluded that evidence to support tamoxifen's preventive effect was very limited. No studies have examined the effect of tamoxifen treatment on ovarian cancer risk.¹²⁵ Studies also indicate that tamoxifen treatment may be unacceptable to many eligible women.^{100,126,127}

Studies examining the effect of oral contraceptives on breast or ovarian cancer are very limited. The limited evidence available, however, suggests that oral contraceptive use decreases the risk of ovarian cancer in BRCA1 and BRCA2 mutation carriers by 40 percent to 60 percent but that it significantly increases the risk of breast cancer.^{29,122,125} Bermejo-Perez et al. conclude, based on the current evidence, that oral contraceptives are not an acceptable risk reduction method for BRCA1/2 carriers.¹²⁵

The most effective risk reduction strategy for BRCA1/2 carriers is prophylactic surgery. Studies have consistently found that prophylactic bilateral mastectomy reduces the risk of breast cancer by 85 percent to 100 percent.^{29,101,125} Prophylactic salpingo-oophorectomy reduces the risk of breast cancer by 53 percent to 68 percent and the risk of ovarian cancer by 85 percent to 96 percent.^{29,122,125} These surgeries, although very effective, are not acceptable or used by most at-risk women. Only 7.5 percent of women reported they would be interested in prophylactic mastectomy,⁹⁶ and only 4 percent of moderate- or high-risk women reported having had a risk-reduction mastectomy.¹⁰¹ Prophylactic salpingo-oophorectomy was more acceptable: 17 percent of women reported they would be interested in the surgery,⁹⁶ and 23 percent of eligible women reported having had the surgery.¹⁰¹ Among women who had undergone risk-reduction surgery, however, 70 percent were satisfied with the procedure.²⁹

Psychosocial benefits. Women may receive psychological benefits from risk assessment, genetic counseling, and testing. A recent review found that risk assessment improved knowledge about breast cancer, risk perception, and psychological well-being and decreased cancer worry among women with a family history of breast cancer.³¹ Women who had completed a family medical history for their physicians in the past year were less likely to experience cancer worry than those who had not.¹²⁸ The association between decreased cancer worry and completing a family medical history may be stronger for women with lower-risk family history characteristics. The collection of a family medical history has also been associated with lower perceived severity of breast cancer but not with perceived susceptibility to breast cancer.¹²⁸

Genetic counseling has generally reduced emotional distress, although most studies have not differentiated effects in noncarriers from those in carriers.²⁹ Some studies have found that breast cancer worry is decreased following genetic testing, although one study found that breast cancer worry increased among mutation carriers.²⁹ A study with participants consisting mostly of African American women found a decrease in anxiety 1 month after testing and counseling in both carriers and noncarriers.¹²⁹ More than 75 percent of participants in this study reported that

reducing uncertainty was a reason to get tested. Focus groups have supported the finding that relieving uncertainty is a significant benefit of testing.⁹²

One study analyzed the effect of genetic counseling and testing on the use of early cancer- detection methods, including mammography, breast self-examination, breast ultrasound, magnetic resonance imaging (MRI), and transvaginal ultrasound.¹²⁴ Overall, high-risk women increased participation in all early cancer detection methods following counseling. However, following testing, there was a reduction in the use of some early cancer detection methods among mutation carriers. It is unclear why this reduction occurred, or whether women received significant benefits from participating in intensified early cancer detection programs. Among women undergoing risk-reduction surgery, 74 percent reported diminished concern about developing breast cancer.²⁹

Health risk of testing. Genetic testing can expose patients to risk from the intervention measures and to psychosocial harms, which are discussed in the next section.

Intensive screening. We identified two studies published since the review by Nelson²⁹ that examined whether low-dose radiation from mammograms might increase the risk of breast cancer among BRCA mutation carriers.^{130,131} A retrospective cohort study of 1,600 BRCA1/2 mutation carriers from Europe and Canada found that women who reported exposure to chest radiation were 1.5 times more likely to have developed breast cancer than women who did not.¹³¹ A prospective study of 213 women found no risk among mutation carriers overall, although there was a small increase (adjusted OR, 1.08; $P = 0.03$) among BRCA1 carriers.¹³⁰

Chemoprevention. Tamoxifen is associated with an increased risk of thromboembolic events, including pulmonary embolism and deep vein thrombosis (RR: 2.21; 95 percent CI: 1.63–2.98); endometrial cancer (RR: 2.42; 95 percent CI: 1.46–4.03); hot flashes, vaginal discharge, bleeding, and other gynecologic problems; brittle nails; mood changes; and problems with sexual functioning.²⁹ Fear or concern about side effects is a common barrier to taking chemopreventive therapy for breast cancer.^{126,127}

Prophylactic surgery. Nelson et al. found little information available on the complications of risk-reduction surgeries.²⁹ They did review one study that found that 21 percent of women who had mastectomies with immediate reconstruction had complications including hematoma, infection, contracture, or implant rupture. Of women who had prophylactic oophorectomies, 5 percent experienced complications including wound infection, perforation of the bladder, distal obstruction of the small bowel attributed to adhesions, and perforation of the uterus. Premenopausal women who undergo oophorectomy lose their fertility and undergo early induction of menopause. Substantial minorities of women who had undergone prophylactic mastectomies were dissatisfied post-surgery with their body appearance (36 percent), feelings of femininity (25 percent), sexual relationships (23 percent), self-esteem (18 percent), level of stress (14 percent), or emotional stability (9 percent).²⁹ We did not find any studies that provided additional information on harms associated with risk-reduction surgeries.

Psychosocial risks of testing. Women who have had genetic testing for HBOC experience less psychological distress or anxiety than anticipated.^{123,132} This may be because women with strong family histories assume they are at risk, and it is women who receive negative results who must

adjust to a different view.¹³³ Coping strategies,^{134,135} pretesting psychological state,¹³² and perceived partner support¹³⁶ were associated with levels of distress. One study found that, compared with traditional genetic counseling, a problem-solving training lowered depressive symptoms.¹³⁷

Family communication of testing results remains a potential source of strain and distress,¹³² as do uninformative test results.¹³⁸⁻¹⁴⁰ Mutation carriers reported greater relationship strain and a greater tendency to withhold their worries and concerns after testing to protect their partners, compared with noncarriers and those with inconclusive results.¹⁴⁰ Those who perceived their spouse or partner as being anxious and unsupportive during the testing process had increased levels of distress, whereas supportive partners were associated with lower levels of distress.¹⁴⁰ Informing children, especially if they are still minors, about genetic risk can be difficult, and requires balancing the right to information with the desire not to cause anxiety.^{141,142} Families often had difficulty deciding how much discussion should occur prior to testing. Single parents may have a more difficult time talking with their children about genetic testing. Children's perceptions of risk and anxiety may be unrelated to the test result. If the result is negative, they may still feel at-risk, and they may be unconvinced about the accuracy of the test.¹⁴²

Women considering genetic testing must decide if and how they will communicate the results to family members. It is important that women receive guidance on how to communicate an inconclusive test result to family members, so that they know how to talk about this information.¹⁴³ Frost also points out that women who receive inconclusive test results may not be motivated to change behavior, so providing screening and other recommendations is particularly important for these women.

In conclusion, genetic testing for HBOC is not associated with exceptional psychological distress, although some women may need counseling assistance to cope with specific issues.

3.3.9 Key Question 8. How Satisfied Are Patients and Providers with Patient Decisions about BRCA1/2 Testing?

The majority of women from high-risk families who undergo counseling and testing for BRCA1/2 mutations are happy with the process and their decision.^{94,97} In fact, in one study, 98 percent of mutation carriers had such a high level of satisfaction that they said they would recommend the test to others.¹⁴⁴ A group of healthy women who had a family history of breast cancer that was not associated with a high-risk of HBOC who received a tailored genetic counseling intervention found the counseling session helpful.⁹⁵ Counseling can also decrease perceptions of risk and worry in women who have a family history of breast cancer, but one that is not consistent with being a BRCA 1 or BRCA 2 mutation carrier.⁹⁴

Chapter 4. Literature Review for Gene Expression Profiling Decision Tools

4.1 Background

Adjuvant therapy is a systemic treatment given to breast cancer patients whose disease does not appear to have spread to other parts of the body but who are at risk of developing metastasis. The purpose of adjuvant therapy is to kill any cancer cells that have traveled from the breast to other parts of the body. Unless their tumors are small and well-differentiated, NCCN recommends that women who have invasive breast cancer and are lymph node negative receive adjuvant therapy. Adjuvant therapy may include chemotherapy, hormonal therapy, or monoclonal antibody therapy. Choosing an adjuvant therapy to minimize both the likelihood of recurrence and toxicity from the therapy is a critical challenge in the management of early breast cancer treatment. Clinicians use patient characteristics and clinicopathological features of the breast cancer when deciding on the recommended therapy. In the past few years, gene expression differences within the tumor cells have been found to predict recurrence and response to chemotherapy. These tests can help to identify women who would benefit from adjuvant chemotherapy.

4.2 Methods

We began the literature review for the GEP CDS tools by identifying the key questions that needed to be answered to develop and evaluate the tools (Table 11). We then abstracted a recent evidence-based review to answer as many of these questions as possible.¹⁴⁵ We identified the remaining information gaps and developed search strategies to fill those gaps (see Appendix A). We searched PubMed using the identified search strategies. For each search, we reviewed the article titles and abstracts and eliminated any that were clearly not relevant. We requested 97 articles for review and abstracted 43. We collected additional information from the test manufacturers' Web sites.

Table 11. Questions regarding the design and evaluation of the GEP CDS tools

Questions
Question 1. What GEP tests are currently available?
Question 2. What are the testing parameters for each test?
Question 3. How is the test interpreted?
Question 4. What is the positive predictive value and negative predictive value of each test?
Question 5. What other characteristics should be considered in treatment decisions?
Question 6. What educational information needs to be included in the tool?

GEP=gene expression profiling.

4.3 Results

4.3.1 Key Questions 1–3. What GEP Tests Are Currently Available? What Are the Testing Parameters for Each Test? How Is the Test Interpreted?

Three GEP tests are currently available for clinical use (Table 12):¹⁴⁵

- Mammaprint,[®] offered by Agendia, uses a microarray to measure the expression levels within tumor tissue of the 70 genes in the risk assessment panel. Mammaprint[®] has FDA approval.¹⁴⁶
- Oncotype DX[®], offered by Genomic Health, measures the expression levels within tumor tissue of 16 genes related to cancer genes and 5 normalizing genes and uses the gene expression levels to calculate the recurrence score (RS).¹⁴⁷ The manufacturer of Oncotype DX[®] originally did not seek FDA approval. The company recently started the application process after negotiations with FDA. Both ASCO and NCCN guidelines recommend the use of Oncotype DX[®] in some cases.^{42,148} ASCO cites the use of Oncotype DX[®] to assess the risk of recurrence in tamoxifen-treated patients, and notes that patients with high RS appear to achieve greater benefit from adjuvant chemotherapy than from tamoxifen.¹⁴⁸ The NCCN guidelines consider Oncotype DX[®] an option for estimating recurrence risk and benefit from chemotherapy for patients whose tumors are between 0.6 cm and –1.0 cm and have unfavorable features for prognosis or patients who are lymph node negative and whose tumors are > 1 cm, hormone receptor positive, and human epidermal growth factor receptor-2 (HER2) negative.⁴²
- The Breast Cancer Gene Expression Ratio Test (BCGER), offered by Quest Diagnostics, measures the expression of the genes HOXB13 and IL17RB, and calculates the ratio of their expression.

Table 12. Clinically available gene expression profiling tests for breast cancer prognosis

Tests Available	Testing Parameters	Test Interpretation
Mammaprint ^{®146}	Women < 61 years old Stage I or II disease Lymph node negative Tumors < 5cm in diameter. No limitation by ER status No limitation by treatment	Used to estimate the risk of future metastases; Test result > 0.04 = Low risk of metastases; Test result < 0.04 = High risk of metastases.
Oncotype DX ^{®147}	Newly diagnosed women Stage I or II disease Lymph node negative Hormone receptor positive OR Newly diagnosed postmenopausal women Stage I, II, or III disease Lymph node positive Hormone receptor positive	RS < 17 = Low risk of recurrence; minimal benefit from chemotherapy RS > 30 = High risk of recurrence; higher breast cancer-specific 10-year mortality; significant benefit from chemotherapy 17 ≥ RS ≥ 30 = Still under investigation
BCGER ¹⁴⁹	Untreated patients Lymph node negative Hormone receptor positive	Ratio correlated with risk of recurrence; the lower the ratio, the lower the recurrence risk

BCGER=Breast Cancer Gene Expression Ratio Test; RS=recurrence score.

There are published reports of other gene expression profiles related to breast cancer, but we have limited consideration to profiles that are commercially available as clinical tests. To make our report easier to read, we synthesize information based on the clinical test and the underlying gene expression profile and refer to the tests by their commercial name.

4.3.2 Key Question 4. How Well Do Gene Expression Profiling Tests Predict Outcomes?

Mammaprint.[®] A study of the predictive value of Mammaprint[®] for the probability of 5 years free of distant metastasis and overall survival found that the 70-gene prognosis signature independently predicted both outcomes among node-negative women with breast cancer.¹⁵⁰ A

followup study¹⁵¹ reported that the 5-year metastasis-free survival rate was 98 percent (SE 2 percent) among patients with good prognosis signatures and 78 percent (SE 6 percent) among those with poor prognosis signatures for an estimated hazard ratio (HR) of 5.7 (95 percent CI, 1.6–20; $P = 0.007$). The overall 5-year survival rate was 97 percent (SE 2 percent) for patients with good prognosis signatures and 82 percent (SE 5 percent) for those with poor prognosis signatures, for an estimated HR of 3.4 (95 percent CI, 1.2–9.6; $P = 0.021$).¹⁵⁰ Mammaprint[®] appears to only slightly improve prediction over conventional criteria, however.¹⁵²

Oncotype DX.[®] Marchionni et al. found one fairly strong study providing preliminary evidence that the RS could predict the chemotherapy benefit in ER positive, lymph node negative breast cancer patients. The review by Piper et al. concluded that Oncotype DX[®] RS was strongly associated with distant disease recurrence or death from breast cancer and that reclassification analysis suggested that it added to classification by conventional criteria, especially in reclassifying women conventionally classified as high risk as low risk.¹⁵² Other studies^{153,154} provided some additional evidence that Oncotype DX[®] RS can predict the likelihood of response after pre-operative chemotherapy. One study found that clinician knowledge of the RS can impact clinical management of patients with ER positive, lymph node negative, and early breast cancer, but it did not report what the patients or doctors understood about the absolute risk of recurrence.¹⁵⁵

Goldstein et al. found that continuous RS alone predicted overall recurrence of breast cancer in both node negative and node positive patients (p -value of test for trend, $P < 0.001$)¹⁵⁶ Among patients with no positive nodes, the 5-year recurrence rate was 0.03 among patients with a low RS, 0.14 among those with an intermediate RS, and 0.13 among those with a high RS.¹⁵⁶ Kok et al. found that the sensitivity of Oncotype DX[®] to predict a short (≤ 6 months) vs. long (> 6 months) time to tumor progression was 73.7 percent (95 percent CI, 53.9–93.5), and its specificity was 46.0 percent (95 percent CI, 32.2–59.8).

Habel et al. found a strong association between breast cancer death when adjusted for tumor size and grade—regardless of tamoxifen treatment—and the Oncotype DX[®] recurrence score among a population-based sample of lymph node negative breast cancer patients not treated with adjuvant chemotherapy.¹⁵⁷ Further, Paik et al.¹⁵⁸ indicates that the 21-gene Oncotype DX[®] recurrence score among node-negative, ER positive breast cancers quantifies breast cancer recurrence likelihood but also predicts the magnitude of adjuvant chemotherapy benefit. Patients with low RS benefit little, if at all, from chemotherapy; however, there is some uncertainty in the estimates among those patients with an intermediate RS ($17 \geq RS \geq 30$) and clinical importance cannot be ruled out.

Piper et al. concluded that Oncotype DX[®] could improve health outcomes among women with hormone-receptor positive, node-negative breast cancer, although they felt additional study was needed to address limitations in the current evidence.¹⁵²

Breast Cancer Gene Expression Ratio Test.[®] Kok et al. found that the sensitivity of the BCGER test to predict a short (≤ 6 months) vs. long (> 6 months) time to tumor progression was 11.1 percent (95 percent CI, 1.4–34.7), but its specificity was 95.2 percent (95 percent CI, 83.8–99.4).¹⁵⁴ A recent study found this test predicted benefit from prolonged tamoxifen treatment among postmenopausal ER-positive patients whose tumors had a lower HOXB13:IL17BR expression ratio, which was not seen among patients with a higher ratio.¹⁵⁹ However, the manufacturer states that the test should not be used to predict response to therapy.¹⁴⁹ Further,

Jansen et al.¹⁶⁰ found that among node negative, ER positive breast cancers, the HOXB13:IL17BR expression ratio was significantly associated with a shorter disease-free survival and the failure of tamoxifen monotherapy. A recent review¹⁵² did not find any studies comparing risk classification by BCGER to classification by conventional methods, nor did we identify any such studies.

Concordance between gene expression profile risk predictions. Some recent studies have found that different gene expression profiles have fairly concordant risk predictions, even though there is little overlap in the genes included in the profiles.^{161,162} Fan et al. examined the predictive or prognostic value of five gene sets, including the gene sets used by Mammaprint[®], Oncotype DX[®], and the BCGER test.¹⁶¹ All the gene expression models except BCGER were significant predictors of relapse-free survival and overall survival. The group of patients that had poor outcomes was those whose tumors had a poor prognostic signature from the Mammaprint[®] gene profile, a high RS, an activated wound response, or were the basal-like, luminal B, and HER2 positive/ER negative intrinsic subtypes. The Mammaprint[®] prognostic signature and wound-response models were all highly correlated ($P < 0.001$); if a patient was classified as having a poor prognosis based on one of the models above, she was also classified as such using the other two models.¹⁶¹ The high concordance between models in the absence of shared genes appears to be due to a high degree of overlap in the represented biochemical pathways. In particular, all four gene expression profiles that were prognostic in this study included genes associated with the activation of the estrogen-signaling pathway.¹⁶¹

4.3.3 Key Question 5. What Other Characteristics Have Been and Should Be Considered in Treatment Decisions?

Patient characteristics, the clinical and pathologic characteristics of tumors, and patient preferences were used to guide treatment before the development of gene expression tests and are still being used alone or in combination with GEP testing. These patient characteristics include patient age, menopausal status, and whether the cancer has spread to the lymph nodes. The tumor characteristics used include stage of disease, tumor size, tumor grade, the presence of ERs, and whether HER2 is activated within the tumor tissue. Several guidelines and algorithms exist to guide adjuvant treatment decisions in early breast cancer, although they differ in the factors used in decisionmaking (Table 13). Available guidelines and algorithms include the following:

- *National Comprehensive Cancer Network.* The NCCN Web site includes detailed guideline-based decision trees for both patients and clinicians based on recurrence risk or expected therapy benefit. The clinician tree incorporates recommendations for Oncotype DX[®] testing and RS into treatment decisions.¹⁶³ The patient tree uses the same parameters except that it does not include RS.¹⁶⁴
- *St. Gallen Conference Consensus, 2005/7.* These guidelines use patient's age, lymph node status, menopausal status, and tumor hormone receptor status, size, grade, blood vessel invasion, and HER2/neu status.¹⁶⁵
- *American Society of Clinical Oncology.* ASCO has guidelines on the use of tumor markers, but we were unable to find any guidelines for adjuvant treatment decisionmaking.¹⁶⁶
- *Adjuvant! Online.* A Web-based program for medical professionals, Adjuvant! computes the 10-year risk of cancer-specific mortality, mortality from other causes, and relapse

risk. It uses the presence or absence of comorbidities in addition to patient and tumor characteristics.¹⁶⁷

- *Adjuvant Consensus*. This is a Web-based program for patients that gathers information about the patient and their breast cancer and gives the appropriate St. Gallen and NCCN recommendations.¹⁶⁸
- *National Cancer Institute (NIH)*. NIH last published consensus guidelines in 2000. The NCI Web page describes the relationship between prognosis and patient and tumor characteristics.¹⁶⁹

Table 13. Characteristics used to guide adjuvant therapy decisions in early breast cancer

Guidelines	Estrogen Receptor	Lymph Node	Age	Tumor Size	Menopausal Status	Grade	Oncogene Activation	Blood Vessel Invasion
NIH (consensus guidelines published in 2000; info here from NCI Q&A undated)	X	X		X	X	X	X	
NCCN (online decision trees aiding treatment decisions for women)	X	X		X		X		
St. Gallen (international consensus group guidelines)	X	X	X	X	X	X	X	X
Adjuvant! Online (online program for medical professionals that computes 10-year mortality and relapse risk; uses comorbidity as well as listed parameters)	X	X	X	X		X		
Adjuvant Consensus (online program for patients that provides St. Gallen and NCCN recommendations)	X	X	X	X	X	X	X	X

NIH=National Institutes of Health; NCCN=National Comprehensive Cancer Network.

Preliminary evidence suggests that GEP predicts prognosis in breast cancer independently of the clinicopathological features used previously. Studies suggest that among node negative breast cancers, the Mammaprint[®] prognostic signature is a better predictor of time from surgery to distant metastasis, overall survival, and disease-free survival than clinicopathological indexes.^{150,151} The Mammaprint[®] prognostic signature adds independent prognostic information to clinicopathological risk assessment.¹⁷⁰ Oncotype DX[®] RS predicted 5-year relapse more accurately than 5-year predictions of relapse from a predictive model based on Adjuvant! Online.¹⁵⁶ Mammaprint[®] signature and Oncotype DX[®] RS were independent prognostic signatures when combined with ER status, tumor grade, tumor diameter, and nodal status.¹⁶¹ In a recent presentation by Liang et al.,¹⁷¹ patients with low Oncotype DX[®] recurrence scores influenced providers' recommendations for adjuvant therapy among women with node negative, ER positive breast cancers and directly reduced associated costs with the reduction in adjuvant therapy. Furthermore, investigators at Massachusetts General Hospital are currently developing a Web-based calculator that calculates risk of breast cancer death and the impact of adjuvant treatment on that risk of death.¹⁷²

4.3.4 Key Question 6. What Educational Information Needs To Be Included in the Tool?

As was discussed in Chapter 3, a recent study identified 14 key themes that should be included in educational materials about genetic testing developed for the public.⁸⁷ The key themes identified in that study were for testing for an inherited condition. Within the context of a test that may be routinely ordered to guide treatment and management decisions, such as GEP, these themes may need modification. The comprehensiveness of the themes provides a good starting point for discussions of the elements and modifications needed for patient education on GEP and adjuvant therapy, however. The table (Table 14) is reproduced here for the reader's convenience.

Table 14. Key themes required in education materials about genetic testing

Theme	Description
Background and effect	Description of frequency and symptoms of condition; difference between being a carrier and having the condition
Treatment and management	Treatment and management options for the condition, their success, and procedures for referrals and follow-up care
Heredity and risk	Information on how the condition is inherited, why the reader might or might not be at risk, the risk of developing the disorder among people who have the faulty gene, the risk to other family members of having the faulty gene or developing the condition, and the risk someone who carries the faulty gene has of passing it onto their children
Type of test	The purpose of the test
Testing procedure	Description of the procedure for testing, the risk of the procedure and whether it hurts
Testing accuracy	Acknowledgement of the limitations of the test, including laboratory or human error, false positive and false negative test results, any local variation in results, and an explanation of why a repeat test may be needed
Follow-up to testing	A description of how and when the reader will receive results and who will provide them. A description of follow-up procedures after each potential test result
Shared decisionmaking	Topics the reader may want to discuss with their family, friends, or health professionals
Psychosocial consequences	The positive and negative emotional and social consequences that might be experienced; a range of emotions may be experienced and is normal; possible that there could be discrimination in employment or health coverage
Consequences for relatives and partner	What an increased risk means to the person being tested and to their family; family members may react differently; misattributed paternity may be discovered
Benefits and risks	Information on benefits such as early diagnosis, disease prevention or treatment, etc. and limitations/risks such as emotional difficulties, strained relationships, difficult decisions, discrimination
Patients rights	Testing is voluntary, results are confidential, and the patient can choose to whom the results are disclosed.
Date and sources	The date of the publication and the sources of the information provided in the document
Additional information and support	Information on services (local preferred), support organizations, other sources of information, and other relevant health professionals

Background and effect. A recent review¹⁷³ reported that in ER negative patients treated by surgery alone, there was an initial large risk of recurrence followed by a rapid decrease. Among ER positive patients, there was a smaller but more persistent risk of recurrence; however, after approximately 48 months, recurrence is higher for ER positive patients. Patterns of recurrence following therapy changed over time. The authors concluded that women with ER negative tumors had a large early chemotherapy benefit followed by a consistently low risk of recurrence. For women with ER positive tumors, chemotherapy benefit was concentrated in the early years following surgery, and they had a higher remaining risk of recurrence risk.¹⁷⁴

Treatment and management. As discussed previously, treatment decisions for breast cancer are based on a number of clinical and pathologic factors. Treatment for breast cancer includes surgery and radiation treatment of local disease, and chemotherapy, biological therapy, or endocrine therapy, alone or in combination, for treatment of systemic disease.⁴² As discussed above, several recommendations exist for determining adjuvant therapy treatment, including the NCCN guidelines and the St. Gallen guidelines.^{42,165} Due to their complexity, they are not summarized here. The NCCN guidelines are available from the NCCN Web site.⁴² The St. Gallen guidelines are available from the Annals of Oncology Web site.¹⁶⁵

Shared decisionmaking. The NCCN guidelines emphasize the need for good patient-provider communication and patient involvement treatment decisions.⁴² For the GEP tool, two decisions will need to be addressed: testing and adjuvant therapy. Women surveyed about the option of GEP tests were interested in having these tests.¹⁷⁵ Participants rated the benefits of the tests higher than concerns about the tests. Most women preferred shared (39 percent) or active (56 percent) decisionmaking about whether to have a GEP test and wanted to be involved in decisionmaking after results were available.¹⁷⁵ While many patients desire shared decisionmaking, a recent study found that only 63 percent of breast cancer patients were able to fulfill their desired role in treatment decisions and that a desire for shared decisionmaking with their physician was least likely of the roles examined to be fulfilled.¹⁷⁶ A recent study of postmenopausal women with breast cancer found that women wanted to receive simple and unrushed explanations, to understand why taking their medication every day is important, and to know about the side effects of their treatments.¹⁷⁷

Psychosocial consequences. In a recent study assessing patient satisfaction, anxiety and decisional conflict for the *Oncotype DX*[®] (21-gene) recurrence score assay, investigators reported that patients were willing to undergo testing, understood results, and used the information in decisionmaking and that results in choices for treatment were impacted by having the recurrence score information.¹⁷⁸

Consequences for relatives and partner. Women deciding on whether to have adjuvant chemotherapy consider the opinions of the partner and children important to their decisionmaking, although the opinion of their specialist is the most important.¹⁷⁹ We found no studies of adverse consequences of GEP testing.

Benefits and risks. We found no studies of benefits or risks of testing outside of its effect on adjuvant chemotherapy. A recent review¹⁸⁰ found that adjuvant chemotherapy affects both physical and psychological aspects of the patient's quality of life. Chemotherapy has more toxic short-term effects, such as nausea and vomiting, hair loss, cognitive and sexual dysfunction, and fatigue, which severely impact the patient's quality of life.¹⁸¹ Additionally, patients should understand the side effects of adjuvant therapy with tamoxifen, or with aromatase inhibitors, although overlapping, can create clinical management issues that impact quality of life.¹⁵³ Montazeri recently published a bibliographic review article that includes a summary of major findings of studies incorporating quality-of-life instruments to assess quality-of-life issues as predictors of survival, psychological distress, supportive care, symptoms, and functioning.¹⁸² They concluded that quality-of-life data provided evidence for clinical decisionmaking by providing valuable information about patient's experiences, but that the current research lacked

patient-centered solutions.¹⁸² Although rare to date, prospective, randomized, longitudinal studies that incorporate a pre-treatment assessment of symptom burden and perceived quality of life are necessary to define the severity and pattern of treatment-related change and subsequently guide intervention strategies. Most effects diminished rapidly following chemotherapy, but the vasomotor symptoms and sexual dysfunction that occur as a result of chemotherapy-induced menopause can persist.¹⁸⁰ While most patients are aware of the short-term consequences of chemotherapy, fewer are aware of the long-term effects. The authors found that these effects were “common, distressing, and inadequately treated” (p. 6).¹⁸⁰ They felt that providing patients with information on the health-related quality-of-life effects of chemotherapy would facilitate informed decisionmaking and guide treatment strategies. Adjuvant endocrine therapy can also have side effects. Adjuvant tamoxifen and aromatase inhibitors both produce menopausal-like symptoms of estrogen deprivation.¹⁸³ Tamoxifen can also cause more serious side effects, including endometrial cancer and thromboembolic disease.¹⁸³ Women on aromatase inhibitors may have musculoskeletal symptoms, hypercholesterolemia, and cardiovascular disease, although it is unclear if these symptoms are a side effect of the aromatase inhibitors or the lack of the estrogenic action of tamoxifen. Although the effects of chemotherapy are usually considered more burdensome than those of endocrine therapy, some studies have found that while small gains in survival are sufficient to make women judge their adjuvant chemotherapy as tolerable, larger gains were needed for women to think hormonal therapy was worthwhile.¹⁸⁰

Communication. The suggestions of O’Doherty et al. on how to address the problems in risk communication and patient perception for women deciding on genetic testing about hereditary breast cancer may also be applicable to women with breast cancer who are making breast cancer treatment decisions. These suggestions, repeated here for the reader’s convenience, are as follows:

- “Encourage the client to use estimates of risk to assist in decision-making rather than as meaningful predictors of future events.”
- “Frame the information in a variety of ways, e.g., the chance of developing cancer, the chance of not developing cancer.”
- “Relative risks...should be avoided when conveying information to a client. Provide information in terms of absolute probabilities, specifying the period over which the absolute risk applies.”
- “Encourage the client to reflect on their professed preferences from different perspectives, such as using different framing, or imagining their situation in 10–20 years’ time.”
- Encourage the client to view decisionmaking in terms of selecting the most appropriate course of action rather than in terms of correct vs. incorrect.”
- “Use numerical probabilities as the basis for providing risk information, but include verbal qualifiers to set the numerical risk in the context of other life events.”
- “Encourage the client to place the risk of cancer in context by outlining what the diagnosis might actually entail for the client. This requires explicit recognition of the client’s life situation (age, well-being, experience, children, etc).”
- “Also outline what the diagnosis may not entail. A diagnosis of cancer may not be as catastrophic as the client believes, especially if the cancer is identified at an early stage.

- “The same principles apply to a discussion about interventions to reduce the risk of an adverse outcome, placing the possible outcomes into the broader context of the client’s life situation.”

Decision support tools may assist patients or providers in deciding about adjuvant chemotherapy. O’Brian et al reviewed three randomized trials of decision aids regarding adjuvant chemotherapy for breast cancer.¹⁸⁴ Two of the studies found that the decision aids increased knowledge and satisfaction with the decision-making process. One trial found that the decision aid used decreased decisional conflict. The effects on treatment action were mixed: one trial found that fewer women in the intervention group chose adjuvant chemotherapy, one trial found that there was increased use in the intervention group, and one found that there was no difference between groups. A study of a provider tool found that it helped clinicians separate the risks and benefits of treatment, compare different treatments in a given context, and provide balanced information about treatment options to patients.¹³ In a study of a computer-based decision aid for patients designed to be user friendly, most patients found it helpful and influential in their decisionmaking.¹⁶ Patients found it easy to understand, and physicians reported that it helped in understanding their patients’ treatment decisions and that they found the information useful themselves.

Chapter 5. Discussion

This review provided much of the information needed to develop the BRCA and GEP CDS tools. Some of these informational gaps can be filled through discussions with the technical expert panel and our clinical partners or through other mechanisms, such as analysis of existing datasets. In some instances, there is no source for the needed information, and development decisions will need to be made based on the best available information and consultation with our technical experts and clinical partners.

An important issue for tool development will be clarifying which decisions need to be made and by whom. For the BRCA tool, there will be multiple decisions that a patient must make, whether (1) she wants to learn her risk of having a mutation; (2) she wants to gather her cancer family history; (3) she would see a genetic counselor if her risk was high; and (4) if advised, she wants to receive a BRCA test. Because the tool will be designed for screening patients in a primary care setting, it will be important to determine if the tool should support all of these decisions or if some would be better supported by genetic counselors (e.g., testing decisions). Similarly, for the GEP tool, there are decisions that the provider must make. For example, (1) whether the patient should receive a GEP test, (2) whether and how to use the test result (recurrence score) in determining treatment recommendations, and (3) how to educate the patient. The patient must decide, given her recurrence score and the treatment recommendations, whether the benefits of adjuvant chemotherapy outweighs the costs.

Our work plan will need to define the type of patient decisionmaking (e.g., shared, informed) that each tool or set of tools will aim to support. USPSTF defines informed decisionmaking as “an individual’s overall process of gathering relevant health information from both his or her clinician and from other clinical and nonclinical sources, with or without independent clarification of values.”¹⁸⁵ Shared decisionmaking is a process used by both the patient and clinician with the goal of informed and joint decisionmaking. In this process, the patient (1) understands the risks or seriousness of the disease or condition to be prevented; (2) understands the preventive service, including risks, benefits, alternatives, and uncertainties;

(3) has weighed his or her values regarding the potential benefits and harms associated with the service; and (4) has engaged in decisionmaking at a level at which he or she desires and feels comfortable.¹⁸⁵ The context in which the BRCA CDS tools and GEP tools will be used and the complex issues that can arise during decisionmaking differ greatly; the same decisionmaking model may not be appropriate for both types of tools. Considerations will need to be made for those patients who do not want to participate in decisionmaking or those who may be unable to perform the cognitive tasks involved in the decision-making process.¹⁸⁵

The review identified possible patient and provider outcomes that other studies of CDS tools have assessed. Determining which outcomes are appropriate and realistic to assess in the context in which each tool will be used will be important.^{9,13-18}

The review identified key features of CDS tools that improved clinical practice such as integration into the clinical workflow, providing support at the time of decisionmaking, and providing recommendations and not just assessments.⁴ For provider tools,¹⁹ the review revealed that the speed of the tool is most critical to success and that simple interventions that fit onto a single screen work best. Asking providers to enter additional data elements should be minimized as the more data elements and entry negatively affects providers' use of the tool. Finally, our review indicated that obtaining early feedback on the tool from providers using the tool in the field and provider training will likely improve acceptance. Planning for how updates to the knowledge base of the tool and will occur will also be critical.

5.1 BRCA CDS Tools

For the BRCA CDS tools, the requirements for the family history data collection are fairly clear. For the most part, the varied screening protocols and risk algorithms rely on the same information, although they use different values to define the high-risk group. We identified three existing family history tools and one soon-to-be-completed tool that could collect the needed cancer family history information. The literature revealed one item of information not currently collected on cancer family history tools should be collected, if possible, to improve the accuracy of the risk calculations, whether women had had an oophorectomy. In particular, the literature showed that the reduction in risk among women who have had an oophorectomy, either to reduce the risk of breast cancer risk reduction or in association with a hysterectomy for other reasons, can bias risk estimates.^{83,84} Women will likely know this information so most computer risk algorithms can incorporate this information into the tool.

At a minimum, the existing family history tools can provide insights into the programming and design of the BRCA CDS tool we will develop. Ideally, the tools could be directly incorporated, with as-needed modifications, into the family history module in our BRCA CDS tool. We are aware that an effort is currently under way to update the existing DHHS family history data collection tool and to develop standards that will allow the inclusion of more complete family history data into electronic medical records.¹⁸⁶ It will be important to be aware of progress in these efforts and to consider the lessons learned from them in our tool development.

The literature review did not identify one best method of identifying women at high risk of carrying a BRCA1/2 mutation, although it did suggest that risk assessment models have been more thoroughly evaluated and are probably more accurate than clinical guidelines. It is unclear which risk assessment model is the best. The models were developed for and have only been evaluated in oncology or high-risk populations, so the parameters of the models are not optimized for primary care. Even in the populations for which they were developed, no one

model is clearly the best choice. Thus, any model chosen will require modification and assessment on data relevant to a primary care setting. We have identified two datasets that will be useful to this assessment.

We identified several resources on patient education about genetic testing in general and HBOC in particular; it may be possible to adapt these for our BRCA CDS. Women identified as high risk will be referred for genetic counseling rather than being tested, which will provide an opportunity for additional, personalized patient risk assessment and education. There is less guidance on the education needs of primary care providers, even though we know providers are often not confident of their knowledge about genetic testing and HBOC. They may need information similar to that provided to their patients.¹⁸⁷

The genetic counseling session will allow women to discuss any concerns, psychological distress, or family tensions related to HBOC or genetic testing. The process of collecting family history data and obtaining a risk assessment for HBOC may cause some women anxiety and distress. In most women, however, responding to a request for a medical family history seems to improve psychological well-being and decrease cancer worry.¹²⁸

In summary, the following major issues remain to be resolved for the BRCA CDS tools:

- data collection on family members' surgeries associated with cancer risk reduction,
- the definition of high-risk women to be incorporated into the tool, and
- which decisions and the type of decisionmaking that the tools will support.

5.2 GEP CDS Tools

At this point, one of our major uncertainties about this tool is how GEP testing is currently incorporated into clinical practice. The literature provided no information on whether it is routinely ordered, by whom, or at what point in the process it is ordered. The information we have received from our oncology consultants suggests that the process of ordering the test differs, often even within the same practice. In some cases, the decision to order the test is made solely by the surgeon or oncologist, while other physicians prefer to discuss the option of GEP testing with patients before ordering the test. Information on current ordering practices will help determine the decision(s) on which the tool will focus and what information needs to be incorporated into the tool. We will seek input on this issue from our technical expert panel, our clinician partners, and other resources as needed.

Several organizations provide guidelines for deciding on adjuvant therapy, and there is at least one publicly available tool that calculates the probability of benefit from adjuvant chemotherapy.¹⁶⁷ This tool and the clinical guidelines have incorporated RS into their calculations or protocols. To our knowledge, the predictive accuracy of risk calculations has not been evaluated. None of the guidelines or available tools include Mammaprint[®] or BCGER as indicators of prognosis. Neither of these tests have been shown to provide information on the likely benefit of chemotherapy.

The educational needs of providers and patients about GEP testing are unclear at this point and will need to be re-examined when we have a more thorough idea of how GEP tests fit into routine clinical practice. Educational information on adjuvant chemotherapy will be needed, including the benefits and adverse effects.

The existing literature provides reasonable evidence of the independent prognostic value of these tests and the predictive value of *Oncotype DX*,[®] although the data still have significant limitations. Some studies present absolute risks, which are more easily understood by patients and clinicians than hazard ratios or survival curves. The literature does not provide enough new

information to improve prediction over the currently available guidelines and outcome prediction tools. Given these findings, our tool may be best focused on educating physicians about GEP testing and the guidelines surrounding its use and assisting them in interpreting the GEP test results may.

In summary, the following issues remain to be resolved for the GEP CDS tools:

- how the GEP testing is used in current oncology practice (or how it is likely to be used in the near future),
- the educational needs of both patients and providers about GEP testing and the best way to present this information so that it is understood by both patients and their providers.

The development of these tools presents an exciting opportunity to improve women's health and experience in the area of breast cancer, but it also presents challenges. Our work plan for tool development discusses how we intend to meet these challenges.

Abbreviations

ACMG = American College of Medical Genetics
AHRQ = Agency for Healthcare Quality and Research
ASCO = American Society of Clinical Oncology
BOADICEA = Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm
BCGER = Breast Cancer Gene Expression Ratio Test
CDC = Centers for Disease Control and Prevention
CDS = clinical decision support
COS = Case Only Study
DEcIDE = Developing Evidence to Inform Decisions about Effectiveness
DHHS = Department of Health and Human Services
EHC = Effective Healthcare
EHR = electronic health record
EMR = electronic medical record
ER = estrogen receptor
FDA = Food and Drug Administration
FHAT = Family History Assessment Tool
FORCE = Facing Our Cancer Empowered
GEP = gene expression profile
GRACE = Genetic Risk Assessment in the Clinical Environment
GRAIDS = Genetic Risk Assessment in Intranet and Decision Support
HBOC = hereditary breast and ovarian cancer syndrome
IPDAS = International Patient Decision Aids Standards
NBOCC = National Breast and Ovarian Cancer Centre
NCCN = National Comprehensive Cancer Network
NCI = National Cancer Institute
NICE = National Institute for Clinical Excellence
NIH = National Institutes of Health
NPV = negative predictive value
NSGC = National Society of Genetic Counselors
PPV = positive predictive value
RAGS = Risk Assessment in Genetics
RS = recurrence score
TPU = transvaginal pelvic ultrasound
USPSTF = United States Preventive Services Task Force
WCGS = Wales Cancer Genetic Service

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Appendix A. Search Strategies

Search for literature on CDS tool design and on the use of CDS in breast cancer treatment or genetic screening

Search

Clinical decision support tools

Strategy

#7. Search decision making[MeSH Major Topic]

#8. Search decision theory[MeSH Major Topic]

#13. "Decision Support Systems, Clinical"[Mesh]

#14 Search #13 OR #8 OR #7 OR "decision making" OR "decision support"

CDS and breast cancer treatment

Search #14 AND "breast cancer" AND (treatment[MeSH Terms] OR therapy[MeSH Terms]) Limits: published in the last 5 years, English

CDS and genetic screening

#38. Search #14 AND genetic screening[MeSH Terms]

Search #28 NOT prenatal

CDS tool design

Search design AND #13

CDS tool accuracy

Search #13 AND accuracy

CDS tool evaluation

Search #13 AND evaluation

Search for literature on collection of cancer family history or BRCA1 or BRCA2 mutation screening

Search

Family history

Strategy

1. medical history taking[MeSH Terms]

2. "family"[MeSH Terms] AND pedigree

3. pedigree Limits: Humans, English

4. #1 OR #2 OR #3 Limits: Humans, English

5. neoplasms[MeSH Terms] Limits: Humans, English

6. cancer Limits: Humans, English

7. "data collection"[MeSH Terms] OR methods OR tools

Limits: Humans, English

8. #91 AND (#88 OR #86) AND #83 Limits: published in the last 5 years, Humans, English

9. assessment OR evaluation AND genetic OR hereditary OR inherited or familial Limits: published in the last 5 years, Humans, English

10. #96 AND #93 AND breast Limits: published in the last 5 years, Humans, English

Prevalence of BRCA1 or BRCA2 mutations

BRCA mutation AND population

Penetrance of BRCA1 or BRCA2 mutations

BRCA AND (penetrance OR risk)

Search for literature on gene expression profiling and adjuvant chemotherapy

Search

Breast cancer

Strategy

#3 Search "breast neoplasms"[mh] OR "breast cancer"[tiab] OR (breast[tiab] AND neoplasm[tiab])

#5 Search ((Gene[tiab] AND expression[tiab]) OR "gene expression profiling"[mh] OR "gene expression"[mh]) AND 2000[PDAT] : 2008[PDAT] AND

"English"[Language]

Search #3 AND #5 NOT ((animals[mh] NOT review[pt] NOT Tumor Cells, Cultured[mh])

Adjuvant Chemotherapy

4 Search chemotherapy OR adjuvant

5 #3 AND #4

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Gene expression profiling tests and breast cancer

1. "breast cancer" AND (MammaPrint or 70-gene)
2. "breast cancer" AND (Oncotype DX OR 21-gene Profile)
3. 1. (("breast neoplasms"[mh] OR "breast cancer"[tiab] OR (breast[tiab] AND neoplasm[tiab]))
2. ((guidelines AND treatment) OR (guidelines AND predictive))
3. #1 AND #2
4. ("educational status"[MeSH Terms] OR "education"[MeSH Terms]) OR ("decision making"[MeSH Terms] OR ("decision"[All Fields]AND "making"[All Fields]) OR "decision making"[All Fields])
5. #3 AND #7

Appendix C. List of TEP Members

**Computer-based Clinical Decision Support Tools (CDS) for
Gene-based Tests Used in Breast Cancer**
BRCA Technical Expert Panel and Peer Reviewers

Name	Affiliation
Janet L. Williams, M.S., C.G.C.	Oncology Services
Blackford Middleton, M.D., M.P.H., M.Sc., F.A.C.P., F.A.C.M.I., F.H.I.M.S.S.	Director of Clinical Informatics Research & Development; Chairman of the Ctr for Information Technology Leadership (CITL) – Partners Healthcare System (Boston); Assistant Professor of Medicine, Harvard
Wilson Pace, M.D., F.A.A.F.P.	Director, AAFP Nat'l Research Network; Professor, Dept of Family Medicine, University of Colorado; Green-Edelman Endowed Chair for Practice-based Research in Family Medicine
Karen Sepucha, Ph.D.	Senior Scientist, Health Decision Research Unit at Massachusetts General Hospital; Instructor in Medicine, Harvard Medical School
Richard L Street, Jr., Ph.D.	Texas A&M University
Margaret Holmes-Rovner Ph.D.	Professor, Health Services Research Center for Ethics & Humanities
W. Gregory Feero, M.D., Ph.D.	Chief, Genomic Healthcare Branch, National Human Genome Research Institute
Anita Kinney, Ph.D., R.N.	Associate professor, Center on Aging, University of Utah
Marc Williams, M.D., F.A.A.P., FACMG	Director, Intermountain Healthcare Clinical Genetics Institute (Utah)
Cecelia Bellcross, Ph.D.	CDC/Office of Public Health Genomics

Appendix D. TEP Conference Call Notes

December 10, 2008

**Computer-based
Clinical Decision Support (CDS)
Tools for Gene-based Tests
Used in Breast Cancer
Notes from BRCA TEP Conference Call on
December 10, 2008**

Prepared for
Agency for Healthcare Research and Quality
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Rockville, MD 20850

Prepared by
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Sue West, Ph.D.
Nedra Whitehead, Ph.D.
Tania Fitzgerald, B.A.
RTI International
Health, Social, and Economics Research
Research Triangle Park, NC 27709

RTI Project Number 09815.008.009

AHRQ BRCA TEP Conference Call Wednesday, December 10, 2008, 2:30–4:00pm EST

Attendees

TEP Members: Wilson Pace, Karen Sepucha, Rick Street, and Janet Williams

AHRQ: Gurvaneet Randhawa

RTI: Linda Squiers, Lauren McCormack, Nedra Whitehead, Sue West, Tania Fitzgerald and Susana Peinado

Baylor CofM: Maria Jibaja-Weiss

Objective

Discuss work plan and tools to be developed for BRCA clinical decisionmaking

To help guide the discussion, the following questions were posed to TEP members for feedback:

1. Are the goals and objectives of the tool appropriate?

One member pointed out that the issue of preparing patients to speak with their doctor is not elaborated upon very much. This member's concern is not including enough information about patient activation and communication with their provider. RTI staff pointed him to the communication portion of exhibit 5 (page 17 in the draft BRCA work plan) and the member was satisfied that this issue will be addressed in more detail in the final work plan. RTI intends to include questions that patients can take with them and guidance for expectations about communication with the provider. This member believes having specific guidance for the providers is good and having similar prompting for patients will also be beneficial.

One member wanted to know if we were intending to go beyond assessing one's risk to actually addressing patient preferences for genetic testing. RTI staff asked for clarification from this member about to what extent we incorporate informed decisionmaking and patients' preferences to our tool. This member suggested that we clarify if patients *have* to have a certain test or what factors they need to consider in their decision to receive a test. This member also mentioned that genetic counselors are trained to handle a lot of these issues and that providers are not expected to cover everything with a patient.

One member does not believe risk calculators are the same as decision aids.

- RTI staff mentioned that the goal of our tool is to help providers determine whether or not to refer a patient for genetic testing. RTI staff added that this could be viewed as a decision aid for whether a patient should talk to a genetic counselor.
- This tool could help identify the appropriate level of concern for those not as high risk.

RTI staff informed the group that the Needs Assessment with providers will be completed soon. This will help define the gaps in knowledge of what patients should be referred, when, to whom, and how. Educating the providers on these points will be very important.

- It was recommended that patient focus groups could greatly inform the development process. RTI staff noted that while RTI would like to conduct patient focus groups, it was not built into the budget.

AHRQ staff reminded the team that this is not a research project but rather a clinical implementation project. We have to stay consistent with these guidelines and collect information that is within the scope of pertinent clinical care. The OMB clinical care exemption process does not allow for collecting data unrelated to clinical care so we can't add other elements for research purposes.

- One member suggested that at least some data about the satisfaction with the tool and patients' anxiety could be gathered. Another added that there are some scales measuring perceived risk and anxiety that are brief and have been validated. The tool will not be adopted by providers if it is too cumbersome so it must be as concise as possible. Perceived severity and barriers could be relevant for patients but not necessary for providers.
- AHRQ staff agreed that some level of satisfaction with care and the tool could potentially be incorporated within the exemption criteria. RTI staff suggested that perhaps the patients' data collection could go through the exemption while the providers could go through an umbrella clearance.
- The team needs to review the outcome measures and decide on them, then it will be possible to see how they fit into the OMB structure. The Final Work Plan will reflect these refined outcome measures.

2. What are your thoughts about the conceptual framework for the tool and evaluation? Have we identified the appropriate outcomes for the tool? Which ones would you consider to be the highest priority?

One member felt the conceptual framework (exhibit 5, page 17) looked very nice and detailed. This member felt that prioritization of the associated outcome variables (exhibit 7, page 19) would be very useful. This member suggested we could add outcomes related to concordance of patients' and providers' views of their interaction, perspective-taking measures.

One member feels that the term "risk level" merits more discussion. This member was unsure what this provider outcome about risk level is related to. This member was also wondering who determines the cut-offs for risk level and recommendations.

- The issues at the heart of this matter are: 1) How accurate is the model? And 2) How do you define risk levels?
- The Needs Assessment could possibly address some of these issues, and even evaluate patients' threshold for their perception and understanding of risk.
- One member added that the patient's perception of risk level will not be measured by the risk number. Hopefully using a family history will help lead to a more accurate decision.
- RTI staff believe a lot of this feeds back to the accuracy of the algorithm we choose.

RTI will be documenting the reason a patient is referred if the standard recommendation does not indicate referral. One member suggested that extreme anxiety is a common reason for referral without documented level of risk. There should be some clinical decisionmaking by the provider beyond the defined thresholds.

3. What do you think about our approach to developing an integrated tool with both a patient and a provider interface?

This question was not asked directly. Instead, TEP members were informed that we will be creating one tool and this will ensure that the patient will not receive their risk status without the provider there to address concerns. There were no objections to this approach.

4. Do you have any suggestions for improving our approach to usability testing or accuracy testing?

RTI staff explained that we have decided to use the BRCAPRO algorithm for the tool. The TEP members did not have any concerns with this approach.

For the usability testing, RTI is proposing to conduct a half-day workshop with the providers to walk them through the tool and procedures. The TEP did not have any suggestions for other approaches.

5. Please provide feedback about the evaluation plan. Do you have suggestions regarding our approach to the implementation evaluation? How about for the outcome evaluation?

This question was asked in conjunction with requesting TEP members' thoughts about the implementation of the design. RTI staff walked everyone through the Implementation and Evaluation model (exhibit 13, pg 30).

Patient Approach – One member described another study he has worked on that had a model nearly identical to ours. This member said we would have to find a primary care practice that is very experienced in research to complete a process with this level of detail. There is lots of interaction necessary to keep participants involved and to complete their requirements. If we could offer some support in completing the followup portion, it may succeed. RTI staff will arrange a separate call with this member to discuss this further.

Provider Approach – RTI proposed that providers could complete a checklist after each encounter but some TEP members feel this could pose challenges for the perception and communication issues discussed earlier. One member emphasized that there must be some system to make sure the form gets into the providers hands for it to be completed. He also suggested that it will probably need to be 1 minute or less to complete or they will not do it. RTI staff asked if it would be more efficient to have the checklist built into the tool but this could pose a challenge if the Web site times out during their discussion or if the doctor has to walk away from the computer. This can be tested in the pilot study.

One member suggested we consider offering CME credits for providers to complete the study. They are easy to apply for and the necessary components are already built into our design.

RTI staff asked the group for their thoughts on a process evaluation. One member believes that you have to pilot the whole process and be able to explain how this tool will function beyond the practice. The implementation of the tools is very important to understand clearly. Another member suggested that we could have research staff rotate through the four data collection sites to collect process evaluation information and observational data. The sites are not local so it would involve extra cost but it could be possible. RTI staff will discuss this possibility further.

Additional Comments

The TEP members inquired as to whether or not we would be able to provide an estimate of how long this process would take to complete in a visit.

RTI staff are not sure if the usability testing would provide this information. The two-week pilot in the field could get a better sense of the time commitment though.

One member also wondered if we would know ahead of time how many high/medium/low risk participants we would see. RTI staff believe there are usually only 7 percent high-risk patients typically seen in primary care practices.

RTI staff asked for TEP members' thoughts about not using the "high/medium/low" labels but rather providing a number or percentage of risk. One member agreed that the "high/medium/low" labels would not be necessary for patients but the general labels (with allowance for a gray area) could be useful for providers.

One potential alternative discussed that would alleviate some of the time constraints from the initial visit could be to identify the risk first and then set up a second visit to discuss the breast cancer risk. The concern is that a regular time slot will not be enough to assess a patient's risk and have a full discussion on what the results mean and recommendations.

One member was concerned that you may see people who experience serious anxiety if they are determined to be at risk. If they were required to set up a second visit to speak with the doctor, could there be an alternate person the patient could talk to right away to alleviate some of the anxiety? A concern about this alternative is that it would bypass the clinician's opportunity to talk to the patient. There could also be potential insurance or coverage issues involved. The biggest concern is that the patient has somewhere to turn if they need it, perhaps to get priority scheduling so they could come back in right away.

AHRQ staff inquired about any technical standards we need to consider as we develop the tool (EMR restrictions or criteria, etc.). TEP members were not aware of any specific issues but RTI will investigate this further and keep it in mind throughout the tool development.

Next Steps:

TEP members will provide written feedback on the work plan by 12/17/08.

RTI will revise the work plan accordingly and the Final Work Plan will be delivered by February 2.

Tool development will begin soon and individual calls for guidance from specific TEP members will be arranged as necessary.

Appendix E. Physician Needs Assessment Results

Breast Cancer Computer Decision Support Tools Needs Assessment Summary – Primary Care Physicians

The team conducted a needs assessment to understand physicians' current practices in collecting family history, experience identifying and referring women at risk for BRCA mutations, and recommendations for integrating the tool into the clinical workflow. Specifically, the team conducted 60-minute telephone interviews with primary care physicians (n=5) at the Baylor and Providence sites. The findings from these interviews are grouped by major themes and highlighted below.

FAMILY HISTORY COLLECTION AND DOCUMENTATION

PROVIDENCE

- Collect family history at new patient visits; update at annual physicals/appointments. No protocol for regularly updating family history.
- Sites ask routine family history questions about first- and second-degree relatives (father, mother, siblings, grandparents).
- Family history is captured on a paper form, which providers described as “lame and old.” Physicians then review the family history form with patients and update it (sometimes substantially) based on their discussion.
 - Physicians aren't sure whether breast cancer is specifically listed on the form. However, they felt satisfied with the form's content/questions.
 - One site has tried mailing family history forms in advance and asking patients to bring completed forms to visit. Only moderate success.
- Once collected, family history is transferred into an open-text box in the EHR. Consequently, family history is not structured in the EHR by illness or relative.
- One physician admitted that sites are not effectively managing family history. The provider stated that the EHR content usually lacks enough detail to be useful or searchable.
- Physicians access the family history at each visit and refer to it when necessary.
- None of the providers has ever used an electronic tool to collect family history.

BAYLOR

- Collect family history at new patient visits; update at annual physicals/appointments. Protocol is to reevaluate family history annually.
- Family history is captured on paper at first visit. Providers request verbal updates at annual visits.
- Patients “generate their own family history” on an open paper form rather than checking boxes. Patients document family history in the waiting room in advance of first appointment.
- Providers were unsure what questions and relatives were included on the family history form. Most recall that form asks about first- and second-degree relatives (parents, siblings, grandparents).
- Patients often have difficulty identifying relatives' type/site of cancer.
- Once collected, family history is documented in the sites' EHR. (No details about how family history is structured in EHR.)
- One provider stated that she previously used a tool (Vista) for collecting family history but now asks for verbal updates. “I don't need it because you get used to asking questions. I don't want a physical tool.”

ASSESSING PATIENT BRCA RISK

PROVIDENCE

- Physicians don't routinely assess for BRCA mutation risk.
- If a patient brings up the topic, physicians said they would investigate it further using online resources (i.e., UpToDate, DynaMed).
- Physicians were skeptical that BRCA screening is a good use of time and resources. They identified several educational needs:
 - 1) Why is BRCA screening a priority? Providers have limited time during patient visits. Why spend time on BRCA risk that could be spent on more common illnesses, like hypertension?
 - 2) What are the elements of an accurate family history? Providers wanted to know how in-depth the family history needs to be.
 - 3) What are the criteria for BRCA genetic testing? What level of family cancer history merits genetic testing?
 - 4) To whom should providers refer a patient if she is at high risk? Physicians weren't sure where to refer patients or how to do so.
 - 5) Is genetic testing covered by insurance? Patients will be curious, and providers want to understand if they're referring patients to a service that's not covered.
- Providers stated that their colleagues would also need to be convinced that BRCA screening is important. They also stated that screening needed to be integrated into the workflow seamlessly. "A lot of physicians have the 'acute care' perspective. You have to find a way to make [screening] smartly and efficiently ingrained into their behavior."

BAYLOR

- Providers examine family history to identify any noticeable cancer trends. However, physicians indicated that they have limited experience screening for BRCA mutations and referring patients to genetic testing.
- Physicians thought that limited education about genetic testing and BRCA mutations would be helpful. However, they expressed interest in having educational prompts built into the tool as well.
- Providers also expressed some subtle skepticism about the value of BRCA screening...and even some reluctance to focus on breast cancer. "I don't have many patients with breast cancer—less than 10 out of thousands—and most don't have a mutation. The majority of breast cancers don't have a family history, and breast cancer is not common."

REFERRAL TO GENETIC TESTING

PROVIDENCE

- Physicians at Providence have never personally referred anyone to genetic BRCA testing.
- One site has an existing protocol for referring patients to genetic testing. However, providers were unsure what the protocol was or where patients should be referred. "Rumor has it that we have genetic counselors. I think Providence has genetic counselors available through an oncology site. But I'm not sure."

BAYLOR

- Both physicians indicated they've referred women with strong family cancer histories to genetic testing. Surprisingly, the physicians referred women to a breast specialist (oncologist) rather than a genetic counselor.
 - "We don't have genetic counselors within our health care system."

PHYSICIAN TOOL USAGE AND INTEGRATION

PROVIDENCE

- Providers felt the proposed BRCA tool would be valuable, especially the family history collection.
- Providers want the tool to be patient-driven and for patients to take ownership. They felt this would improve patient-physician interaction.

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- Some physicians were willing to use the tool during patient visits; others preferred to use the tool in advance. Those who preferred advanced use wanted site staff to include a printout summary in the patient docket and to flag high-risk patients.
- Physicians liked the idea of integrating tool output into the EHR (if possible). Alternatively, they would like the tool to be hosted on a Web site. This would allow them to compare a patient's cancer family history and BRCA risk assessment to their existing medical record.
- The primary barrier to using the tool is time constraints. Some physicians stated they'd prefer to schedule a follow-up visit with the patient to discuss the tool results.
- Physicians emphasized that the tool needs to (a) provide an interpretation of patients' risk levels and (b) recommend next steps. What do the different risk levels mean? What is the chance that a patient will have a BRCA mutation? Who should be referred to genetic testing vs. who should not be referred? How should providers use the tool results?
- Convincing providers that BRCA screening is worth their time was cited as the primary barrier to tool usage.

BAYLOR

- Physicians expressed some reluctance to using the tool, as they felt it may be too burdensome and take too much time.
 - "It depends on how quick it is. Breast cancer is so rare: We don't want to over-invest in a tool."
- Providers suggested that the tool could best be integrated into clinical workflow by using it at the first visit and annual physicals, when family history is traditionally collected.
- Physicians recommended linking the family history and tool output to the sites' EHR. This would allow them to access the tool information during exam visits.
- Complexity of the tool was cited as the major barrier to tool usage. "You just want to make sure it's an improvement over current practice."
- Providers also expressed concern about tool ownership. Who will maintain the tool? Who will protect and own the data that patients enter?

PATIENT TOOL USAGE

PROVIDENCE

- Physicians felt that most patients were capable of using a computer-based BRCA tool.
- However, providers cited Internet access, computer familiarity, navigation difficulties, and privacy concerns as potential barriers.
 - One physician, in particular, felt Internet access was a major barrier. "It's very difficult for our site's population to access the Internet."
 - Another physician emphasized that the tool should assure patients that their health information is secure. The tool should explain how the info is used and who will have access to it.
 - Reading and education level could also be a concern. One provider recommended aiming for a fourth-grade reading level in the tool.
- Physicians recommended that the tool include straightforward, simple language for patients. "Be straight with the patient. 'If you don't have X, you're at average risk.'"
- Providers agreed that patients' ability to correctly identify family cancer history would vary. "Don't expect that everyone will give an accurate answer. Part of the workflow should be to review the cancer history with the patient."
- Providers thought the tool could help to assuage patients' genetic testing and breast cancer fears.
- Providers thought the tool should educate patients on several key facts—the genetic aspect of breast/ovarian cancer, the value of family history, and the risk of cancer vs. the risk of BRCA mutation.
- Some providers thought the tool should provide patients with their risk assessment results. Others thought that telling patients they were "high risk" could cause panic. Instead, these providers suggesting telling high-risk patients to "discuss their BRCA risk with your doctor."
- **Physicians stated that one of the BRCA tool's primary purposes should be to objectively educate patients about genetic testing and when it is and isn't merited.** In the providers' experience, it is much more common for women at low risk to hear about BRCA mutations and demand genetic testing than it is for high risk women to avoid genetic testing.

BAYLOR

- Physicians expressed concern that the tool would be too burdensome on patients. They also preferred that patients complete the tool in the waiting room, rather than at home or in advance of the visit.
 - “How long would it take a patient to complete it?” [INTERVIEWER: “Ten minutes.”] “Ten minutes! No one will use it! It needs to be very fast and automated.”
 - “It should ask the patient if they have any family history of breast cancer or ovarian cancer. If they don’t, the tool should terminate right there.”
 - “Could the tool include a prebuilt family tree and yes/no questions? It needs to be super short and fast.”
- Providers also stated that some patients will have difficulty identifying the type of cancer in a family history.

ADDITIONAL ISSUES

PROVIDENCE / BAYLOR

- The providers felt that a Spanish-language version of the tool would be valuable.
- Provider stated that having the tool collect all family history—not only cancer history—would be valuable. Because most women are likely to be at low risk for BRCA mutations, providers felt that the tool’s collection of family history would encourage more physicians to adopt it.
- Providers were concerned that genetic testing results could impact a patient’s insurance status.
 - “Insurance companies say they don’t [use genetic test results], but I think they do. They can cherry-pick populations to cover.”
 - “We let the patient know upfront that it (genetic testing) might not be covered. The genetic test results can also impact insurance.”

Appendix F. Health IT Feasibility Assessment Results

February 18, 2009

Computer-based Clinical Decision Support (CDS) Tools for Gene-based Tests Used in Breast Cancer

Feasibility Study Summary Report BRCA Tool

Prepared for
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RTI Project Number 0209815.008

The team conducted a feasibility study to understand sites' IT capabilities and to identify potential barriers to BRCA tool functionality and adoption. Specifically, the team conducted 60-minute telephone interviews with IT professionals and informatics experts (n = 3) at the Baylor and Providence sites. The findings from these interviews are grouped by major themes and highlighted below.

OPERATING SYSTEMS/INTERNET ACCESS

All primary care sites—both Baylor and Providence—use PC computers with the Windows XP operating system. The site computers have consistent Internet access through LAN networks, and the sites also have wireless Internet capabilities. Microsoft Internet Explorer is the default Web browser on most computers.

Both Baylor and Providence have policies that restrict Internet access to some sites. Generally, prohibited sites include Webmail portals (i.e., Yahoo, Gmail), auction sites (i.e., Craigslist, eBay), and sites with video capabilities or embedded video (i.e., YouTube).

Tool Implications: The BRCA Web-based tool should be designed to work with the Windows XP operating system and with Internet Explorer. Video shouldn't be included in the tool, as it may be inadvertently blocked by the sites.

ELECTRONIC HEALTH RECORDS

Both the Baylor and Providence primary care sites use the GE Centricity electronic health record (EHR) system. (available at: www.gehealthcare.com/usen/hit/products/centricity_practice/emr_index.html)

In general, Centricity has the capability to document patient visits, track major diagnoses, order tests/arrange e-prescribing, document test results, and in some cases, receive test results electronically. The EHR can also be used to manage billing (Baylor) and to link to outside Web sites approved by the EHR vendor.

Centricity has the capability for popup alerts (e.g., drug-drug interactions, drug allergy alerts), and the Baylor sites use this capability. That said, Baylor IT professionals confided that most physicians find these alerts annoying, and most ignore them.

The EHR system can also generate reports from searchable data fields. However, some data are entered into open-text fields (e.g., reason for visit) rather than restricted fields (e.g., diabetes diagnosis, Y/N) and are not searchable. Because family history is captured in open-text fields at the primary care sites, it would not be searchable or extractable from the EHR.

Providence has arranged for lab test results from Providence labs to be automatically sent and integrated into their EHR system. Lab results from outside vendors, however, are still received hardcopy and scanned into the system as a visual file, such as a PDF (nonsearchable).

Finally, Centricity has the capability for secure messaging, and some Baylor physicians use this feature. This allows physicians to send a secure message through the

EHR to other physicians or to patients. Physicians/patients receive an email alerting them that they have a secure message; then they log in to the Centricity Web portal to view the message. Direct e-mail exchanges between physicians and patients are not supported by Centricity, and IT professionals indicated that most physicians prefer not to e-mail patients anyway. (Moreover, Baylor has e-mail addresses for less than 30 percent of its patients.)

***Tool Implications:** These findings have several implications for the BRCA tool. First, because all sites use the Centricity EHR, the tool should be customized to this system as much as possible. For instance, if family history and tool output is sent directly to the EHR, it should be customized and linked with the existing fields in the Centricity system.*

Second, these findings confirm our approach of collecting family history directly from patients rather than extracting it—or pieces of it—from electronic medical records. Extraction is likely not possible because family history is stored in open-text data fields.

Third, while secure messaging is a feature of the EHR, it is used sparingly and not all physicians embrace it. Thus, secure message reminders to update family history or to attend the visit are unlikely to be received by most patients.

Finally, these findings suggest that tool output (family history and BRCA risk) are likely to be stored as PDFs or visual files in the EHR. In other words, the tool output will not be searchable at a later date and probably cannot be integrated into restricted EHR fields.

TOOL OUTPUT AND EHR INTEGRATION

There is no one straightforward method for integrating tool output (family history/BRCA risk) into the EHR system, and IT professionals suggested three potential approaches, each with advantages and disadvantages.

Option 1: Hotlink to Web-based Tool Embedded in the EHR

One possible solution is to create a hotlink in the EHR records of participating patients that, when clicked on, takes providers to the Web-based tool. Providers would then be able to review and, if desired, download the patient's family history and BRCA risk status.

The Centricity EHR system has the capacity for embedded hotlinks, but the link would need to be inserted by the EHR vendor (rather than the site). Because certain Web sites are blocked by the vendor—and by site IT policies—we would need to ensure that the site receives administrative approval. IT professionals also stated that providers use this approach with existing resources, such as state immunization registries.

This approach has several advantages. First, providers could access tool output in real time during a patient visit and wouldn't need to enter data into the EHR prior to the appointment. Second, a hotlink would eliminate incorrect matching of patient records; providers could confirm with the patient that they're reviewing the correct tool output. This approach would also minimize the burden on site staff, who wouldn't need to enter or match tool output prior to appointments. Finally, the hotlink approach would be flexible, allowing providers to review the tool output whenever they prefer.

Disadvantages of the hotlink option include login requirements and the need for site-patient matching. Because the link will allow providers to view patient health information, the physician portal will need to be secure and require a login/password. If this login and password are not automated, this is one more piece of information physicians will need to memorize. Moreover, because physicians should be able to view tool output for their patients only, we will need to ensure that each patient is correctly matched with their clinical site (e.g., Participant A is at the Baylor North Garland site).

Option 2: Electronic Transfer of Tool Output to EHR

A second solution is to automatically transfer tool output to the appropriate EHR and house the data in each patient's medical record. Once a patient completes the tool, their family history and BRCA risk status would automatically be sent to the site and stored in the patient's EHR.

Centricity has the capability to store information and results from outside parties (e.g., lab tests, tool output); however, the information is stored as a visual file attachment because the EHR does not have existing fields for the tool output. Alternatively, new data fields could be created for family history and BRCA risk status, but Providence was uncertain that creating new fields would be acceptable.

There are several advantages of the automatic transfer option. First, tool output is stored directly in a patient's EHR, so physicians will not have to log on to the Web-based tool or sift through output from various patients. Second, the tool output becomes a permanent part of the patient's record and would still exist if the RTI tool were ever decommissioned. Finally, this approach requires almost no effort from site physicians or staff.

That said, there are multiple challenges to implementing this approach. First, we would need to ensure that tool output is written and transmitted in a language that the EHR can read (e.g., HL7, etc.). Second, because the process is automatic, the tool needs to be able to correctly match users with (a) their clinical site and (b) their EHR record. Thus, the tool would need to collect some type of identifying information (e.g., EHR number, name and DOB, etc.). Finally, the EHR and the site might have firewalls or other security measures that block incoming information. Consequently, we would need to work with the IT administrators—as well as the EHR vendor—to ensure the tool and the EHRs can “talk.”

Option 3: Electronic Transfer of Tool Output to Site, Manual Entry into EHR

Another option is to automatically transfer tool output to site personnel, who would then manually enter or scan the information into the appropriate medical record. Once a patient completes the tool, their family history and BRCA risk status would be sent (via e-mail or secure messaging) to site staff. The staff could then correctly match the output to the patient's medical record and enter the information.

As with Option 2, this approach is advantageous because tool output is stored directly in a patient's EHR and becomes a permanent part of a patient's medical record. In addition, this option would eliminate the need for syncing the tool and EHR language and for navigating around EHR security measures.

However, this approach has new disadvantages. First, site staff still need to be able to match tool output with patient records, so the tool will need to collect identifying information (e.g., EHR number, name and DOB, etc.). Second, the tool output will need to be transferred securely to site staff, and sites may not have this capability. Finally, this approach increases the burden on site personnel (and perhaps physicians), which may aggravate the evaluation sites and minimize tool adoption after the study.

(Note: Baylor was more open to this approach than Providence. The Providence sites have fewer staff members and do not have scanning capabilities onsite.)

Tool Implications: These findings have major implications for tool design, and the team needs to select which option is best for transferring tool output to site EHRs. Each approach has advantages and disadvantages, and no option is inherently more attractive or feasible than the others.

PATIENT ACCESS TO TECHNOLOGY

Patients at both Baylor and Providence have limited access to site technology and no access to their electronic medical records. Baylor has a patient portal where individuals can access secure messages from physicians or receive appointment reminders; Providence does not use this technology.

Both sites have wireless access, which patients can use to access the Internet from laptops. (At some sites, patients need to request an access code to use the wireless network.)

Tool Implications: As expected, patients will not be able to enter family history directly into the EHR or update their EHR records. Moreover, the sites are set up so that patients can complete an online post-test at the clinics in an exam room or other private area.

PROVIDER ACCESS TO TECHNOLOGY

The Baylor and Providence sites have computers in every exam room that physicians can use to access the EHR system and other information during patient appointments. Most physicians choose to use these computers, but others carry their own tablet computers from room to room (and use wireless access).

Physicians at the sites have different preferences for how they use computers during patient appointments. Some prefer to review health records prior to the appointment; other prefer to access health records on the exam room computer during the visit. Some physicians favor keeping multiple windows open during an exam (e.g., EHR, physician desk reference, etc.); others prefer to have only the EHR open.

Tool Implications: The most important implication is that physicians can and will access the EHR and the Internet in exam rooms. Thus, physicians will have the capability to access the Web-based BRCA tool in real time while seeing patients.

Moreover, the findings suggest that physician preferences for using computers and the EHR vary widely. Consequently, we should design the tool to have some flexibility in when and how providers review patients' family history and BRCA risk. (For instance,

some may want to review the family history before meeting with patients rather than during the appointment.)

ADDITIONAL ISSUES

IT professionals mentioned three additional issues that might impact tool design.

First, IT professionals confirmed that several criteria can be used to match tool output to patient EHR records. The most common suggestion was to use patient identification numbers (stored in the EHR), which allow exact matching and would cause no harm if accidentally disclosed. Another suggestion was to use identifying information, such as full name and date of birth. This option is less attractive because duplicate entries are possible (although unlikely) and because the information may be damaging if disclosed.

Second, IT professionals reiterated that physicians will be skeptical of the tool and that the tool's sensitivity/specificity should be very high. If the tool incorrectly calculates patients' BRCA risk status, physicians will probably consider the tool a burden.

Third, the sites emphasized that having senior staff—especially physicians—manually enter family history and risk status into the EHR would be a major burden. In fact, some IT representatives suggested that physicians may be reluctant even to validate patients' family history.

Tool Implications: Regardless of how the tool transfers output to EHRs, some patient-identifying information will need to be collected. These findings suggest that patient identification numbers may be the most appropriate and least sensitive method for matching records.

March 13, 2009

Computer-based Clinical Decision Support (CDS) Tools for Gene-based Tests Used in Breast Cancer

Feasibility Study Summary Report GEP Tool

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The team conducted a feasibility study to understand sites' IT capabilities and to identify potential barriers to GEP tool functionality and adoption. Specifically, the team conducted 30-minute telephone interviews with IT professionals (n = 2) at the Baylor and Providence sites. The findings from these interviews are grouped by major themes and highlighted below.

OPERATING SYSTEMS / INTERNET ACCESS

Both oncology sites use PC computers with the Windows XP/XP Professional operating system. The sites have consistent Internet access through LAN networks, and the Baylor site also has wireless Internet capabilities. Microsoft Internet Explorer is the default browser at both sites.

Both Baylor and Providence have policies restricting Internet access and usage. Specifically, Baylor policies restrict access to sites with streaming video (e.g., YouTube), and Providence policies prevent users from downloading any software onto clinic computers.

Tool/Study Implications: The GEP tool—if ultimately used by providers—should be designed to work with the Windows XP operating system and the Internet Explorer browser. Additionally, video and mandatory downloads should not be included in the tool, as they may be inadvertently blocked by the sites.

ELECTRONIC HEALTH RECORDS

Neither oncology site currently uses an electronic health record (EHR) system, and both sites maintain and rely on paper medical records. However, by the time of the evaluation, Baylor will likely have implemented an EHR system while Providence may still be relying on paper records.

Baylor has selected IKnowMed as the site's EHR vendor and hopes to implement the EHR completely by the end of March 2009. However, implementation may take longer than expected, and the March deadline is flexible. Baylor is optimistic about IKnowMed and sees enhanced access to Web content and Web-based tools as a major advantage of EHRs.

Providence is also considering adoption of an EHR system but has not yet selected a vendor. The site has identified two possible vendors, and its goal is to select an EHR system and begin implementation in 2009. In general, Providence seemed less optimistic about EHRs and cited two major barriers to adoption—cost and a lack of oncology-focused systems.

Both IT professionals explained that oncology EHRs are more complex than primary care systems. In addition to more detailed and nuanced diagnoses, oncology sites need to document complex chemotherapy regimens, which are not easily categorized.

Because neither site is currently using an EHR, the IT professionals were unsure how easily test results, tool output, or other information could be integrated into the records.

Tool/Study Implications: These findings have several implications for the GEP tool and its evaluation. First, if we create a provider-focused tool, we need to design it so that it doesn't rely on sending data to an EHR (i.e., tool output ultimately stored in EHR). Instead, we might design the tool so that output / treatment recommendations can be downloaded as a PDF or RTF file and printed for inclusion in a hardcopy medical record.

Second, the findings suggest that many oncology sites may not have EHRs because (a) the EHR systems are still evolving, (b) the cost is prohibitive, and (c) oncology records aren't easily categorized

or standardized across practices. Thus, we should ensure that the tool is designed to work with both sites that have EHR systems and sites with paper records.

Finally—if tool output is accessed by providers at all—we need to ensure a consistent evaluation protocol. Because Baylor will likely have an EHR system and Providence will not, we might want to confirm that providers are accessing, viewing, and storing tool output in ways that will not confound evaluation results. (For example, if one site can easily access tool output via the EHR and one site cannot, that may influence providers' perceptions of the tool's value and ease of navigation.)

PATIENT ACCESS TO TECHNOLOGY

Patients at both oncology sites have limited access to technology and, currently, no access to their medical records. Baylor offers wireless Internet access to patients (via a secure password), but does not intend to allow patients access to the EHRs. Conversely, Providence envisions that patients will have read-only access to their EHR files with the new system (via a Web portal), but the site does not offer wireless Internet access.

IT professionals indicated that providers at both sites rarely or never communicate with patients by email. Providers generally believe that eschewing email helps protect their time, and they encourage patients to discuss issues face-to-face instead. Likewise, the sites indicated that their patient population tends to be older, less computer savvy, and less comfortable with email.

Tool/Study Implications: These findings have three implications for the study and GEP tool. First, because there is limited Internet access (especially at Providence), patients may not be able to complete a post-visit questionnaire on-site at the clinics. This is likely to decrease the completion rate and limit study findings. At both sites, we will need to ensure that patients have access to either a network-connected computer or a laptop with wireless Internet access.

Second, because patients are less computer savvy, email recruitment methods and email appointment reminders are likely to be ineffective for this study. Instead, we should encourage sites to recruit individuals and remind them of their appointment by telephone.

Third—and most importantly—these findings suggest that a significant number of patients may not be initially comfortable using a computer-based tool. If we ultimately create a patient-focused tool, we need to ensure that the technology, navigation, and content are as simple and straightforward as possible. We might also need to explore alternative ways for patients to access the tool, as some may not have home computers or may not want to view sensitive information on public computers. Interviews with site oncologists may be beneficial in exploring this issue further.

PROVIDER ACCESS TO TECHNOLOGY

Providers at both oncology sites have consistent access to technology; however, neither site currently has computers in the exam rooms. Baylor is in the process of installing a computer in each exam room and anticipates that the installation will be complete by mid-March 2009. Providence providers have computer access in their clinic offices.

IT professionals indicated that providers at both sites were extremely comfortable with technology—they use computers and email one another frequently. At Providence, the oncologists also use Blackberries, Palm Pilots, or other handheld devices regularly.

The only caution offered by the IT professionals is that providers are occasionally frustrated by computer delays and dislike long periods of computer “down time.” As one professional stated, “Sometimes the [computer] hourglass stares at you. Nobody likes the hourglass.”

Tool / Study Implications: The main implication of these findings is that providers may or may not be able to access the tool in exam rooms and in real-time during patient appointments. If we create a provider-focused tool—or want the patient and provider to view the tool output together—we need to brainstorm when and how providers will access the tool.

One option might be to enable providers to download tool output onto their handheld devices (e.g., Blackberries, Palm Pilots, etc.). However, this may create security/privacy concerns, and not all providers have handhelds. Another option may be to create a printable summary that patients can bring to their oncologists or that site personnel can add to the paper medical records.

ADDITIONAL ISSUES

IT professionals mentioned two additional issues that might impact study design and protocol.

First, IT professionals stated that finding an exam room or other space where patients can complete an exit questionnaire will be challenging. While an unoccupied room is usually available, the room will change throughout the day, making it difficult to direct patients to right space or to set up a network-connected computer.

Second, Providence confirmed that, while they do not currently have an EHR, the site’s scheduling and billing software is Internet based. Thus, the Providence site may be able to quickly identify eligible participants from computer records.

Tool/Study Implications: Space limitations—along with limited Internet access—might prevent patients from completing postvisit questionnaires on-site at the clinics. Thus, we may need to develop a different protocol for securing these questionnaires.

In addition, Providence’s online scheduling and billing software may speed recruitment by allowing the site to quickly identify eligible individuals.

Appendix G. Patient Content Cognitive Testing Reports

BRCA Cognitive Testing Summary

**Round 1: Tool Content
July 7, 2009**

Claudia Squire, Doug Rupert, and Susana Peinado

Participant Demographics

Table 1 provides the participant demographic information for the seven participants completing an interview in round 1. Participants were recruited by a professional recruiting company in Raleigh, North Carolina.

Table 1. Participant Demographics for Round 1—Tool Content Testing

	Age	Education	Race	Breast or Ovarian Family Cancer History	Diagnosed with Cancer
Participant 1	54	Some college	White	Breast	No
Participant 2	48	Post college experience	African American	Ovarian	No
Participant 3	51	High school	African American	Neither	No
Participant 4	58	Ph.D.	African American	Breast	No
Participant 5	36	Some college	White	Neither	No
Participant 6	52	High school	White	Neither	No
Participant 7	36	Some college	White	Neither	No

General Issues

- Formatting – Some respondents commented on the font being too small, not enough white space, and other formatting concerns. These issues should be taken into account when programming the tool. Usability testing will be a better way to evaluate formatting problems.
- Use of Plain Language – Simplify language wherever possible. Some respondents commented that the information in some sections was dense and difficult to read (this was mainly an issue in step 6). Respondents frequently suggested that words should not be too technical. Concepts should be explained in layman’s terms.
- Some women were surprised by low risk of BRCA mutations (1 out of 100) and wondered why they should spend time on the tool.
- In general, respondents thought the layout of the tool was helpful. They appreciated the bold topic headings and found it easy to locate key information. Some also expressed satisfaction with the balance of detail and brevity.

Introduction/Purpose of Tool

- Although this section says that the tool will tell you your chances of having a gene mutation (and not your risk of developing cancer), some respondents seemed to miss this and thought the tool could tell them their risk of getting cancer. Others were unsure whether the tool would calculate mutation risk or cancer risk.

- One woman recommended including a graphic that shows the different stages of learning one's risk. Risk of BRCA mutation → Genetic test to confirm BRCA mutation → Risk of breast/ovarian cancer.
- One respondent suggested adding something in the beginning that would “pull me in more,” such as statistics, why I would want to go further, or “did you know that...?”
- One respondent wondered whether everyone could get access to this tool because some people don't have computers (Ex: “What about the elderly?”) and not everyone reads.
- Most women expected that their physician would refer them to this type of tool.
- Respondents understood the concept of family history and cancer family history well.
- Most respondents would want to use the tool after reading the introduction. However, one respondent wasn't sure if she would want to know because: “I don't think anyone wants to know if you have cancer.” She said most people would rather “wait until the doctor says something rather than seek it out on your own.”
- Other topics that may help alleviate confusion include:
 - Purpose of Tool – Making the purpose clearer.
 - Usefulness of Tool – After getting further along in the tool, a couple of respondents had questions about how useful the tool is. One respondent said that she thought it would be easier just to have a cancer family history worksheet to bring to the doctor. Another said that if she had a history of cancer in her family she would discuss it with her doctor rather than use a computer tool. Another wanted to know the benefit of knowing one's risk (“What's the benefit of early detection?”).
 - Physician Collaboration – Explain upfront how this tool will be used in collaboration with one's doctor. Specifically, after using the tool, women should talk with their doctor about their results.
 - Sponsor – One respondent said that if she saw that the tool was sponsored by the government in the introduction, she would be more likely to use the tool.
 - Tool Login – Explain that users can complete the tool in multiple sessions.

Step 1 – Learn about Hereditary Breast and Ovarian Cancer

- Respondents consistently misinterpreted and misunderstood BRCA1 and BRCA2. Only a few understood the concept well.
 - In some cases, respondents thought that BRCA was another term for breast cancer, rather than a gene mutation. This was caused by the sentence: “BRCA is short for Breast Cancer.” (“BRCA is another way of saying people have cancer.”)
 - Other respondents missed the BRCA acronym entirely and, consequently, didn't understand the term in later passages.
 - The concept of two different mutations (BRCA1, BRCA2) was also confusing. Some women thought BRCA1 was shorthand for breast cancer and BRCA2 was the gene mutation.
 - *Recommendation: Explain the concept of a BRCA mutation as simply as possible. Eliminate “BRCA is short for breast cancer,” as it leads to more confusion. If possible, eliminate use of BRCA1 and BRCA2; instead, we should discuss a single concept—BRCA mutation.*

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- Many women felt the first step was informative and said they learned new information, such as men could get breast cancer, the risk of a BRCA mutation is generally low, Jewish women are at higher risk, etc.
- The concept of gene mutations was confusing.
 - One respondent thought mutations could come from your bloodline, but also from surgery or the environment.
 - Another described a mutation as an “altered gene,” but thought it could continue to change.
 - Another woman didn’t understand the difference between a gene mutation and cancer itself. (“I thought cancer was a type of mutation.”)
 - Another respondent suggested that the discussion of mutations would not be understood by many women, particularly if the tool is trying to reach women of all economic levels.
 - One woman wanted to know if she could inherit two gene mutations—one from each parent. (“Does that mean I’m twice at risk?”)
 - Two other women wanted to know why genes could mutate.
 - Several respondents believed mutations could possibly skip generations.
- When talking about genetics, three respondents used or preferred the phrase “runs in families.” [This phrase was removed from the content at the storyboard meeting. Maybe it should be added back in.]
- In the section “How can I find out if breast or ovarian cancer run in my family,” two respondents said that it would be helpful to know more about who they would need to gather cancer history on. For example, one respondent asked if it was just immediate family, and if not, how far she needs to go back for the tool to be useful.
- Almost all Black women wanted more information about how the risk of a BRCA mutation differed by race/ethnicity. (“What’s the risk for Black women? You’d called out Jewish women, but what about other groups?”)
- *Recommendation: Clearly state that the risk of a BRCA mutation is the same for all other racial/ethnic groups.*
- The term “Ashkenazi Jewish” was confusing to most women and probably needs further clarification. (“How do you know if you have Ashkenazi Jewish heritage? What’s the different between that and other Jewish heritage?”)
- Likewise, women were unsure when to “count” Ashkenazi Jewish heritage. (“Is one Jewish relative enough?”)
- Most women understood the written risk statements.
 - Several respondents thought the statistic seemed low considering all the women who get breast cancer. They thought all or most breast cancer was caused by a mutation.
 - Conversely, one respondent didn’t know how to interpret 1 in 100 and compared it to a lottery ticket to provide some context. (“I don’t know if 100 is considered a big number or not. 1 in 100...I’m thinking that’s possibly a high risk because when you think about a lottery ticket, those are good odds.”)
 - For the risk statements, one respondent desired percentages in addition to fractions. For example: Fewer than 1 in 100 people, or less than 1 percent.
- Almost all women had difficulty interpreting one or more of the risk graphics.

- Many women found it hard to understand that the three graphics were displaying three different concepts.
- Some women were confused by the phrase “By Age 70” in the titles. (“I’m getting closer to 70, so my risk is getting higher.” “Why is the risk so high at 70?”)
- *Recommendation: If possible, eliminate the phrase “By Age 70” from the graphic titles. This only seems to confuse respondents.*
- The colors—pink and black—also seemed to confuse women because they were used differently in the three graphics. (Pink is used to denote three different conditions—BRCA mutation, breast cancer, and ovarian cancer. Thus women didn’t really know what a pink figure was representing.)
- The use of contrasting colors was effective, though. Women understood that there was some difference between the pink and black figures (even if they weren’t sure what pink and black represented).
- *Recommendation: Select different colors to denote different conditions. For instance, green figures could denote those with BRCA mutations in the first graphic. Pink figures would denote those with breast cancer in the second graphic. Blue figures would denote those with ovarian cancer in the third graphic.*
- Women had difficulty reading the graphics’ text; they felt the font size was too small.
- Nevertheless, women generally grasped the comparative nature of the graphics. Most understood that the second and third graphics were showing some risk compared to the general population.
- *Recommendation: Include risk text immediately below or in front of each corresponding risk graphic.*
- Some women missed the information on HBOC occurring at younger ages, perhaps because it was eclipsed by the risk graphics.
- *Recommendation: Move this information before the risk graphics.*
- Some participants had difficulty conceptualizing personal risk despite grasping population-level risk.
 - For instance, one woman explained that only 1 out of 100 women would have a mutation. When asked her personal risk of having a mutation, however, she replied: “50/50. The flip of a coin.”

Step 2 – Decide if You Want to Know if You Might Have a BRCA Mutation

- In the section, it may be helpful to have a link at the third bullet to provide more information on how the calculations are done. Although none of the respondents suggested this, all asked at various points in the process how the tool calculates chances of having a mutation.
- In the section “What should I know about gathering my cancer family history,” the title doesn’t seem to match the information in the section. One respondent said she was expecting to read about the process she should use to gather her family history. When asked what a better title would be, she suggested something like “What are the pros and cons of gathering my cancer family history.”
- Respondents identified several challenges to collecting family history.

- Most respondents talked about the challenges of getting family history information from relatives who were older—didn't know what the illness was (just symptoms), weren't willing to share or comfortable sharing, or didn't go to the doctor.
- One respondent wanted to know how "invasive" she should be. Specifically, how much information would she need?
- In the section "What should I know before I decide to calculate the chances I have a BRCA1 or BRCA2 gene mutation," one respondent thought that the information was good, but the title didn't match.
- In the section "What if I don't know all the information for my family members," one respondent wanted to know if there is a minimum amount needed in order to be useful.
- One respondent wanted to know whether there was going to be ongoing research to improve the tool, whether there were going to be updates, and whether it would stay current.
- In the same section, one respondent didn't know what DNA was. It may be helpful to have definitions for some terms that pop up when you put the mouse over a word.
- Respondents were a little flummoxed by the concept of tool accuracy.
 - A few respondents wanted more information on how the accuracy of the tool is calculated.
 - Two respondents interpreted the first statement as saying they have a 50 percent chance of having it.
 - Another respondent was surprised by the concept of tool accuracy. ("You mean it's malfunctioning?") She felt the tool was either working correctly or it wasn't.
 - Almost all respondents were concerned about the statistic that 7 out of 100 women the tool identified as not having a higher chance of having a mutation will have it.
 - One respondent said accuracy might affect her decision to use the tool. She was concerned that it could give people a "false sense of security."
 - Another asked if someone is told they don't have a higher chance of having a mutation should they do anything to follow up.
 - *Recommendation: We may need to provide more detail to address these concerns.*
- Most women would choose to continue using the tool, but several expressed concerns or caveats.
 - One respondent felt that if you're not Jewish, it would "make more sense just to do what the doctor says and not go through any of this. Just knowing my family history would be enough to tell me." This respondent said she would therefore not continue on with the tool.
 - One respondent said that after reading step 2, she would want to talk to someone, maybe a doctor to help her understand more and answer some questions one on one.
 - Conversely, one woman felt that the tool was a good excuse for exploring family history.
- In the section "It's time to make a decision," most respondents noticed the symbol.
 - When asked what the symbol meant to them in this context, some respondents said they thought it symbolized someone weighing their options.
 - Another said she thought it was there to emphasize the section.

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- Two respondents thought that it stood out a little and suggested either using symbols in other places or not at all.

Optional Content – Key Facts about Genetic Testing

- A couple of respondents commented on the formatting. For example, one woman thought that the sentences under the first bullet should either be moved up as part of the bullet or indented under the first bullet.
- In addition, respondents thought that the way the pros and cons of genetic testing sections were formatted made it difficult to follow.
- Two respondents were concerned about the expense of getting tested, how much it would cost. One also wondered how common it is for insurance providers to cover testing.
- Another respondent wondered why it would take so long to get the results and worried they the woman could be in a different stage of cancer by the time she got the results back. She therefore wondered what the benefit was.

Step 3 – Gather Your Cancer Family History

- One respondent questioned the accuracy of the output considering most people wouldn't have information for their entire family: "The more information you have, the more accurate. How many people have all the information? Most wouldn't, so would run the chance of not having an accurate assessment."
- One respondent liked the tips for gathering family history, but would like more tips/instruction on exactly how to go about doing it. For example, questions they could ask; how to introduce the subject to people. Maybe provide a narrative to model how one woman goes about this.
- Two respondents questioned whether you could get useful cancer history information from obituaries, birth certificates, and other documents mentioned.
- *Recommendation: Clarify the role of these documents. They won't provide illness information, but they can provide age and age at death.*
- When asked about other strategies for collecting family cancer history that should be included, one respondent suggested enlisting help from other family members such as cousins or siblings and forming a committee.
- All respondents were unconcerned about the time required to enter family history. They said if they decided to proceed, they wouldn't be concerned about time. ("I'd enter it until I was done.")
- *Recommendation: Consider dropping the estimate since few users are concerned about the amount of time it will take. Moreover, an accurate time estimate might be elusive since it will depend on how many family members they have.*
- It may be helpful to provide a form that women can give family members to fill out. One respondent said that her family members probably wouldn't feel comfortable talking about cancer history, and she was concerned that they wouldn't respond to a request to send

information unless they had specific lists. An easy to fill out form may be helpful in these circumstances.

Step 4 – Learn Your Risk of Having a BRCA Mutation

- Three respondents felt this decision point was unnecessary. They said that if someone completed their cancer family history, then they had effectively decided to use the tool. If they decided not to, they would have already stopped.
- *Recommendation: Since women could potentially receive upsetting information, it seems appropriate to keep the section even if it feels repetitive to some.*
- One respondent said she would collect her family history even if she decided not to use the tool.
- One respondent said it would be helpful if the tool had a login, so that she could pick up where she left off.
- In terms of the type of output they expected, two respondents said they would like to see numbers, such as percentages or probabilities.

Step 5 – Understand Your Risk

- A few participants were dissatisfied with the tool output.
 - Two respondents said they thought that the information they received would be more detailed. For example, one woman thought that “average” and “increased” risk seemed “vague.”
 - When asked about the statistics that explained the categories, one woman had a hard time distinguishing between less than 1 and 100 and at least 1 in 100: “So someone with an average risk could have a chance of .9 out of 100 and someone at an increased risk could be 1.1 out of 100? What does that tell me?”
 - One R suggested using percentages (e.g., less than 10 percent).
- Several participants felt the term “average risk” was unhelpful.
 - Some respondents interpreted “average risk” as meaning that there’s a chance you may have it and a chance you may not.
 - One respondent specifically said that no matter what, she looks at everything as a 50/50 chance.
 - Another respondent said: “I’d think, what the heck is “average”? The term “average” is confusing to me. I don’t like the term “average,” but that could be just me. Could be 50 percent, one or the other.”
 - Instead, some respondents would prefer to be given a percentage because the category had no meaning to them.
 - Conversely, another respondent said she would be skeptical about a number. (“I’m not just going to rely on the numbers because I know that there’s still a chance I could get cancer.”)
 - Three respondents said that if they were at average risk, they would just keep doing what they’ve been doing: having regular mammograms, checkups, etc.
 - *Recommendation: Consider renaming the “average risk” category. One option is to have a category of “increased risk” and “not at increased risk.”*

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- Respondents understood the concept of “increased risk” and grasped that it was not a confirmation of a gene mutation. All women focused on what the next steps would be (e.g., see a doctor, make a plan).

Step 6 – Make a Plan with Your Doctor

- Almost all respondents thought this section was very helpful, particularly the tips for talking with their doctors.
- Nevertheless, many respondents felt that the section had a lot of information that required concentration to read. It may be possible to simplify the language in some places. Especially for women at increased risk, it may be an overwhelming amount of information.
- A couple of women suggested formatting changes to make the material easier to read. For example, bolding “first, second, and third” under step 6a and 6b to make the steps stand out. One woman thought that the square boxes used in the “Questions about genetic testing for BRCA1 or BRCA2” were distracting.
- One respondent wanted the role of the genetic counselor to be called out more prominently. She recommended boxing the description because it’s easy to miss otherwise.
- Respondents generally thought the tips and questions were very helpful.
- Other suggested tips/questions to include:
 - Take a friend with you to the doctor so you don’t miss something. (“You may have a million questions in your head until you get to the doctor’s office.”)
 - “Don’t feel intimidated by your doctor. Some people are afraid to ask questions. Take charge; it’s your health.”
 - Ask about the latest, updated screening available. This respondent said this is important because doctors often don’t let you know about new tests because they can be more expensive.
- One respondent wondered whether her doctor would really be able to answer these questions or whether she would need to see a specialist.

Miscellaneous Findings

- Several respondents liked the title of the tool better than the alternatives.
- Another respondent liked the term “Risk Assessment” and suggested working that into the title.
- In providing suggestions for strengthening the tool, one respondent said that the amount of information was overwhelming, and she would like to have a person to talk her through it. One option may be to have a narrator walk a user through the tool. This isn’t the same as having a live person, but maybe it would help to address this somewhat.

Appendix H. Usability Testing Reports

February 2010

Computer Based Clinical Decision Support Tools for Gene-Based Tests Used in Breast Cancer

Usability Testing of the Provider Web Site

Prepared for
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RTI Project No. 0209815.008.003

Computer Based Clinical Decision Support Tools for Gene-Based Tests Used in Breast Cancer

Usability Testing of the Provider Web Site

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1. Introduction

This report provides the Agency for Healthcare Research and Quality (AHRQ) with an overview of the usability testing task completed by RTI International for the *Clinical Decision Support Tools* project. The purpose of this task is to conduct a set of interviews to test the “usability” of the Cancer in the Family provider Web site, specifically, to characterize users’ experiences with navigating the site, their reactions to the site layout and content, and their reactions to the prospect of integrating the provider tool within their clinical workflow.

2. Usability Testing Procedures

As part of this task, we conducted six usability interviews at RTI’s office in Research Triangle Park, North Carolina and one interview offsite in Chapel Hill, NC. We completed one round of interviews over a period of three weeks in December, 2009. No changes were made to the Web site during the testing period so all physicians provided feedback on the same content. At least seven days prior to the scheduled interview, participants were received a Web address, a Physician Education Module Review Worksheet, and instructions for accessing the content and providing feedback on the BRCA Basics and Beyond Basics sections of the Cancer in the Family provider Web site. A trained interviewer conducted the interviews using a semistructured interview guide developed by RTI, beginning with a discussion of the review worksheet. Each interview lasted approximately 90 minutes. After the interview, respondents received an honorarium of \$300.

3. Recruitment Procedures and Eligibility Requirements

Respondents were recruited by RTI International staff from the University of North Carolina at Chapel Hill Preventive Medicine Program and the Duke University Department of Community and Family Medicine. To be eligible for the study, respondents had to be a practicing primary care physician without specialty in oncology or surgery. Table 3-1 provides a breakdown of participant characteristics.

Table 3-1. Interview Participant Characteristics

Respondent	Degree/Specialty	Gender
R1	MD/Preventive Medicine Resident	F
R2	MD/Preventive Medicine Resident	F
R3	MD/Family Medicine	F
R4	MD/Obstetrics & Gynecology	M
R5	MD, MHS-CL/Family Medicine	F
R6	MD/Family Medicine	F

4. Results

In this section, we discuss general findings and page-specific findings. General findings are related to topics that cut across Web pages. Page-specific findings are organized by Web page.

4.1 General Findings

The clinicians interviewed all responded favorably to the tool. According to respondents, the primary care physician’s role in the discussion a patient’s individual risk and their responsibility to recommend screening for BRCA mutations were of particular interest. Clinicians provided recommendations on the general characteristics of the tool, the educational content, reviewing the risk

results produced by the tool, and the terminology used throughout the tool. After reviewing the findings, the usability team made recommendations for addressing these issues.

- Some respondents raised concerns over a few particular images displayed alongside the educational content that depict a male mammography technician and male physicians reviewing results with patients. Of concern to these respondents was that the majority of technicians are women and many women are going into family medicine.

Recommendation: Critically review all images currently in the tool and select replacements for those identified by reviewers.

Decision: This recommendation was adopted.

- All respondents reviewed the educational content. Those with feedback on the layout of the material universally preferred the use of succinct, bulleted content, collapsed beneath each subject heading that could be expanded and reviewed on demand.

Recommendation: Ensure that all educational content in the Beyond Basics section is formatted in the compressed format to mirror the BRCA Basics section for consistency and ease of navigation.

Decision: This recommendation was adopted.

4.2 Page-Specific Findings

BRCA Basics

- Respondents indicated that Beyond Basics seemed less organized and concise as the Basics section. Comments included that there were too many sections to click through, that some headings seemed redundant with the Basics section, and that some sections were just not helpful.

Recommendation: Review all sections that respondents felt were redundant or unnecessary and delete duplicative material, particularly in the following sections:

- The Importance of BRCA Screening in Primary Care
- Information on the PCP's Role
- Learn More About Ashkenazi Jewish Founder Mutations section

Decision: This recommendation was adopted.

- The Detailed Information for Providers Involved in Cancer Screening or Caring for Cancer Patients section, which linked to external CME activities, was not well received by the respondents. Citing a preference for other forms of CME and being surprised by being redirected to a site (Medscape) that required them to log in were the leading comments.

Recommendation: Delete the Detailed Information for Providers Involved in Cancer Screening or Caring for Cancer Patients section and links to external sites that require login.

Decision: These recommendations were adopted.

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- A few respondents expressed a desire to better understand the tool’s accuracy and sensitivity/specificity. The team should discuss the possibility of including this section.

Recommendation: Critically review content that addresses accuracy and edit as needed.

Decision: Upon review of the educational content in the BRCA Basics and Beyond Basics sections, the project team decided that the statements regarding the accuracy of BRCAPRO results were sufficient.

References

- Respondents had no significant feedback on the reference section. Respondents were either indifferent to it or supportive of the quality of citations.

Recommendation: No changes recommended.

Additional Resources

- Respondents generally favored the resources offered in the tool. Some indicated a preference for the embedded URLs that encouraged accessing additional content under a specific topic area. Others preferred a single section for resources, separate from the educational content.

Recommendation: Present resources in a manner that integrates both user preferences for access by creating a tab entitled “Additional Resources” that compiles all of the external links in a single bulleted list, including introductory description. Retain the embedded, in-line text references to external resources.

Decision: This recommendation was adopted.

Glossary

- Respondents were generally supportive of the glossary feature. Of the respondents who commented, many indicated that the use of hover-over definitions within the educational content would be an improvement.

Recommendation: Activate the keyword highlights for the glossary terms throughout all pages, as handled in the patient tool.

Decision: This recommendation was adopted.

- Many respondents said they were unfamiliar with the HBOC acronym and suggested writing out “hereditary breast and ovarian cancer” instead.

Recommendation: Review content and confirm that the first instance of HBOC is fully expressed. Add HBOC to the glossary.

Decision: This recommendation was adopted. The first instance of the term HBOC was written out in full text followed by a parenthetical indication of the abbreviation to include a hover-over definition and a link to the provider glossary. All subsequent uses of the term hereditary breast and ovarian cancer were consistently expressed as the abbreviation HBOC.

Patient List

- Overall, respondents found the patient list to be useful, but some aspects of navigation, layout, and functionality were confusing. We received a variety of specific suggestions that are listed below.

Recommendations:

- Develop a patient username convention: first three letters of last name + birth year.
- Replace “Initials” column with “Primary Provider” column. This field will be completed by patients and will indicate the patients assigned primary care provider.
- Allow the list to be sorted alphabetically/numerically by column. For instance, clicking on the Primary Provider column would alphabetically sort patient records by their provider.
- Use the Appointment Date column for primary sort of patient list.
- Delete the LastLoginDate column.
- The results icons (Increased Risk, Not at Increased Risk) are helpful; however, providers were confused when the icons linked to the Sharing Results content. Continue to display results icons, but disable the link to the Sharing Results sections.
- Rename the “View Output” column as “Risk Results PDF.”

Decision: These recommendations were adopted.

Sharing Results – Increased Risk

- Respondents indicated that the content in the Increased Risk section was valuable. While several stated that they probably wouldn’t use the talking points verbatim during appointments, they felt the talking points were useful and helped to lay out the key information. Some indicated a preference for something to give their patient to summarize their discussion.

Recommendation: We recommend creating a Visit Summary PDF. Physicians could tailor the summary document by selecting key pieces of information about and individual’s BRCA risk and general information on HBOC on this page and create a customized PDF (similar to the Patient Action Plan).

Decision: This recommendation was not implemented prior to pilot testing, but will be considered for the final version of the tool should feedback from the providers in the pilot test support this approach.

Sharing Results – Not at Increased Risk

- Respondents found the content in the Not at Increased Risk section was valuable. While several stated that they probably wouldn’t use the talking points verbatim during appointments, they felt the talking points were useful and helped to lay out the key information.

Recommendation: We recommend creating a Visit Summary PDF. Physicians could tailor the summary document by selecting key pieces of information about and individual’s BRCA risk and general information on HBOC on this page and create a customized PDF (similar to the Patient Action Plan).

Decision: This recommendation was not implemented prior to pilot testing, but will be considered for the final version of the tool should feedback from the providers in the pilot test support this approach.

Output PDF

- Respondents were disappointed that the output document did not specifically include the patient's risk result. However, respondents liked that the document was printable and savable, and they preferred having both the family history table and pedigree chart available. We received a variety of specific suggestions that are listed below.

Recommendation:

- Rename the "View Output" document as "Risk Results PDF."
- Revise format of the Risk Results PDF to be more physician focused and to include patients' customized risk results.
- Modifications to the family history table:
 - Eliminate initials column
 - Highlight rows that contain breast or ovarian cancer history
 - Change breast history column so that: 0 = blank field, 1 = uni, 2= bilat
- Format the pedigree charts in landscape view on the Risk Results document.
- Modifications to the pedigree chart:
 - Increase legend size (if possible)
 - Remove "age at cancer diagnosis" numbers from the chart and the legend
 - Adopt the following cancer symbols
 - B = unilateral breast cancer
 - B2 = bilateral breast cancer
 - O = ovarian cancer

Decision: These recommendations were adopted.

Additional Comments/Suggestions

- Respondents acknowledged that public hosting of the tool on the Web increases its accessibility while away from clinic, in the office, in the home, or while traveling if they had a patient with concerns about her risk results. Only when probed did this raise concerns related to security and privacy. Respondents expressed little concern for integrating the tool within their workflow; however some indicated they were unsure of how the patient's results would be integrated with a facilities electronic health record.

Recommendation: Consider if alternate methods exist for transferring data between the webtool and standing EHRs

Decision: This recommendation was not implemented before pilot testing.

Conclusion

After analyzing the data, the usability team met to review findings. The following changes were made to the tool based on testing:

- Critically review all images currently in the tool and select replacements for those identified by reviewers.
- Ensure that all educational content in the Beyond Basics section is formatted in the compressed format to mirror the BRCA Basics section for consistency and ease of navigation.

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- Review all sections that respondents felt were redundant or unnecessary and delete duplicative material, particularly in the following sections:
 - The Importance of BRCA Screening in Primary Care
 - Information on the PCP's Role
 - Learn More About Ashkenazi Jewish Founder Mutations section
- Delete the Detailed Information for Providers Involved in Cancer Screening or Caring for Cancer Patients section and links to external sites that require login.
- Present resources in a manner that integrates both user preferences for access by creating a tab entitled "Additional Resources" that compiles all of the external links in a single bulleted list, including introductory description. Retain the embedded, in-line text references to external resources.
- Activate the keyword highlights for the glossary terms throughout all pages, as handled in the patient tool.
- Review content and confirm that the first instance of HBOC is fully expressed. Add HBOC to the glossary.
- Improve design and layout of the Patient List by:
 - Develop a patient username convention: first three letters of last name + birth year.
 - Replace "Initials" column with "Primary Provider" column. This field will be completed by patients and will indicate the patients assigned primary care provider.
 - Allow the list to be sorted alphabetically/numerically by column. For instance, clicking on the Primary Provider column would alphabetically sort patient records by their provider.
 - Use the Appointment Date column for primary sort of patient list.
 - Delete the LastLoginDate column.
 - The results icons (Increased Risk, Not at Increased Risk) are helpful; however, providers were confused when the icons linked to the Sharing Results content. Continue to display results icons, but disable the link to the Sharing Results sections.
 - Rename the "View Output" column as "Risk Results PDF."
- Improve the design and layout of the Output PDF by:
 - Rename the "View Output" document as "Risk Results PDF."
 - Revise format of the Risk Results PDF to be more physician-focused and to include patients' customized risk results.
 - Modifications to the family history table:
 - Eliminate initials column
 - Highlight rows that contain breast or ovarian cancer history
 - Change breast history column so that: 0 = blank field, 1 = uni, 2= bilat
 - Format the pedigree charts in landscape view on the Risk Results document.
 - Modifications to the pedigree chart:
 - Increase legend size (if possible)
 - Remove "age at cancer diagnosis" numbers from the chart and the legend
 - Adopt the following cancer symbols
 - B = unilateral breast cancer
 - B2 = bilateral breast cancer
 - O = ovarian cancer

5. Appendix

5.1 BRCA Tool Usability Testing Guide: Providers

Interview ID#: _____

Interviewer/Notetaker Initials: _____

Date: _____

Time Begin: _____

Time End: _____

INTRODUCTION

Thank you for your willingness to take part in the conversation. Your opinions are very important to us.

Review the following points:

- RTI, a nonprofit organization that does health-related research, and the Agency for Healthcare Research and Quality, within the U.S. Department of Health and Human Services, are working together to develop a Web-based tool that women and primary care physicians can use to learn about hereditary breast and ovarian cancer, collect their family history of cancer, and calculate their risk of having a BRCA1 or BRCA2 mutation.
- We're going to break today's interview into two parts. First, we'll ask you a few questions about the educational module that was sent in advance. Second, we'll ask you to use the site as if you were a provider. We'd like to get your feedback on how easy or difficult the site is to use, as well as what you think about the way the site looks. At one point, we'll ask you to input health information for mock patients and patient's family members. I will provide you with fictional data for this purpose. You will not be asked to provide any personal information or the personal information of your patients.
- Anything that you say today will be kept private. Your name and other identifying information will not be used in any reports that result from our discussion today.

Provide a copy of the informed consent and review with the participant:

- The informed consent explains the study and what you are being asked to do.
- Please take a few minutes to review the form and sign it if and when you are ready.
- I will also give you another copy of the form to keep for your records.
- There are phone numbers of researchers at RTI that you can call if you have any questions about the study after today.
- Do you have any questions before we begin?

I. EDUCATIONAL MODULE

First, I'd like to focus on the educational module that will be a part of this tool. Before primary care physicians use the tool with patients, we'll ask them to complete the module. They can also reaccess the module at any time.

Did you have time to review the educational module that we sent in advance?

[IF YES] Great. I'd like to spend some time talking about the module's content. [COLLECT EDUCATION MODULE WORKSHEET]

[IF NO] Okay, we'll start by reviewing the educational content that physicians will complete before using the tool. [DIRECT TO PROVIDER EDUCATION MODULE]

What are your first impressions of the education module?

What are your first impressions of the content?

How much of the educational content did you review?

Which sections, in particular, did you review?

Why is that?

How much of the content was new to you?

How useful was the module?

What content/sections were most helpful?

What content/sections were least helpful?

What would you add to the educational module to strengthen it?

What would you remove from the module to strengthen it?

How receptive would your colleagues and other primary care physicians be to the module?

How could we make the module more useful to them?

What could we do to encourage physicians to read the module?

Is there anything else I should know about the module that we didn't discuss?

II. SITE INTERFACE

At this point, I'd like to have you sit at the computer and use the tool. I'll ask you to perform some different tasks with the tool, and I'll also ask some followup questions.

As you review the tool, I'd like to ask you to "think aloud." In other words, share your thoughts and reactions as you review and use each feature.

Login Process

Please log into the tool using these credentials. [Hand participant index card with login credentials.]

How easy or difficult would it be to login during a clinical encounter with a patient?

Why would it be [easy/difficult]?• What are some advantages or disadvantages of this login approach?

How would you prefer to access and login to the tool?

Why is that?

What are the advantages and disadvantages of allowing physicians to access the tool from multiple computers?

How confident are you that the tool will protect patients' data and keep it private?

How well does the login process help to protect patient health information?

Patient List

You'll notice a list of mock patients who've been using the tool and entering their family history.

What are your first impressions of the patient matrix?

Probe on ease of use, layout

How easy or difficult would it be to locate a specific patient in this list during a clinical encounter?

Notice that the tool includes a username and initials for each patient. How would you expect to receive the patient's username for purposes of identification?

How would you prefer to receive it?

How could we make it easier to identify or locate the right patient?

How could this section of the tool be improved?

How would those improvements help?

Reviewing Risk Results

You'll notice that the tool provides a risk summary and output for each patient.

What are your first impressions of the risk summary (i.e., increased vs. not increased risk)?

How useful are the two risk categories that the tool provides?

What else would you like to know about a patient's risk result?

You'll notice the output report ("View Output") in the patient list. What would you expect to see in this report?

One of the pieces in the output report is a family tree with the patient's cancer history. What type of information would you want to see in this tree chart?

[DIRECT PARTICIPANT TO OPEN REPORT] What are your first impressions of the actual content?

Which format—table or pedigree chart—is most helpful?

How could we make the report more valuable?

Where in the tool would you go to learn more about a patient's risk result?

You'll notice the "Sharing Risk" tabs at the top of the tool. What would you expect to see on these tabs?

[DIRECT PARTICIPANT TO CLICK ON TAB] What are your first impressions of the actual content?

How would you use this tab during a clinical encounter?

How could we make the tab more valuable?

Pretend for a moment that I'm the patient. In your own words, how would you present an "increased risk" result to me?

How would you discuss screening recommendations with me?

Based on my risk result and patient information, what screenings would you recommend?

Again, pretend for a moment that I'm the patient. How would you check that I understand my BRCA risk?

How would you check that I understand the screenings you've recommended?

III. HANDOUTS / CHECKLISTS

Pedigree Charts

You might have noticed that the tool will create pedigree charts for each patient. These charts display the patient's family tree—one chart for the mother's side, one for the father's side—and indicate which relatives have breast or ovarian cancer.

I'd like to show you three different options for the pedigree charts and find out which one you prefer.

Which presentation of risk results do you prefer?

Probe on ease of use, layout, etc.

Visit Checklist

What are your first impressions of the checklist?

What do you think is the purpose of the checklist?

When would you fill out the checklist for each patient?

IV. WRAP-UP AND CLOSING

What other features did you expect to find in this tool?

Why would you expect those features? • How would those features strengthen the tool?

Overall, how easy or difficult would it be to use this tool with patients?

How likely would you be to adopt this tool in your practice?

Why is that?

What are the barriers to tool adoption?

What are the advantages of tool adoption?

1. What else can we do to strengthen this tool?

Thank you again for your time. Your feedback today has been very helpful!

Debrief

1. Is there anything not working properly on the site that needs to be fixed before the next interview?
2. Are there potential recommendations for changes that came from this interview?
3. Additional comments.

5.2 Provider Education Module Worksheet

CANCER IN THE FAMILY: COULD YOU HAVE A GENE CAUSING HEREDITARY BREAST AND OVARIAN CANCER?

Physician Usability Testing

Thank you again for your willingness to pilot test the *Cancer in the Family* decision support tool for physicians and patients!

Before your in-person interview on [DATE], we'd like you to review the tool's educational module for physicians and provide feedback on the module's strengths and limitations. You can access the module by visiting the Web site below:

<http://brca.rti.org>
Username: prov1A
Password: brca1!

Please provide feedback on the module using the text boxes below. You can enter your feedback electronically or handwrite it. **Please bring this worksheet with you to your interview.**

What are the strengths of the BRCA Basics section?

Your notes:

What are the limitations of the BRCA Basics section?

Your notes:

What are the strengths of the Beyond Basics section?

Your notes:

What are the limitations of the Beyond Basics section?

Your notes:

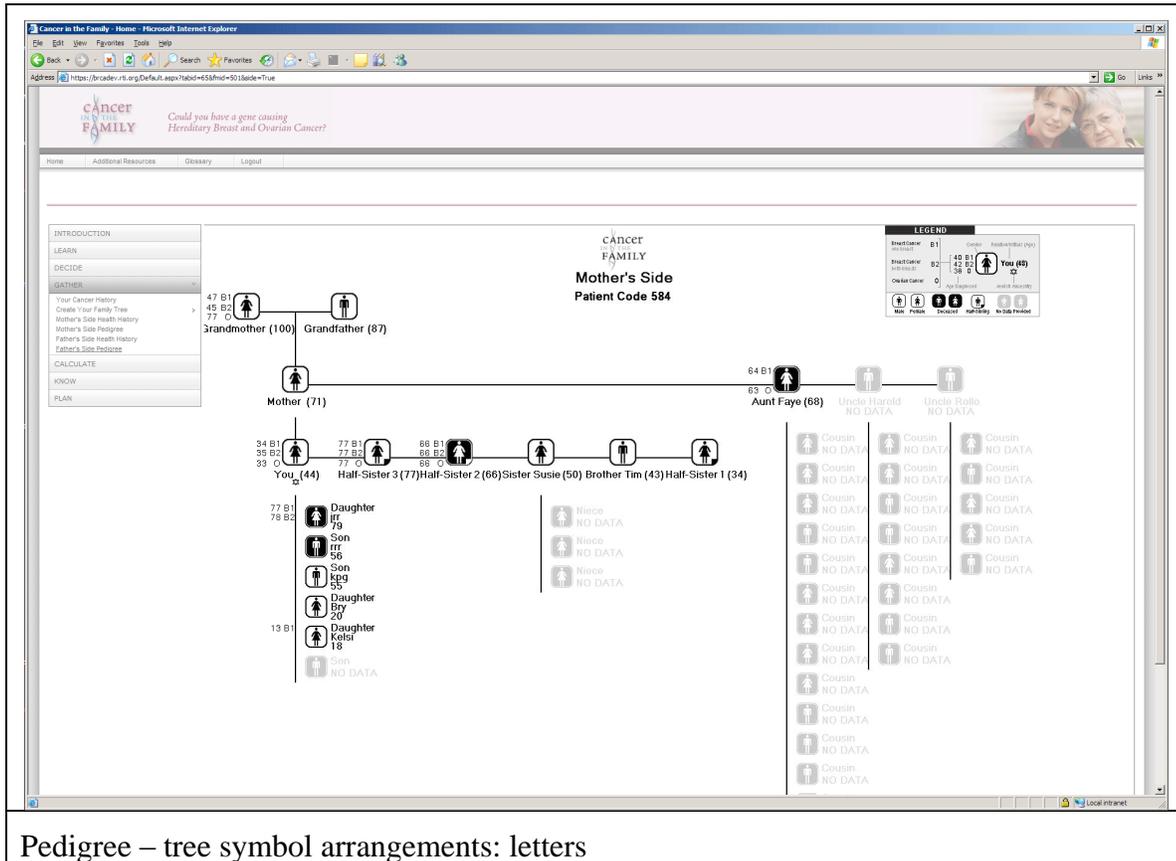
What are the strengths of the Glossary and Resource Guide?

Your notes:

What are the limitations of the Glossary and Resource Guide?

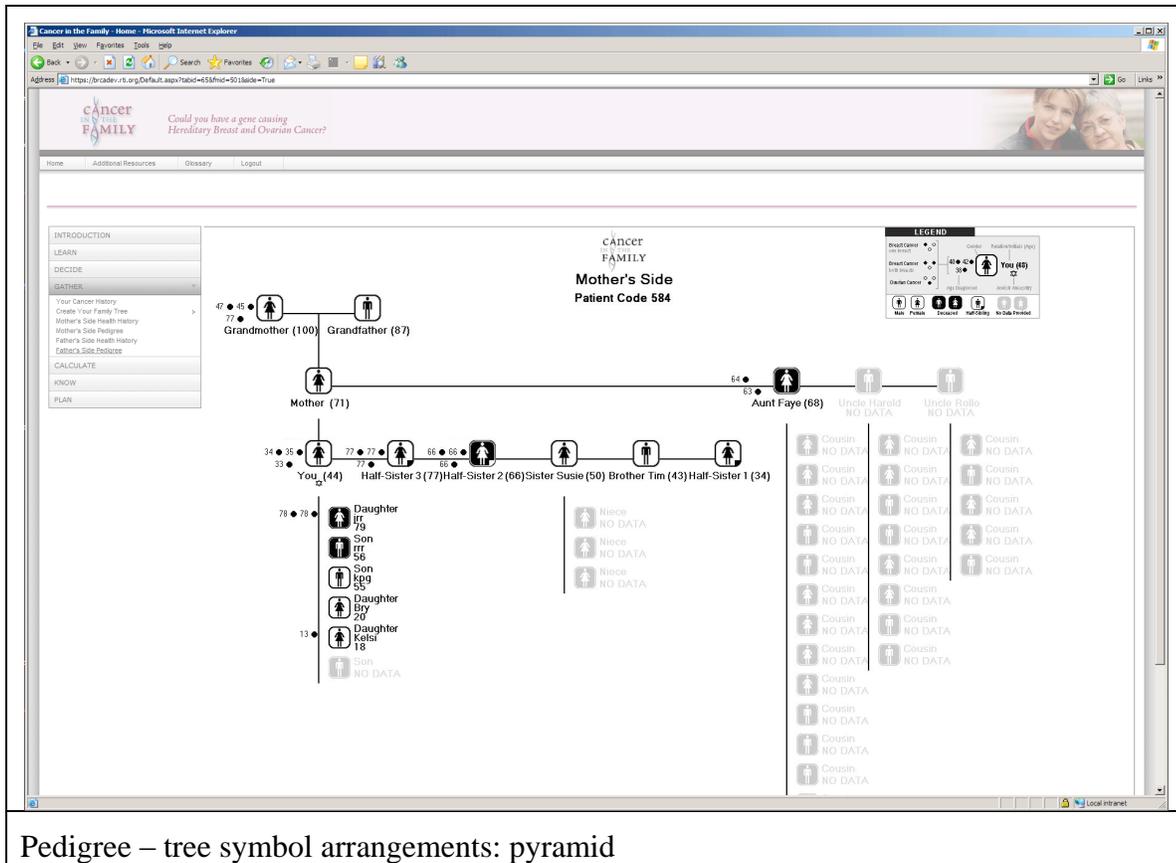
Your notes:

5.3 Output PDF and Pedigree Handouts



Pedigree – tree symbol arrangements: letters

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Pedigree – tree symbol arrangements: pyramid

**Appendix I. Patient and Provider Output from Tool Provider
Usability Report**

CANCER IN THE FAMILY

COULD YOU HAVE A GENE CAUSING HEREDITARY BREAST AND OVARIAN CANCER?

Your Action Plan

Your Risk Result

You may be at increased risk for having a BRCA mutation

Now that you know your chances of having a BRCA1 or BRCA2 mutation, you should talk to your primary care provider about next steps.

This printout is your action plan. It provides tips on talking to your doctor, lists the questions you want to ask your doctor, and depicts your family tree and family cancer history. Bring this printout to your next appointment and share it with your doctor.

Remember, this tool simply tells you your chances of having a BRCA1 or BRCA2 mutation. It cannot tell if you actually have a mutation, and it cannot tell if you have cancer. You and your doctor should discuss your family history and decide together if genetic testing makes sense.

Tips for Talking to Your Doctor

Here are some suggestions for talking to your doctor about your family cancer history.

1. Give information.
Tell your doctor what you know about your family's history of cancer. Don't wait to be asked.
2. Ask questions.
Ask the doctor any questions you have, especially if you don't understand something.
3. Write down questions before your visit.
This will help you remember what to ask. To help you think about questions to ask, click on [Step 6](#) in the tool.
4. At the beginning of the visit, tell your doctor that you have questions.
Don't wait until the end of the visit when time is short.
5. Take notes.
It can be hard to remember everything your doctor tells you. Bring a notebook or a piece of paper to take notes during your visit. You can also bring a family member or friend with you who can take notes while you listen carefully to the doctor.
6. Ask for a summary to take home.
Ask for written instructions or information you can take with you.

Your Family History – Mother's Side

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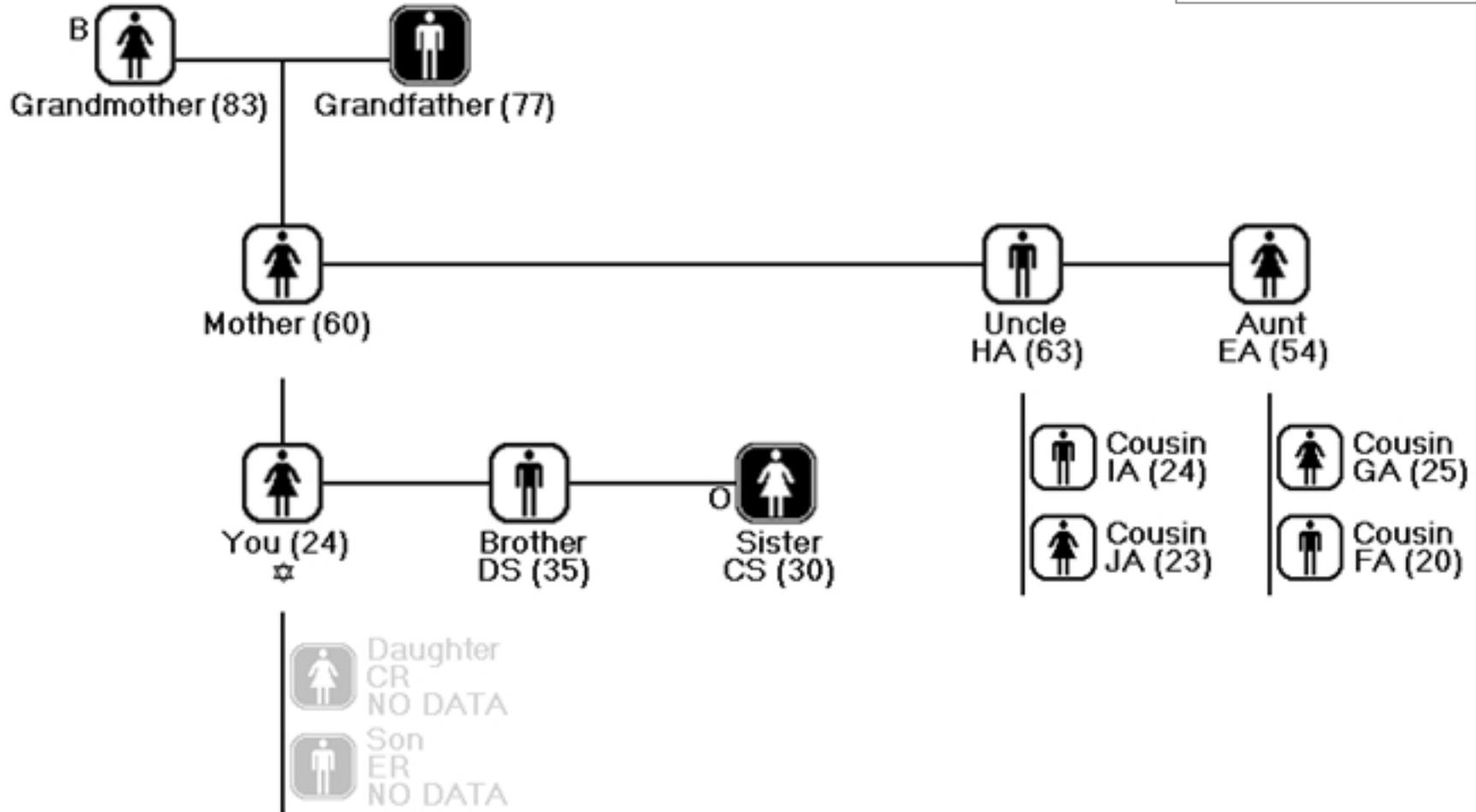
LEGEND

B = Unilateral Breast Cancer (1 breast)
B2 = Bilateral Breast Cancer (both breasts)
Ovarian Cancer

Gender: B (Female), O (Male)
Relation/Initials (Age): You (48)

Jewish Ancestry

Male Female Deceased Half-Sibling No Data Provided



Your Family History – Father's Side

Effective Health Care Program Research Report Number 30

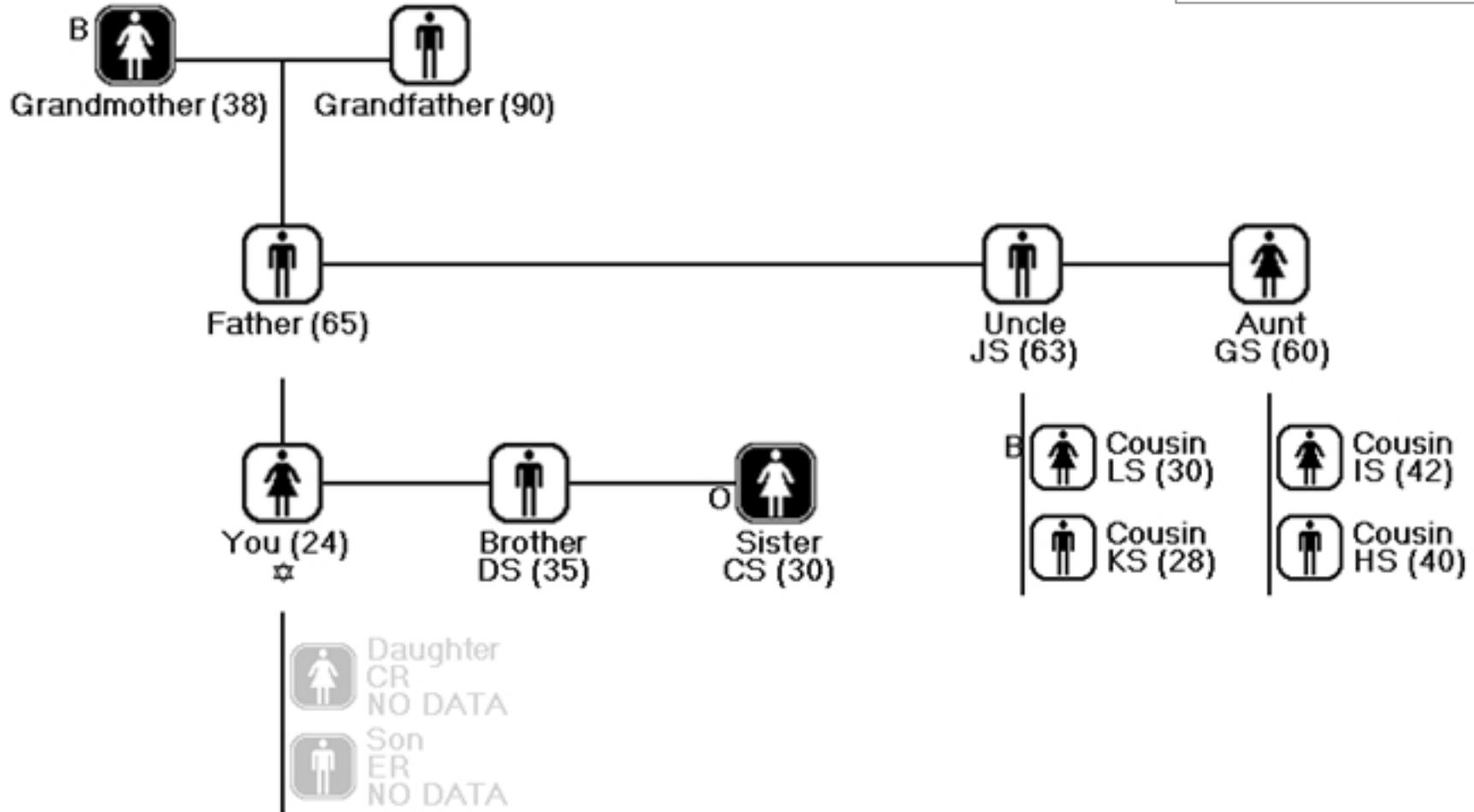
LEGEND

B = Unilateral Breast Cancer (1 breast)
B2 = Bilateral Breast Cancer (both breasts)
Ovarian Cancer

Gender: B (Male), O (Female)
Relation/Initials (Age): You (48)

Jewish Ancestry: ☆

Male Female Deceased Half-Sibling No Data Provided



Questions for Your Doctor

Given my family's history of cancer, would genetic counseling be helpful?

Your notes:

Can you recommend a genetic counselor? Can you refer me to him or her?

Your notes:

What can I expect when I talk to the genetic counselor?

Your notes:

What other information should I take with me to the genetic counselor?

Your notes:

Besides my family history of cancer, what else might increase my chances of getting breast or ovarian cancer?

Your notes:

Questions for Your Doctor (cont'd)

How will I know if having the test to see if I have the gene mutation is right for me?

Your notes:

Questions for Your Doctor or Genetic Counselor

What is the test like for the gene mutation?

Your notes:

How much does the test cost?

Your notes:

How long will it take to get my results?

Your notes:

Do I want to ask my health insurance plan to pay for my test?

Your notes:

What would a positive test result (having a BRCA gene mutation) mean for me?

Your notes:

Appendix J. Technical Documentation

July 2010

**Computer-based Clinical Decision Support (CDS)
Tools for Gene-based Tests Used in Breast Cancer
Technical Documentation
Version 2.0**

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Effective Health Care Program Research Report Number 30

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None of the investigators has any affiliations or financial involvement that conflicts with the material presented in this report.

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Chapter 1. Introduction

This document is designed to provide the reader with an overview of the background to the development approach for the *Cancer in the Family* BRCA clinical decision support (CDS) tool as well as software requirements, technical specifications, and deployment instructions. Thus, the sections of this report are organized accordingly. Specifications are identified in *Section 3* with Use Cases.

Scope

The purpose of the *Cancer in the Family* tool is to provide a CDS tool (i.e., Web application) that effectively communicates information about BRCA1 and BRCA2 genetic mutations and the associated screening test to patients and providers and to promote informed decisionmaking. To inform the design and development of the tool, our project team conducted a literature review⁵ and obtained input and guidance from our technical expert panel (TEP) members and the project's peer reviewers.

The goal of the tool is to facilitate appropriate referral of women for genetic counseling based on their individual risk level, as calculated by family history and other relevant data. The long-term objective is to have a tool that is available to and adopted by the clinician for use in real-time decisionmaking at the point of care and results in routine screening for BRCA mutations in primary care. The tool, as developed, adheres to all current relevant U.S. Department of Health and Human Services (HHS) requirements, such as compliance with Section 508 of the Americans with Disabilities Act to allow access to disabled persons. The tool is flexible to allow easy incorporation of new clinical or software knowledge; easy to maintain; capable of working on different IT platforms, systems, and architecture; adaptable to allow different user interfaces and outputs; and easy to modify.

Tool Objectives

- Provide patients with a user-friendly computerized tool to record detailed cancer family history data.
- Empirically assess patients' risk of having a clinically significant BRCA1 or BRCA2 mutation using cancer family history data and an algorithm accurate for a primary care population.
- Educate patients about hereditary breast and ovarian cancer, its risks, genetic counseling/testing,⁵ and cancer surveillance practices.
- Educate patients about how to talk to their doctor about their risk for BRCA mutations.
- Support patients' exploration of their values and preferences for involvement in decisionmaking about genetic risk assessment, counseling, and testing.
- Present providers with patients' risk assessment results and guidelines for referring patients to a genetic counselor.
- Offer providers guidance on educating patients about their risk and choice of next steps (e.g., seeing a genetic counselor, regular cancer screenings).
- Facilitate patient-provider communication about patients' values and preference for involvement in decisionmaking about genetic risk assessment, counseling, and testing.

Patient Tool Workflow

Patient portion of the tool. A woman enters cancer family history data into the tool at home, allowing her to consult family members and other sources as needed. The tool asks the user to enter data about her cancer family history for three generations and provide additional

⁵ The tool assumes that the genetic counselor will provide high- risk patients in-depth education about genetic testing and the availability of clinical interventions to reduce the risk of breast or ovarian cancer among BRCA mutation carriers.

demographic (e.g., ancestry) and selected health status information. Once the data are as complete as possible, the tool calculates her risk for a genetic mutation (e.g., increased risk, not at increased risk). The tool incorporates a modified version of the algorithm BRCAPRO for risk assessment. BRCAPRO is a Mendelian risk model. Mendelian models calculate the probability a person carries a BRCA1 or BRCA2 mutation by representing the mode of inheritance of BRCA mutations and the correlation between phenotype (cancer status) and genotype (mutation status) as mathematical relationships. The tool estimates the probability a person carries a mutation as a percentage between 0 and 100. The value at which a woman will be classified as belonging to a particular risk category (not at increased risk vs. increased risk) is determined by an analysis of retrospective data by the BRCAPRO algorithm. Risk categories have been determined and verified through accuracy testing and consultation with Dr. Giovanni Parmigiani from Johns Hopkins University, the developer of BRCAPRO and a consultant to this project.

The tool then directs the user to educational information targeted at her risk level (see Table 1).

Table 1. Content of brief patient educational information, by risk status

Increased Risk	Not at Increased Risk
<ul style="list-style-type: none">• Definitions of terms (e.g., familial risk)• Information on what proportion of hereditary breast and ovarian cancer is associated with a BRCA1/2 mutation• Interpretation and explanation of risk score for having mutation• Naming and describing the test to identify a genetic mutation• Options other than testing (e.g., interventions to detect cancer early) and their pros and cons• Responses to frequently asked questions• A summary of possible interventions for women with a positive family history whose affected relatives do not have a mutation in BRCA1 or BRCA2• Importance of sharing family history information throughout the family	<ul style="list-style-type: none">• Definitions of terms (e.g., familial risk)• Reminder that risk status is based on current cancer family history information and risk could change if/when history changes• Information on what proportion of hereditary breast and ovarian cancer is associated with a BRCA1/2 mutation• Interpretation and explanation of risk score for having mutation• Interventions to detect cancer early and their pros and cons• Responses to frequently asked questions• Importance of sharing family history information throughout the family

After completing the cancer family history, there is an option to print a summary that contains users' family history information and pedigree, risk category, and recommended next steps, which will include talking to their doctor about the results and suggestions about how to start conversations with providers and family members. To assist with communication between patients and providers, patients will be able to print a list of key questions and concerns appropriate to their risk category that they can bring with them to their appointment, as well as guidance for what to expect when talking with their physician.

To further support patients (and physicians) in the process of informed decisionmaking, women who are assessed by the tool as being at high risk are given additional information about genetic counseling and testing and what to expect during this process. This provides information that patients should consider when making a decision about whether to talk to a genetic counselor and pursue genetic testing. For women who are not at increased risk, the tool provides screening guidelines for each age group.

Provider Tool Workflow

Provider portion of the tool. Based on recommendations from the TEP, the provider section of the tool includes an educational module that contains the following information:

- an overview of hereditary breast and ovarian cancer,
- reasons to screen primary care patients,
- data on what proportion of hereditary breast and ovarian cancer is associated with a BRCA1/2 mutation,
- prevalence of BRCA mutations,
- interpretation and explanation of risk scores and suggestions for how to explain them to patients,
- a summary of the preventive and follow-up options and their benefits and risks,
- a summary of possible interventions for women with a positive family history whose affected relatives do not have a mutation in BRCA1 or BRCA2, and
- links to resources to locate genetic counselors and insurance coverage for genetic counseling.

In addition to this educational module, providers are able to use the tool to review a patient's cancer family history and risk score prior to or during the appointment. At the visit, the patient and provider would make any corrections or other modifications to the information the patient entered and reassess the risk level if necessary. The tool also provides reminders to the provider to actively engage the patient in a discussion, regardless of whether genetic counseling is recommended and, if counseling is recommended, to discuss why and the process for undertaking the testing. To facilitate this discussion, the tool offers providers appropriate, targeted messages to give to patients and will prompt providers to check patients' understanding (e.g., with the "teach back" method).

Development Approach

The general approach this project implemented used the Software Development Lifecycle (SDLC) as discussed in the following sections. The scope of work included developing a Web portal that integrated a CDS tool used by patients and providers to gather a patient's family history, run a BRCAPRO algorithm which calculates the risk probability of having a genetic mutation linked to Hereditary Breast and Ovarian Cancer (HBOC), and provide educational information about genetic counseling. Information gathered during a pilot study with primary care providers to determine efficacy was then utilized to make usability adjustments to the tool.

The systems development tasks included:

- architecting the system,
- establishing the hosting environment,
- deploying and maintaining the portal platform with security roles,
- implementing the content for the sites,
- developing a mechanism to allow patients to build a family tree with family cancer history,
- implementing a Web-accessible version of the R statistical engine,
- developing the pedigree interface and generator,
- producing PDF outputs of the BRCA calculation and pedigree,
- developing a provider interface for accessing patient information,
- overseeing the testing and error resolution, and
- producing a flash video tutorial.

Cross-phase activities. At the beginning of the project, the baseline project management infrastructure was put into place, which included the creation of a share drive and folder structure to store documentation, a project in Bugzilla (an issue tracking system), a project in Visual Source Safe (VSS) for source control, and the establishment of initial documentation. These constituted the cross-phase activities of the SDLC.

Concept phase. During the concept phase, the proposal recommendations were discussed with the project team and the client to determine the overall objectives. The high-level process flow and required systems were recorded and barriers to success were identified for remediation. General workflow for both patients and providers were documented through storyboards and sitemaps.

Requirements phase. Once the objectives and process flow of the project were finalized and approved by the Project Director and the client, meetings with relevant staff were initiated to gather requirements for the system components necessary to implement the project. The requirements documentation was produced to inform the system design. It was determined from the requirements phase that the systems to be developed needed to include

- a portal Web site that could support multiple roles, including providers, patients, and site coordinators;
 - a clinical decision aid for hereditary breast and ovarian cancer for both patients and providers;
 - eight surveys to evaluate the efficacy of the tool;
 - a Web-accessible version of the R statistical engine running BRCA PRO;
 - a pedigree generator;
 - a provider interface for accessing patient information;
 - PDF reporting; and
 - a flash video tutorial.
- These are further documented in the Use Case section of this document in *Section 3*.

Design and implementation phase. With the requirements phase completed, the systems were then designed to meet the requirements. Mockups and prototypes were produced at scheduled milestone points to confirm compliance with user expectations. When a workable design had been architected and agreed to by the project team, the systems staff moved to the implementation phase of the SDLC process.

Each component of the system was mapped to a relevant version of a specification document and was referenced by the configuration plan. The configuration plan implemented documentation version coordination with source control versions.

All code was managed as one entity, integrated as a system Web portal. Code was checked into and out of VSS as necessary for proper version and source control management.

Code was tracked and versioned so that the most current version was readily apparent and available within the VSS code repository. Version numbers indicated the status of the code within its life cycle.

Source code deployed to the staging and production servers were referred to as “released” and labeled in the source code repository according to the following versioning convention:

Changes determined to be major will move the version number in full integer (x.0) increments. Example: Version 2.0 => 3.0.

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Changes determined to be minor will move the version number in fractional (0.x) increments.

Example: Version 2.0 => 2.1.

The release target was the version that was being tested on staging and was ultimately to be released to production. All staging releases destined for a particular target release shared the same major and minor version number.

With subsequent changes to the code after being deployed to staging, the second fractional increment increased each time the code was deployed to the staging server.

1. Example: v2.1.0 = first staging release for target release v2.1
 v2.1.1 = second staging release for target release v2.1
 v2.1.2 = third staging release for target release v2.1
 v2.1.x = subsequent staging releases for target release v2.1

Once the code was tested and approved on staging and ready for production, the version deployed to production was labeled according to the major and minor version of the target release.

2. Example: v2.1 = first release of version 2.1 to production (based on completely tested and verified staging release v2.1.7)

Code that was changed because of a high-severity issue and deployed to the production server was labeled as 0.x.x, where the integer and first fraction are the released version and second fraction is the bug-fix increment, as needed.

3. Example: v2.1 = first release of version 2.1 deployed to production
 v2.1.1 = first bug fix deployed to production
 v2.1.x = subsequent bug fix(es) deployed to production

Testing and release phase. Once the initial implementation produced a system that met the stated objectives and requirements, it was presented to the project team for feedback. This feedback was incorporated into the implementation before system testing began. Testing procedures are outlined in *Chapter 4*. Once tested and accepted by the Project Director and client, the final product was released into production.

Chapter 2. Design Overview

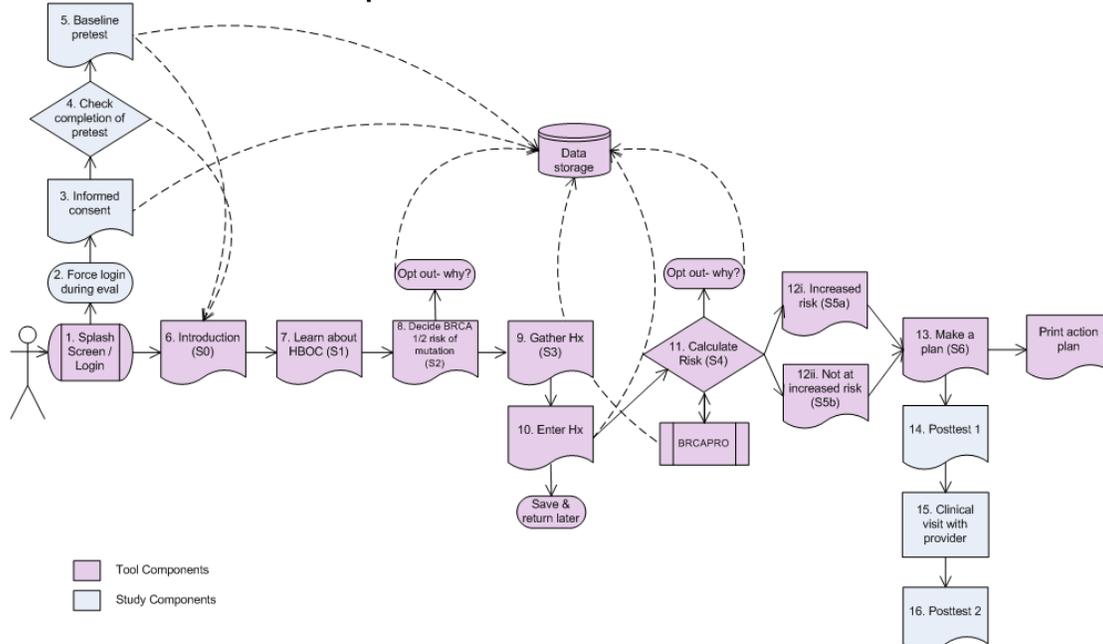
Design Specifications

Creating the design specifications of the patient and provider sites was approached iteratively and centered on the existing structure of the didactic content for each type of end user. Concept site maps were drafted, critiqued, and updated based on reviewer feedback and cognitive testing of the learning material. Once finalized, these diagrams were used as a guide for programming each page of the site.

The patient and provider workflow site maps shown in Figures 1 and 2 (full size version in *Appendix B* and *Appendix C*, respectively) are currently color coded to reflect those system components that are a part of the evaluation, in light blue, and those components that are central parts of the tool that will persist in the final release, shaded in purple.

Patient Workflow Site Map

Figure 1. Patient workflow site map



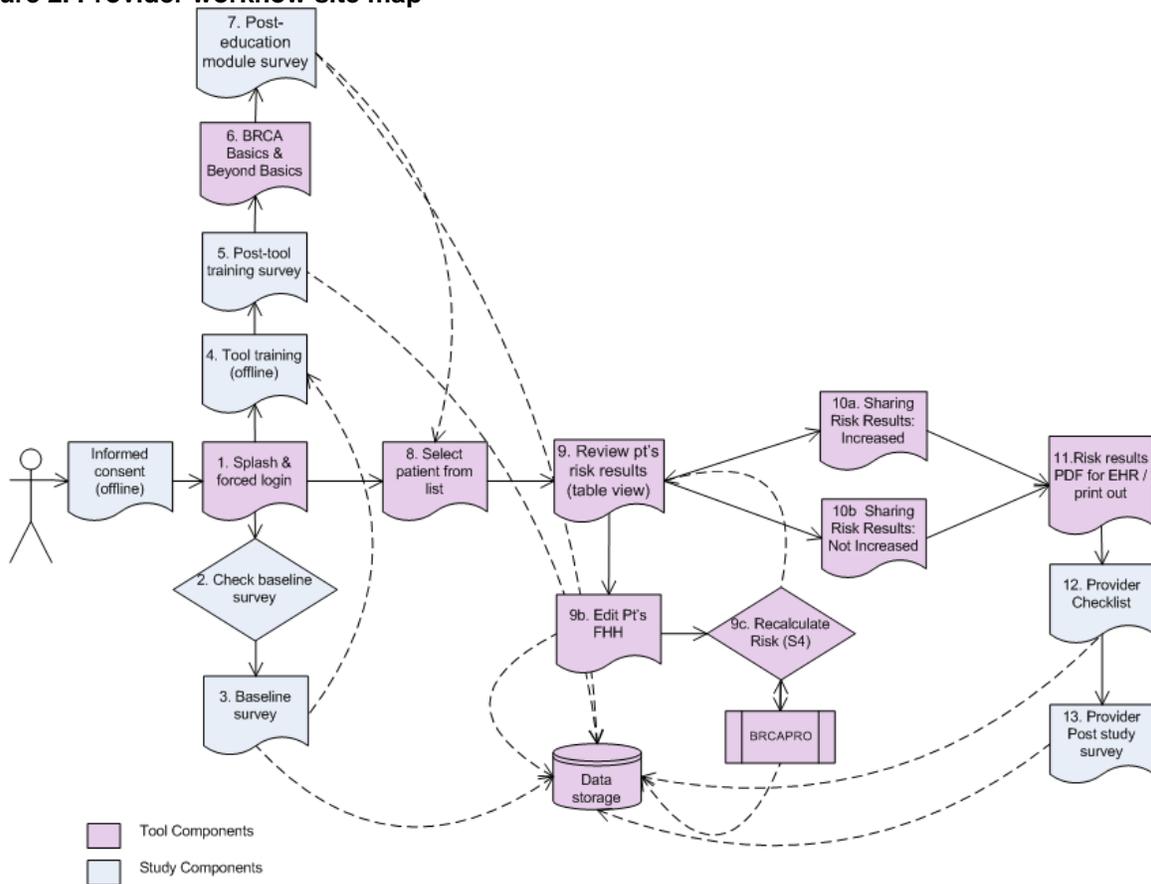
The site map shown in Figure 1 depicts the flow a patient end user would experience during the evaluation of the tool. This 16-step process, from end to end, is as follows:

- Splash screen. This page welcomes the user, and offers a “Take a Tour” video link that allows the public to see what the tool is all about, how burdensome it is to complete the risk assessment process, and how the results can be used by an individual’s physician.
- During evaluation, we forced login to the tool.
- During the evaluation phase, informed consent was obtained electronically at the beginning of the user’s first visit. Upon each subsequent return, users were redirected from the login back to the last page they viewed. There is no consent form programmed in the final release.

- For evaluation purposes, the *Cancer in the Family* Web tool confirmed that a user has completed the baseline pretest before allowing her to access the tool's content. If this check reveals she had not completed the pretest, users continued to Step 5. Once Step 5 had been satisfied, returning users were redirected from this stage to Step 6 below.
- A Web-based assessment of users' knowledge, attitude, and behaviors surrounding BRCA can cancer risk was administered during their first visit.
- Represents the users' return to the final release of the tool. General introductory learning material is presented in this section.
- Next, women learn more specifics about hereditary breast and ovarian cancer.
- There are two decision points in the flow of the Web tool. The first asks users to consider if they wish to determine their risk of having a BRCA mutation. Users who decline are requested to indicate why they choose not to do so and are free to continue reviewing the introductory content. Those women who affirm that they are interested in learning their risk for mutation proceed to the next step in the Web tool.
- Gathering a complete family history is an essential step in deriving an accurate assessment of risk. This section explains why these data are important and provides some tips for communicating with family members about their medical history. In addition, this section includes a worksheet that users print out for offline data collection.
- Once data collection is complete, users return to the Web tool and enter their family members and each individual's cancer history.
- The second of two decision points is reached once family history data have been entered. At this stage, users are prompted to confirm their interest in learning their risk. For those who decline, a record of family history is still maintained should they wish to share these data with providers or other family members. For those who confirm they want to calculate their risk, the Web tool engages the BRCAPRO algorithm to compute a user's risk based on their family history.
- Risk results
 - Increased risk results are provided to women with a reminder of what the BRCAPRO results mean and recommendations for next steps.
 - Not at increased risk results are provided to women with a reminder of what the BRCAPRO results mean and recommendations for next steps.
- The "make a plan" step encourages women to consider what concerns they have and tips for engaging in shared decisionmaking to determine the most appropriate, individualized next steps during their followup clinical visit. The product of this review is a printable action plan for women to bring to their appointment, including specific questions they have to discuss with their provider.
- During the evaluation, participants completed a Web-based post-test measuring their knowledge, attitude, and behaviors surrounding BRCA can cancer risk.
- Each participant returned to their participating primary care provider's office for a followup clinic visit to discuss their risk results.
- After their clinic visit, participants were prompted to complete an additional post-test.

Provider Workflow Site Map

Figure 2. Provider workflow site map



- As shown in Figure 2, during the evaluation, we obtained informed consent from participants offline and assigned each clinician login credentials that were specific to each individual practitioner and clinical evaluation site. Providers were directed to the same splash screen as patient users to log in.
- Provider end users were directed to complete a baseline Web survey on their first visit, and the Web tool verified completion of this assessment before permitting access to the tool.
- The baseline survey was designed to assess providers' knowledge, attitude, and behaviors as related to BRCA screening and cancer risk in primary care.
- During the evaluation phase, all providers who were participating in the study received offline training on how to access the didactic content and how to use the Web tool at the point of care.
- The post-tool training survey assesses participants' understanding of the benefits of using the tool and their comprehension of the evaluation process.
- Didactic content was developed to be self-directed, self-paced, and formatted for quick review. The BRCA Basics section provides a high-level overview of BRCA mutation and cancer risk, while Beyond Basics reviews how the tool is used in practice at the point of

care and allows providers to review examples of risk results before doing so with a patient.

- The posteducation module Web survey assessed knowledge change in providers who had completed the didactic sections of the *Cancer in the Family* Web tool and was the final step in the evaluation process before permitting users to access final release content.
- The centerpiece of the provider navigation experience is the patient list (**Appendix D**). The patient list is the first page a provider sees once they have logged in successfully. Sorted primarily by appointment dates, the list is designed to allow clinicians to identify their patient and their risk results and link to their detailed risk results and family history from one page.
- Reviewing a patient's risk results presents users with a narrative summary of their results, a family history overview in both a table view (**Appendix F**) and pedigree (**Appendix G**).
- The sharing results section offers two options:
 - Increased risk results are provided alongside pointers for what to discuss with women during the visit to facilitate shared decisionmaking with respect to next steps, including referrals.
 - Not at increased risk results are provided alongside pointers for what to discuss with women during the visit to facilitate shared decisionmaking with respect to next steps, including referrals.
- The PDF output of the risk results is available for providers to save to their local computer, then upload to an electronic health record (EHR) as an attachment, or to print for scanning and/or referrals.
- On completion of the patient encounter, providers were prompted to complete a checklist detailing their use of the tool.
- The post-study survey aimed to measure any changes in providers' knowledge, attitude, and behaviors as related to BRCA screening and cancer risk in primary care.

Interface Requirements

The user interface of the patient and provider tools was largely a product of the underlying learning material. Our designers sought to optimize a Web experience that complemented the flow of this material; however, developing expectations and concepts around the user experience began long before authoring any of the didactic material.

In October 2008, we delivered the *Computer-based Clinical Decision Support Tools for Gene-based Tests Used in Breast Cancer: Literature Review* to AHRQ. This review included a section relevant to development entitled *Features and Content*, which provided a summary of the seminal research in CDS development, including the feature set and functionality of 32 existing CDS tools. Another source that was used to inform our design and development was drawn from the foundation of the work by Bates et al. (2003), *Ten Commandments for Effective Clinical Decision Support: Making the Practice of Evidence-based Medicine a Reality*. Our design team was able to use such products for the provider side of the Web tool, alongside the International Patient Decision Aid Standards (IPDAS) checklist for the patient side of the tool from the very beginning of interface design. Our interdisciplinary project team was encouraged to continue referring to these resources throughout every phase of the development life cycle.

In February 2009, we delivered *Computer-based Clinical Decision Support Tools for Gene-based Tests Used in Breast Cancer: Feasibility Study Summary Report* to AHRQ. This report

was based on a series of 60-minute interviews with clinicians in primary care and oncology; hospital administrators; and health care system IT specialists. Results contributed to a sound formative base on which we developed the *Cancer in the Family* Web tool. Technical specifics focused on our evaluation sites but were generalized in the ultimate design of the tool, including prevalence operating systems in use, Internet access in the clinical setting, use of EHRs, tool output options and the potential for EHR integration, and both patient and provider access to technology.

Preliminary iterations of the user interface were wire framed and reviewed internally by the content creators, engineers, and developers. Ad hoc heuristic feedback was incorporated until the final pre-usability testing prototypes were completed. Multiple rounds of usability testing among the target populations of patient and provider end users were executed to obtain input to refine and finalize the design. We anticipate making some slight changes to the final release version of the Web tool based on any actionable feedback obtained during the evaluation.

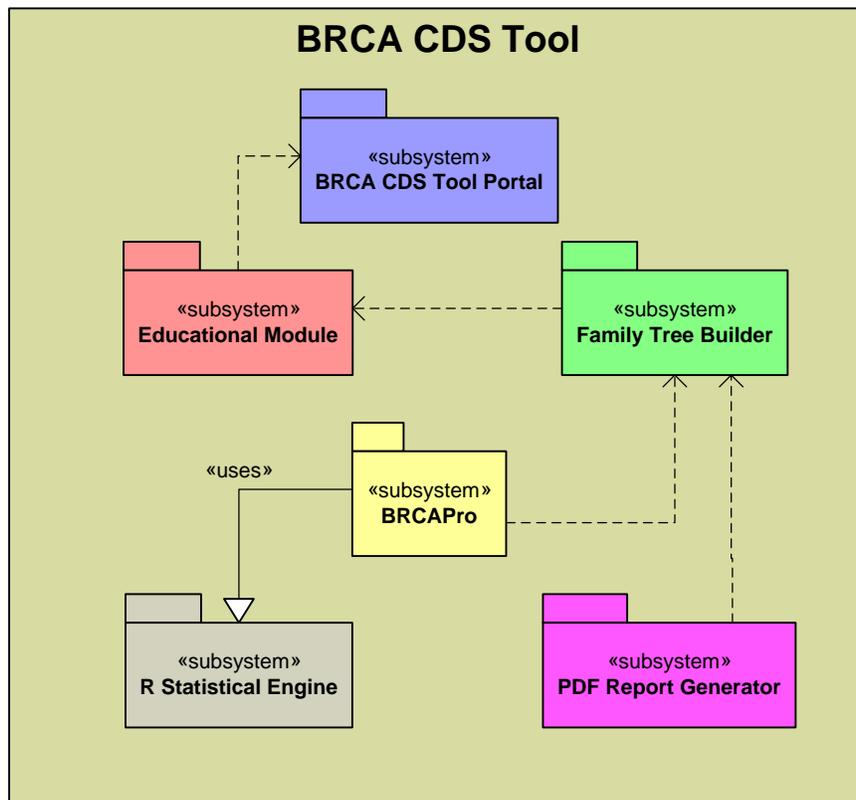
Chapter 3. System Design Specification

Each use case included in this document consists of an identifier, a name, a brief description, and a use case specification. The specification contains both a main flow of events and zero or more alternate flows of events. A use case diagram and a list of all the associated requirements are included in each use case section.

BRCA CDS Tool Design Overview

The diagram below, **Figure 3, BRCA CDS Tool Overview**, is a high-level model of the BRCA CDS tool and the interfaces that are used in the use case models included in this document. The use cases in subsequent use case specifications further illustrate the purpose of these interfaces.

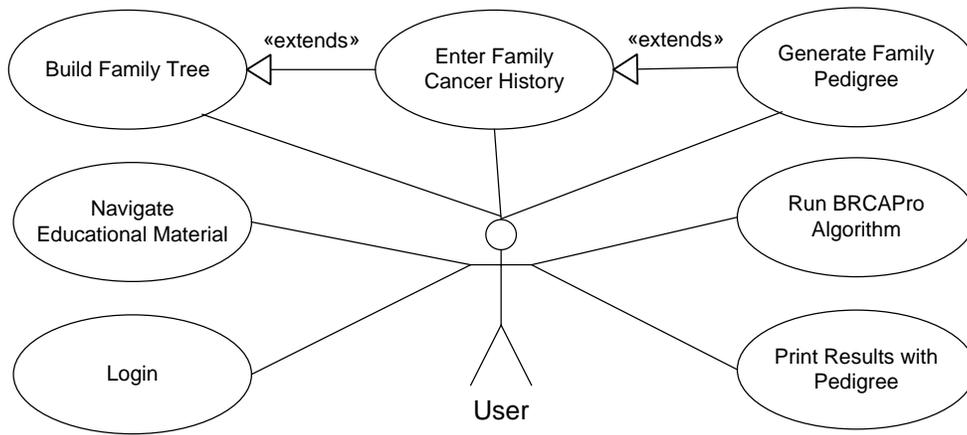
Figure 3. BRCA CDS tool overview



Patient Use Case Overview

The diagram below, **Figure 4, Patient Use Case Overview**, is a high-level model of the patient use case model. The figure depicts the different functionality the system will provide a patient. The system's functionality is illustrated by an individual use case. The use cases in the diagram are further detailed in subsequent use case specifications.

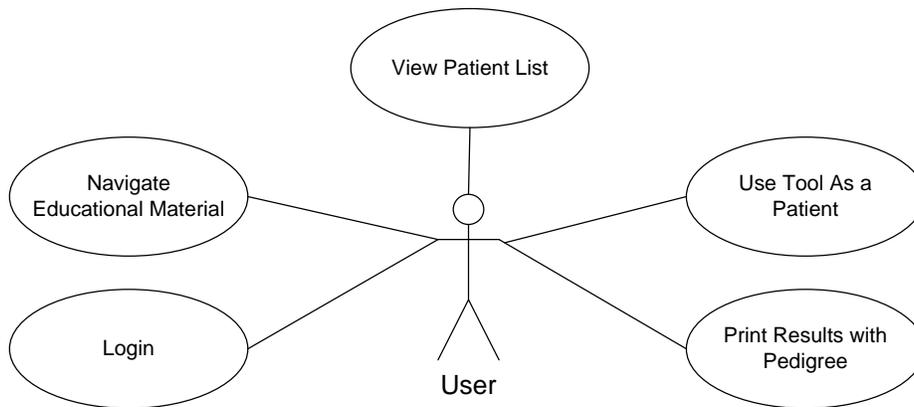
Figure 4. Patient use case overview



Clinician Use Case Overview

The diagram below, **Figure 5, Clinician Use Case Overview**, is a high-level model of the clinician use case model. The figure depicts the different functionality the system will provide a clinician. The system's functionality is illustrated by an individual use case. The use cases in the diagram are further detailed in subsequent use case specifications.

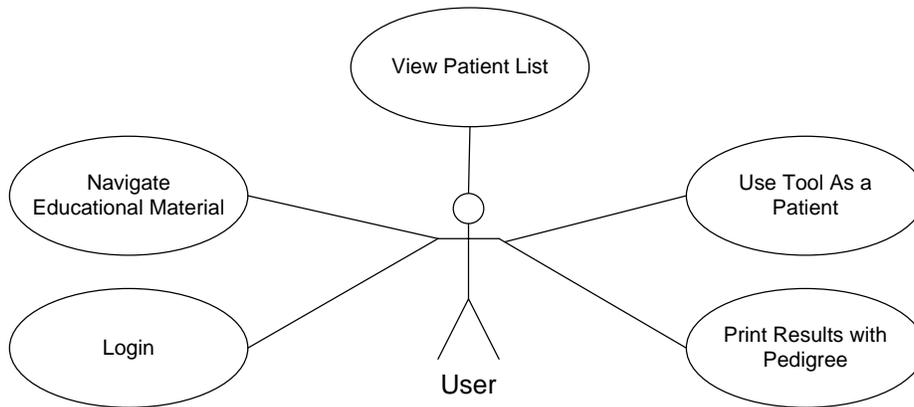
Figure 5. Clinician use case overview



Site Coordinator Use Case Overview

The diagram below, **Figure 6, Site Coordinator Use Case Overview**, is a high-level model of the site coordinator use case model. The figure depicts the different functionality the system will provide a site coordinator. The system's functionality is illustrated by an individual use case. The use cases in the diagram are further detailed in subsequent use case specifications.

Figure 6. Site coordinator use case overview



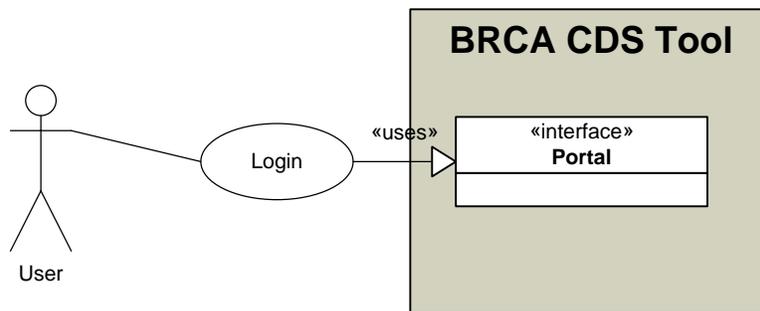
Use Cases

The following section provides detailed use cases for the release *Version 1.1* of the BRCA CDS tool application. Each use case is represented by three components. The components are a use case model, a use case specification, and a listing of features that relate to the use case.

Patient/Clinician Shared Use Cases

UC11: User Login. *Brief Description.* This procedure describes the steps needed by end users to log into the BRCA CDS tool application, illustrated in Figure 7. Users are assigned a user name and password that they enter into the appropriate form on the BRCA CDS tool Web site. Once authenticated, the application directs the user to the appropriate content.

Figure 7. User login



Specification:

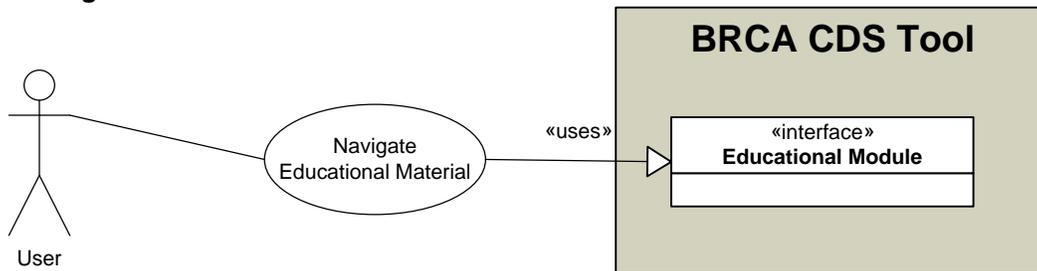
Use Case Name	User Login
Purpose	Provide users with the ability to login to the BRCA CDS tool application.
Actors	Patients, clinicians, and site coordinators
Precondition	The user has a Web browser opened and has been provided valid credentials to access the portal.
Normal Flow	The user navigates to the BRCA CDS tool Web portal. The Web application displays the login form on the home page. The user enters his/her preassigned user credentials that include a user name and password. The user may optionally check the [Remember Login] checkbox. The user selects the [Login] button. The Web application displays appropriate Web content to the user based on the user's security role.
Alternative Flow	
Post Condition	
Special Considerations	

FEAT110: Login. The system will allow a user to log in with unique credentials consisting of a user name and password.

FEAT111: Remember Login. The system will allow a user the option of storing their login information in a cookie with a 2-week duration on the user's personal computer.

UC12: Navigate Educational Material. *Brief Description.* This procedure describes the steps needed for end users to navigate educational material as part of the BRCA CDS tool, illustrated in Figure 8.

Figure 8. Navigate educational material



Specification:

Use Case Name	Navigate Educational Material
Purpose	Provides a manner for users to navigate educational material.
Actors	Clinicians and patients
Precondition	A user has Web browser open and navigated to the BRCA CDS tool Web site.
Normal Flow	<ol style="list-style-type: none"> 1. UC11 2. Patients are directed to a series of tabs that contain educational material. These include Introduction, Learn, Decide, Gather, Calculate, Know, Plan. 3. The patient clicks on the tab subsequent to the one being viewed. 4. On the Decide tab, the patient encounters a decision point. 5. The patient clicks [Yes] and [Submit] to continue to the next tab. 6. UC21 7. UC22 8. UC23 9. UC24 10. Educational content relevant to the risk level of the patient is displayed. 11. UC25
Alternative Flow 1	<ol style="list-style-type: none"> 1. Follow the normal flow of events for Steps 1–4. 2. At Step 5, the patient clicks “not at this time.” 3. A message appears inviting the patient to complete the process later. 4. Additional content tabs are disabled and unavailable for navigation until the response is changed to [Yes].
Alternative Flow 2	<ol style="list-style-type: none"> 1. Follow the normal flow of events for Steps 1–4. 2. At Step 5, the patient clicks [No]. 3. The patient is presented with a text box asking for further explanation. 4. The patient enters a response in the text box and clicks [Submit]. 5. The patient account is deactivated.
Alternative Flow 3	<ol style="list-style-type: none"> 1. Providers are directed to a series of tabs that include BRCA Basics, Beyond Basics, Sharing Results—Increased Risk, Sharing Results—NOT at Increased Risk, References, Additional Resources, Glossary. 2. Providers click on a desired tab to view content. 3. Content is provided in collapsible lists. 4. Provider clicks on an item to expand the content of the list item for additional information.
Alternative Flow 4	<ol style="list-style-type: none"> 1. Follow the normal flow of events for all steps in Normal Flow and Alternative Flow 1 and 2. 2. At Step 2, use the [Prev] or [Next] button found at the bottom of the screen to navigate to the prior or next tab, respectively. 3. Rejoin the flow at Step 3.
Post Condition	The patient or clinician will have been able to navigate through the pages of available education content.
Special Considerations	Security roles determine whether patient or clinician content is displayed. For patients, risk level and age dynamically determine content displayed.

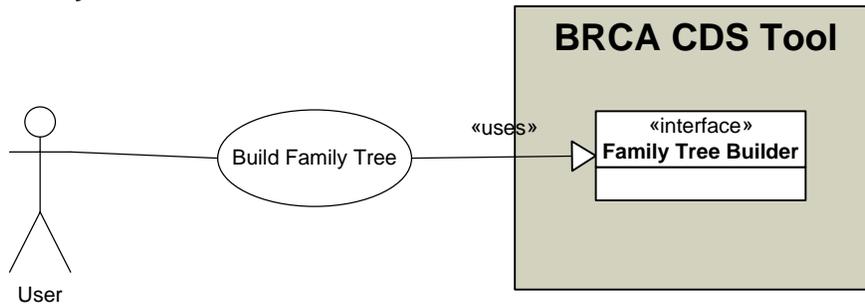
FEAT120: Security Roles. The education module must be capable of displaying role-specific content.

FEAT121: Navigation. The system must provide means to navigate through various educational components with preconditions determining access to each component. For example, a response to a decision point question may determine access to additional educational components. Users must be able to navigate to previously viewed sections of material.

Patient Use Cases

UC21: Build Family Tree. *Brief Description.* This procedure allows end users to build a family tree and print a worksheet to be used for collecting health history for members of the family tree they create, illustrated in Figure 9.

Figure 9. Build family tree



Specification:

Use Case Name	Build Family Tree
Purpose	Provides a manner for users to build a family tree by adding relatives and then produces a worksheet to assist with gathering family cancer health history.
Actors	Patients
Precondition	The patient has logged in and answered “yes” to the decision point in the Decide tab of the Education Module.
Normal Flow	<ol style="list-style-type: none"> 1. The patient navigates to the Gather tab of the Educational Module. 2. The patient clicks on [Enter Your Cancer History] in the menu. 3. The patient enters Age, Race, Jewish Ancestry, Breast Cancer Hx, and Ovarian Cancer Hx. 4. The patient clicks [Save]. 5. The patient clicks [Enter Your Family Tree > Your Children] 6. The patient enters the number of daughters with initials for each one and the number of sons with initials for each one. 7. The patient clicks [Save]. 8. The patient clicks [Next]. 9. The patient repeats 6-8 for Siblings, Nieces and Nephews, Maternal Aunts and Uncles, Maternal Cousins, Paternal Aunts and Uncles, Paternal Cousins. 10. After clicking [Next] on the Paternal Cousins page, the patient is presented with a page where she may print her family cancer history worksheet. 11. The patient clicks [Open Your Family Cancer History Worksheet]. 12. The patient uses the browser print function to print the output.
Post Condition	A PDF form is created depicting each member of the patient’s family with questions necessary to derive information to run a more accurate BRCA ^{PRO} analysis of the patient’s BRCA mutation risk.
Special Considerations	

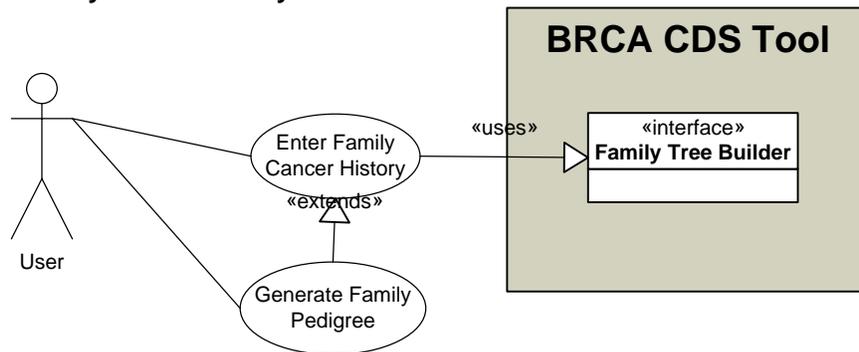
FEAT210: Bulk Add Family Members. The system must provide a method for adding multiple family members at one time and uniquely identifying the family members for the patient without providing personally identifying information (PII).

FEAT211: Add/Edit/Delete Family Members. The system must provide a method for adding/editing/deleting single instances of family members once the initial family tree has been created.

FEAT212: Account for Duplicate Patient-Provided Identifiers. The system must provide a method for allowing patients to add the same set of initials to more than one type of family member.

UC22: Enter Family Cancer History and Generate a Pedigree. *Brief Description.* This procedure provides the steps needed for patients to add their family’s cancer history to the BRCA CDS tool and generate a family pedigree, illustrated in Figure 10.

Figure 10. Enter family cancer history



Specification:

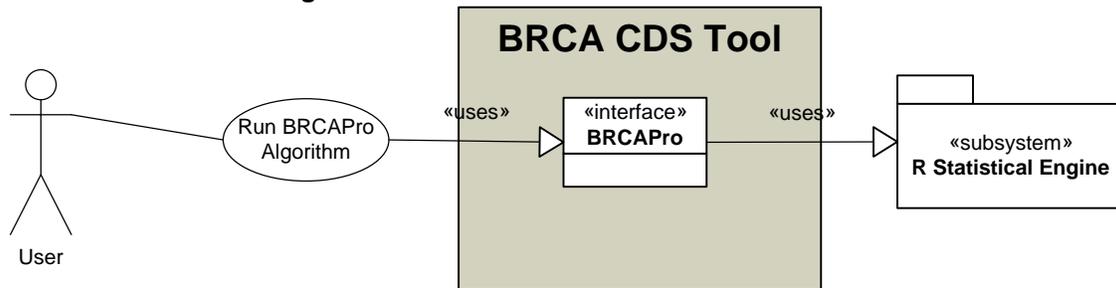
Use Case Name	Enter Family Cancer History
Purpose	Provide a manner for patients to enter/update the BRCA CDS tool with cancer history for their families.
Actors	Patients
Precondition	The patient has her Web browser open and has previously created a family tree. The patient has also logged into the BRCA CDS tool Web site.
Normal Flow	<ol style="list-style-type: none"> 1. The patient clicks on the Gather tab. 2. The patient selects [Enter Mother's Side Cancer History]. 3. The patient completes the form using the information collected by her from her family members in the Family Cancer History Worksheet (generated in UC3). 4. The patient clicks [Save All]. 5. The patient clicks [Next]. 6. The patient is presented with a family pedigree for her mother's side that can be reviewed before proceeding. 7. The patient click's [Next]. 8. The patient completes the form using the information collected by her from her family members in the Family Cancer History Worksheet (generated in UC3). 9. The patient clicks [Save All]. 10. The patient clicks [Next]. 11. The patient is presented with a family pedigree for her father's side that can be reviewed before proceeding.
Post Condition	The BRCA CDS tool has all information necessary to run the BRCAPRO algorithm and the patient is ready to proceed to the Calculate tab.
Special Considerations	

FEAT220: Update Family Cancer History Data. The system will provide a method for updating the cancer history for each member of the family tree identified by the patient. Family members for whom no data are entered will be ignored during the calculation.

FEAT221: Generate Pedigree. The system will generate a graphical pedigree representing the inputs collected during the Family Tree Building and Family Cancer History processes.

UC23: Run BRCA PRO Algorithm. Brief Description. This procedure describes the steps needed for the BRCA CDS tool to run the BRCA PRO algorithm for a patient, depicted in Figure 11.

Figure 11. Run BRCA PRO algorithm



Specification:

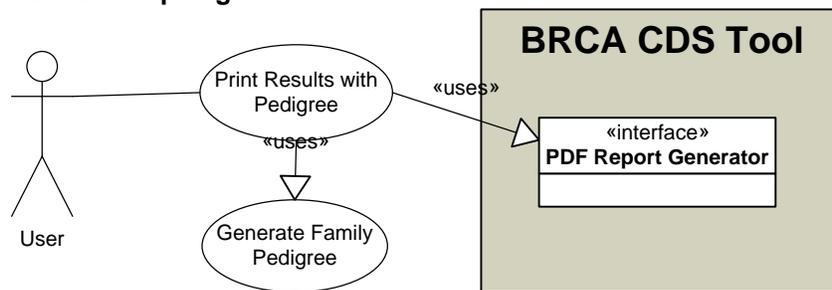
Use Case Name	Run BRCA PRO Algorithm
Purpose	Provides a manner for the patient to run the BRCA PRO algorithm.
Actors	Patients
Precondition	The patient has completed entering her cancer history, built her family tree, and entered her family cancer history. The patient is logged in and on the Calculate tab.
Normal Flow	<ol style="list-style-type: none"> 1. The patient is presented with a decision point that asks the patient if she would like to have the tool calculate her chances of having a BRCA gene mutation. 2. The patient selects [Yes]. 3. The patient clicks [Calculate Chances of BRCA Mutation] button. 4. The BRCA CDS tool uses the patient's information to run the BRCA PRO algorithm using the R statistical engine. 5. A result of Increased Risk or NOT at Increase Risk is displayed on the page. 6. The patient clicks [Next] at the bottom of the page to move to the next tab.
Alternative Flow 1	<ol style="list-style-type: none"> 1. Follow the normal flow of events for Step 1. 2. At Step 2, the patient selects [No]. 3. The patient is presented with a text box and a request to explain why she has chosen not to calculate her risk at this time. 4. The patient is also presented with a message that she can come back at a later date and change her response to [Yes] and calculate her risk. 5. The patient enters text in the text box. 6. The patient clicks [Save No Answer]. 7. The patient ends her session.
Post Condition	The patient has calculated her BRCA risk probability.
Special Considerations	

FEAT230: Provide Decision Point for Calculating BRCA Risk. The system will provide a yes/no question to confirm that the patient wants to calculate her BRCA mutation risk probability. If “no” is selected, the system will collect an explanation.

FEAT231: Run BRCAPRO Algorithm. The system will use the patient-provided data to run the BRCAPRO algorithm using the R statistical engine. The results will be displayed on the screen to the user in the form of “Increased Risk” and “NOT at Increased Risk” along with the date the algorithm was last run for the patient.

UC24: Print Results with Pedigree. *Brief Description.* This use case describes the steps needed to print the results for the BRCAPRO calculation along with the pedigree and other supporting information, depicted in Figure 12.

Figure 12. Print results with pedigree



Specification:

Use Case Name	Print Results with Pedigree
Purpose	Provides a means for generating a report of results, pedigree, and other relevant information.
Actors	Patients
Precondition	The patient has calculated her BRCA mutation risk probability. The patient is logged in and on the Plan tab.
Normal Flow	<ol style="list-style-type: none"> 1. The patient with an “Increased Risk” result is presented with the option to create a list of questions by checking prewritten questions in each of the following categories: 2. Selecting Questions to Ask Your Doctor 3. Questions about genetic testing for BRCA1 or BRCA2 4. Questions about the test itself 5. Questions about the results 6. Questions about family implications 7. Questions about family history 8. Other questions 9. The patient is also provided with open text boxes to type her own questions. 10. The patient selects questions and optionally types in her own questions. 11. The patient clicks [Your Results and Questions]. 12. The system generates a report that displays the selected/typed questions, the patient’s results, family tree, cancer history, and pedigree. 13. The patient uses her Web browser’s print functionality to print or save the report.
Alternative Flow	<ol style="list-style-type: none"> 1. The patient with a “NOT at Increased Risk” result is presented with the option to create a list of questions by checking prewritten questions in each of the following categories: 2. Selecting Questions to Ask Your Doctor 3. Resume normal work flow at Step 2.
Post Condition	The patient has a report with the results of a BRCAPRO calculation based on patient-provided inputs, a graphical family pedigree, a tabular representation of her family tree and cancer history, and patient selected/typed questions to ask her provider and/or genetic counselor.
Special Considerations	Risk results determine which questions are visible for selection and inclusion on the dynamically generated PDF report.

FEAT240: Question List. They system will allow a user to create a question list from predetermined lists of questions, based on risk result. This question list will include open text boxes for each category to allow the user to type free-form questions to be included in the resulting question list. “Increased Risk” patients will have the following categories:

- Selecting Questions to Ask Your Doctor
- Questions about genetic testing for BRCA1 or BRCA2
- Questions about the test itself
- Questions about the results
- Questions about family implications
- Questions about family history
- Other questions

“NOT at Increased Risk” patients will have the following categories:

- Selecting Questions to Ask Your Doctor

FEAT241: Report Output. The system will dynamically generate a PDF report that includes the following:

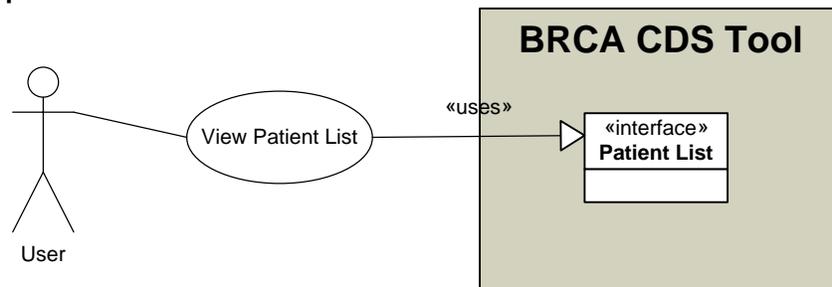
- BRCAPRO Result of “Increased Risk” or “NOT at Increased Risk”

Family pedigree—graphical representation suitable for sharing with a genetic counselor
 Family tree with cancer history in tabular format
 Patient selected/provided questions from question list

Clinician/Site Coordinator Shared Use Cases

UC31: View Patient List. *Brief Description.* This procedure describes the steps needed by clinicians and site coordinators to view patients who have been given credentials to use the BRCA CDS tool for their specific practice/site, depicted in Figure 13.

Figure 13. View patient list



Specification:

Use Case Name	View Patient List
Purpose	Provides users the ability to view patients who have been given credentials to use the BRCA CDS tool for the clinician's practice/site.
Actors	Clinicians and Site Coordinators
Precondition	The user has a Web browser open and has navigated to the BRCA CDS tool.
Normal Flow	<ol style="list-style-type: none"> UC11 The Web application displays a patient list based on the user's security role that lists patients for the user's specific practice/site. <p>The list displays the following for clinicians: User Name (clickable link) Patient ID Appointment Date/Time Provider Name Results as "Increased risk" or "Not at Increased Risk" Risk Results PDF (clickable link)</p> <p>The list displays the following for site coordinators: User Name Patient ID Appointment Date/Time Provider Name Results Date Risk Results PDF (clickable link) Edit (clickable link)</p>
Alternative Flow	
Post Condition	
Special Considerations	Security role determines if a user is allowed to see the patient list and further determines which practice's list to show.

FEAT310: View Patient List. The system will display a patient list for providers and site coordinators immediately upon logging into the system. The patient list will be context aware and display only the patients for the user’s practice/site.

The list displays the following for clinicians:

- User Name (clickable link)
- Patient ID
- Appointment Date/Time
- Provider Name
- Results as “Increased risk” or “Not at Increased Risk”
- Risk Results PDF (clickable link)

The list displays the following for site coordinators:

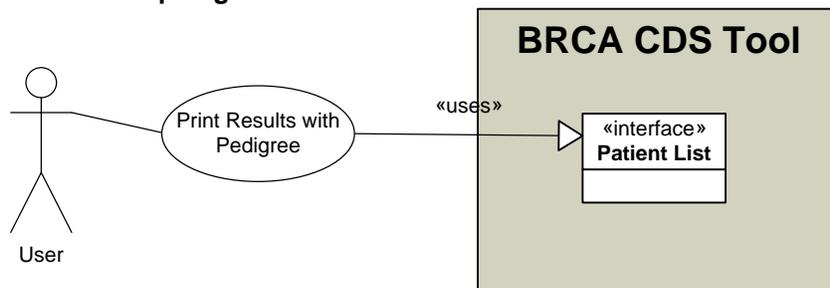
- User Name
- Patient ID
- Appointment Date/Time
- Provider Name
- Results Date
- Risk Results PDF (clickable link)
- Edit (clickable link)

FEAT311: Sorting. The system will allow a user to sort the list in ascending or descending order by clicking on the following column headings:

- User Name
- Patient ID
- Appointment Date/Time
- Provider Name
- Results/Results Date

UC32: Print Results with Pedigree. *Brief Description.* This procedure describes the steps needed by clinicians and site coordinators to print the risk results and pedigree for a specific patient, depicted in Figure 14.

Figure 14. Print results with pedigree



Specification:

Use Case Name	Print Results with Pedigree
Purpose	Provides users the ability to print risk results and pedigree for a specific patient.
Actors	Clinicians and Site Coordinators
Precondition	The user has a Web browser open and has navigated to the BRCA CDS tool.
Normal Flow	<ol style="list-style-type: none"> 1. UC11 2. UC31 3. The user identifies the patient in the Patient List for whom he/she wishes to print results. 4. The user clicks on the Risk Results PDF icon for the patient. 5. The system opens a PDF file displaying the results of the patient's BRCAPRO risk calculation, pedigree, and family tree in tabular form with cancer history. 6. The user uses the Web browser's print or save functionality accordingly.
Alternative Flow	
Post Condition	The user has printed or saved the patient's risk result with pedigree.
Special Considerations	Security role determines if a user is allowed to see the patient list and further determines which practice's list to show.

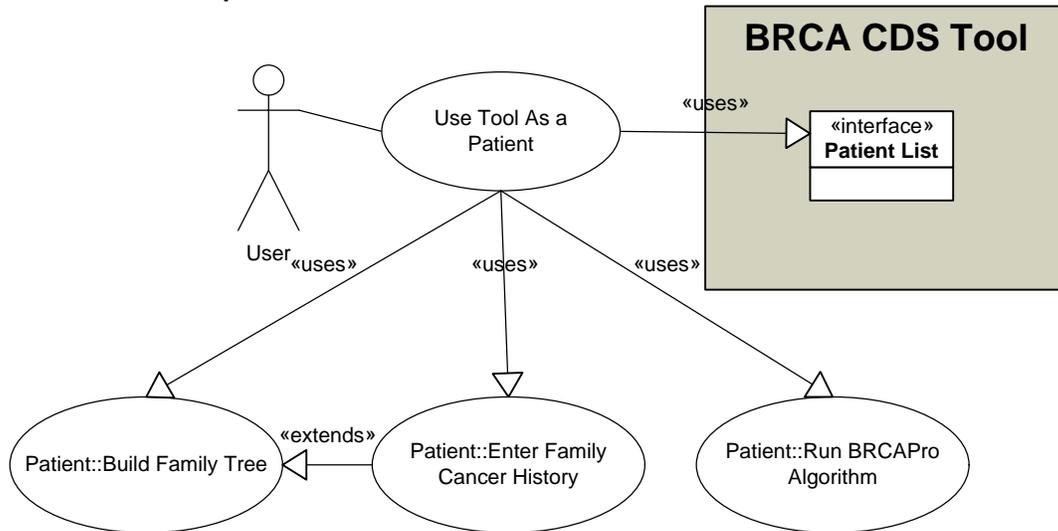
FEAT320: Clinician Results Report. The system will generate and display a PDF patient report for clinicians that includes:

- User Name
- Risk result as "Increased Risk" or "Not at Increased Risk"
- Mutation Probability Score as generated by BRCAPRO
- Tips for Talking with Your Patient (contextually related to risk result)
- Family tree in tabular form with cancer history
- Graphical pedigree with symbols relevant to cancer history

Clinician Use Cases

UC41: Use Tool as a Patient. *Brief Description.* This procedure describes the steps needed by clinicians to use the BRCA CDS tool as a specific patient in order to change/update family history information and rerun the BRCAPRO calculation, depicted in Figure 15.

Figure 15. Use tool as a patient



Specification:

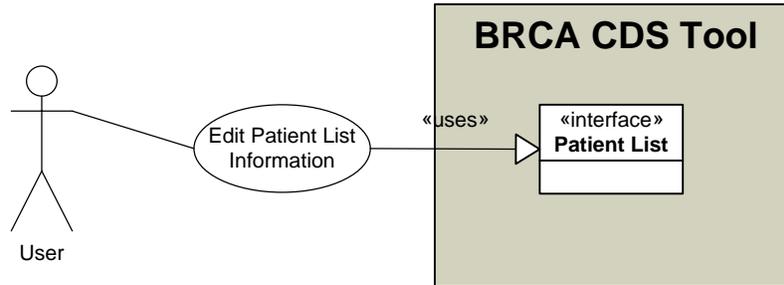
Use Case Name	Use Tool as a Patient
Purpose	Provides users the ability to use the BRCA CDS tool as a specific patient in order to change/update patient information and rerun the risk calculation.
Actors	Clinicians
Precondition	The user has a Web browser open and has navigated to the BRCA CDS tool.
Normal Flow	<ol style="list-style-type: none"> 1. UC11 2. UC31 3. The user identifies the patient for whom he/she wishes to make changes to cancer history and/or rerun the risk calculation. 4. The user clicks on the User Name (clickable link). 5. The system impersonates the patient and displays the patient's interface. The system displays a heading indicating "Running Patient Tool as [Patient's User Name]." A link is also displayed that says, [Return to Patient List]. 6. UC21 7. UC22 8. UC23 9. The user clicks [Return to Patient List] link.
Alternative Flow	
Post Condition	
Special Considerations	

FEAT410: Run Tool as Patient. The system will allow a clinician to select an individual patient from the patient list and have the patient interface display with notification that the clinician is running the patient tool as that patient. A link will be provided to allow the clinician to return to the Patient List. The clinician will be able to interact with the patient tool, just as the patient, to add/edit/delete family members, update cancer history, and run the BRCAPRO risk calculation.

Site Coordinator Use Cases

UC51: Edit Patient List information. *Brief Description.* This procedure describes the steps needed by site coordinators to edit Patient List information for a specific patient, depicted in Figure 16.

Figure 16. Edit patient list information



Specification:

Use Case Name	Edit Patient List Information
Purpose	Provides users the ability to edit Patient List information.
Actors	Site Coordinators
Precondition	The user has a Web browser open and has navigated to the BRCA CDS tool.
Normal Flow	<ol style="list-style-type: none"> 1. UC31 2. The user identifies the patient for whom he/she wishes to edit Patient List information. 3. The user clicks on [Edit] (clickable link). 4. The system expands the row to show the following text fields for: Patient ID Appointment Date/Time Provider Name 5. The user enters information in the available text fields. 6. The user clicks [Update]. 7. The system updates the Patient List information for the patient.
Alternative Flow	<ol style="list-style-type: none"> 1. Follow the normal flow of events for steps 1–5. 2. At step 6, the user clicks [Cancel]. 3. The system returns the user to the Patient List with no data changed.
Post Condition	
Special Considerations	Only the site coordinator has permissions to edit Patient List information.

FEAT510: Edit Patient List Information. The system will allow a site coordinator to edit certain Patient List information for patients who are assigned to the site coordinator’s practice/site. The information that can be edited is the
 patient ID,
 appointment date/time,, and
 provider name.

Chapter 4. System Testing

Once the initial implementation had been produced that met the stated objectives and requirements, the system was presented to the project team for feedback. This feedback was incorporated into the implementation before system testing began. Testing procedures are outlined in the following sections.

Test Plan

Unit Testing

Unit testing was performed by programmers as they built each system. This was used by the developer to verify the system was ready to be turned over to the testers for system acceptance testing. This type of testing was at the discretion of the developer, and no formal documentation of the testing was required.

Integration Testing

Integration testing for these systems was included as part of the system testing.

System Testing

In the test environment, testing was conducted and/or performed by the project team using scripts developed from requirements documentation (use cases) as a guide.

Actionable findings from testing were entered into Bugzilla, an issue tracking system, for resolution.

Acceptance Testing

For acceptance testing, all systems were presented to the Project Director who provided written (email) acceptance of the final product. Feedback and approval messages were stored on the project share in a directory designated for systems development.

Regression Testing

Regression testing was performed to verify that corrections and/or updates applied to the system did not adversely affect previously programmed features. The programmers, as well as system testers, performed regression testing as they made changes. The exact test was the responsibility of the tester and varied depending on the system and the change made.

Accuracy Testing

Data Requirements

To calculate a risk score, BRCAPRO needs the following data for the individual for whom the risk is to be calculated: age, race, Jewish ancestry, history of breast or ovarian cancer, and whether the individual has had an oophorectomy. If the individual has had either type of cancer, BRCAPRO gathers the age of diagnosis and, if breast cancer, whether it was unilateral or bilateral. In addition, the BRCAPRO calculation needs cancer history for the following family

members: parents, siblings, half-siblings, children, nieces and nephews, maternal grandparents, paternal grandparents, maternal aunts and uncles, paternal aunts and uncles, maternal cousins, and paternal cousins. For each of these individuals, BRCAPRO collected information on whether they are living or dead; if living, current age (if deceased, age of death); and history of breast and/or ovarian cancer. If the family member has had breast cancer, BRCAPRO also collects the age of diagnosis and whether it was unilateral or bilateral breast cancer. If a relative has had ovarian cancer, BRCAPRO collects the age of diagnosis. BRCAPRO also incorporates whether female relatives have had an oophorectomy into the calculation.

Method

We constructed 100 hypothetical families for testing the CDS tool. Each family consisted of a female consultant and the following family members: mother, father, maternal and paternal grandparents, sister, brother, son, daughter, maternal aunt and uncle, and paternal aunt and uncle. Cancer histories and ages were varied to reflect a range of expected risk levels. In addition to these cases, other cases were constructed to test specific aspects of the tool or estimation as needed.

Results

We compared the risk estimates for the 100 hypothetical families from our CDS tool with those from BRCAPRO to ensure the results were the same. We also manually entered the family history for 20 families into the tool interface. We developed six additional cases to test the effect of race following a BRCAPRO upgrade that included race-specific prevalence estimates. Following iterative testing and correction of errors, the estimates from the CDS tools and from BRCAPRO agreed to at least the fourth decimal place.

508 Compliance

The Research Computing Division at RTI has extensive experience managing, developing, and maintaining portals in full compliance with the Americans with Disabilities Act (ADA) (including Section 508 regulations), other federal regulations, and privacy and security requirements.

In addition to visual and manual inspection, compliance testing included some of the testing tools like AccVerify (checks Web sites/applications for most conformance standards), Web Accessibility Toolbar (aids in manual examination of Web pages for a variety of aspects of accessibility), CommonLook (verifies whether PDFs are accessible and meet the requirements of Section 508), Java Ferret (allows users to select different methods to select an object to be examined, such as focus, mouse, F1 button, etc.), Microsoft Navigator (a screen reader utility that offers capability in reading dialog boxes and window controls), and Microsoft Object Inspector (a tool that permits testers/developers to view property values of an application within a user interface).

ADA compliance for the *Cancer in the Family* Web tool was provided in the following areas:

4. Section 1194.21: Software applications and operating systems.

- a) Keyboard access:** The applications' Web pages are designed such that the navigation and/or execution is possible from a keyboard where the function itself or the result of performing a function can be discerned textually.

- b) **Accessible features:** The application will not disrupt or disable activated features of other products and/or operating systems that are identified as accessibility features.
 - c) **Focus:** A well-defined on-screen indication of the current focus is provided that moves among interactive interface elements as the input focus changes (on tabbing). The focus is programmatically exposed so that assistive technology can track focus and focus changes.
 - d) **User interface elements:** Sufficient information about user interface elements such as buttons, dropdown menus, check boxes, radio buttons, etc. are available to assistive technology.
 - e) **Bitmap images:** Whenever bitmap images (icons) are used to identify controls, status indicators, or other programmatic elements, which are mainly used to indicate action, they are used consistently throughout the application.
 - f) **Text:** Textual information in the application is also available to the operating system's assistive technology.
 - g) **Contrast:** The Web pages will not override user-selected contrast and color selections and other individual display attributes. This ensures that users with color blindness and macular degeneration are served.
 - h) **Animations:** When animations are present, all the animation information and functionality will also be provided in accessible formats.
 - i) **Color:** All Web pages are designed such that any information conveyed with color will also be conveyed without color.
 - j) **Availability of color and contrast settings:** The application is designed such that a variety of color and contrast settings are provided so the user can adjust to their desired settings.
 - k) **Page flickers:** Web pages do not use flashing or blinking text, objects, etc.; screen flicker was limited to less than 2 per second or greater than 55 per second to reduce the risk of optically induced seizures.
 - l) **e-Forms:** All electronic forms have the necessary information, field elements, directions/cues, and functionality required to complete and submit the form.
5. **Section 1194.22: Web-based intranet and Internet information and applications.**
- a) **Text:** A text equivalent for every nontext element, such as images, links, Java applets, flash files, video files, audio files, and plug-ins, are provided. This could be an alt text description or content described clearly in the adjacent text.
 - b) **Multimedia:** Alternatives for multimedia presentations are synchronized with the presentation. Video files have transcripts.
 - c) **Color:** All Web pages are designed such that color is not the only means to convey information or an action. An alternative method, such as text labels, was used in combination with color to identify emphasized text or to indicate an action.
 - d) **Style sheets:** All documents are organized such that they are readable without requiring an associated style sheet. Font size and contrast are regulated along with any style sheets or format issues to ensure that text and images are easily recognized.
 - e) **Rows and Column headers:** Every data table has descriptive and unique row and column headers. This will help in providing audible identification to the cell by naming the row and column before the cell content.
 - f) **Markup:** A markup is used to associate data cells when data tables have two or more logical levels of row and/or column headers.

- g) Flashing and blinking items:** Web pages have been developed without any flashing or blinking items.
- h) Text page:** The Web pages have been designed such that compliance to Section 508 requirement is accomplished within the Web page. In rare situations, when compliance is not accomplished this way, a text-only page alternative was provided.
- l) Scripting languages:** Use of scripting languages was limited, but if any pages do use it to display content, or to create interface elements, the information provided by the script shall be identified with functional text that can be read by assistive technology.
- j) Applets/plugin-ins:** Web pages have been designed such that use of applets and plug-ins are either eliminated or limited.
- k) e-Forms:** All electronic forms have text labels for every control (text fields, radio buttons, checkboxes, and text areas) that specify the type of information to be imported into each field. DHTML scripting of the form will not interfere with assistive technologies and is keyboard accessible.
- l) Skip repetitive navigation links:** Users have the option/means to skip repetitive navigation links and move directly to the page content.
- m) Timed response:** In situations where the user needs more time to read or operate input controls, the user will have provision to indicate more time is required.

Chapter 5. Deployment Guide

Environment

DotNetNuke (DNN) (available at: <http://www.dotnetnuke.com>) is an open-source Portal and Content Management Framework, based on Microsoft's .NET technology. DNN offers a robust, extensible and fully functional framework for developing a broad range of commercial portal applications. The Web site is running under the DNN framework, version 4.9.4. All code runs on a Windows server that has .NET 2.0 installed. A user manual for operating and maintaining this open-source Web portal can be found at the following location:
<http://www.dotnetnuke.com/tabid/787/default.aspx>.

The BRCA mutation probability calculation uses the R statistical engine. The R program must be installed on the same Web server that is serving up the Web site pages. Since installing a program such as R is usually not allowed on shared environments, the *Cancer in the Family* Web site is running on a separate virtual machine (VM).

R Statistical Engine

With the R “engine” installed, the Web site code creates a process and runs a DOS command prompt (cmd.exe). A version of cmd.exe is located in the brcadata folder under the Web site, and this is the one that is run by the app. The process runs the CMD prompt and runs the following command line:

```
6. R -vanilla -no-restore <(input filename.r) >output.txt
```

The “R” is R.EXE located in the R bin folder. Before running the cmd prompt, the Web site code sets the DOS PATH environment variable to the R folder, so DOS can find the R.EXE program and other DLLs for R.

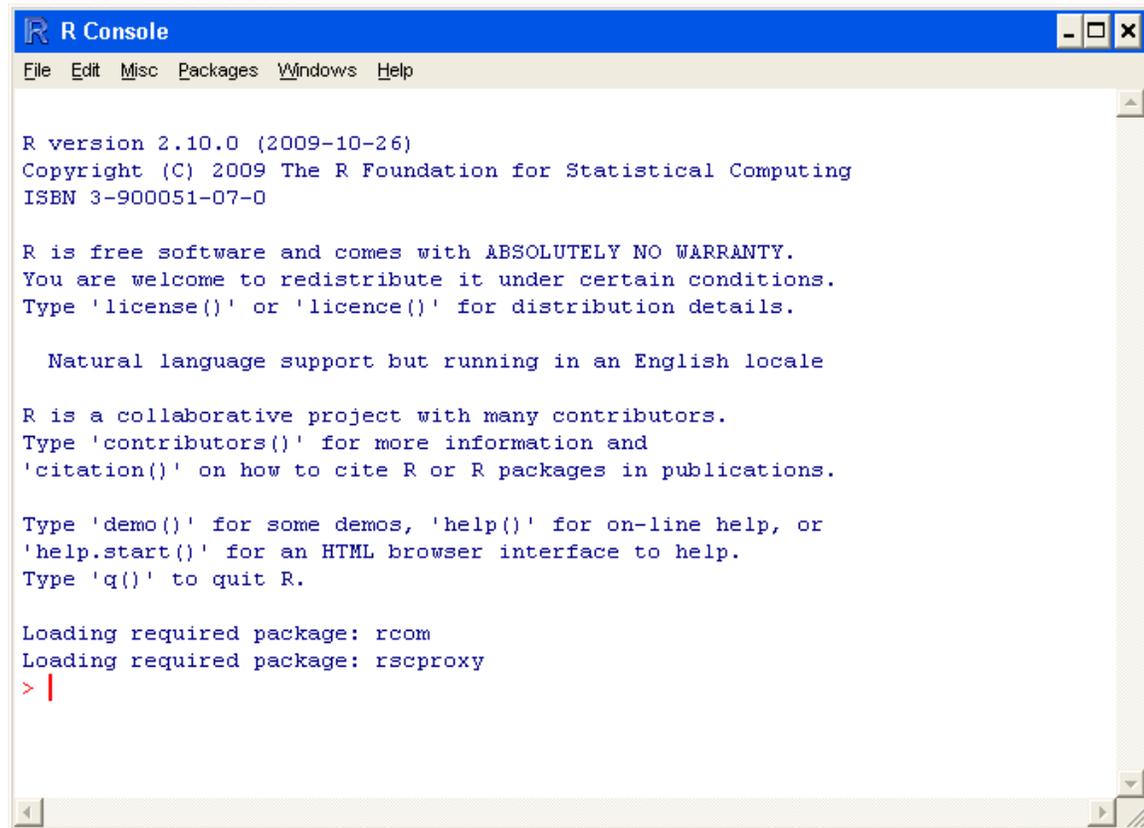
The `-vanilla` and `-no-restore` are command line flags for R. See R documentation for full explanation.

The “<” is standard DOS input redirection, which means the R program receives its inputs from an input file. The contents of the input file are built by the Web site code.

The “>” is standard DOS output redirection, which means instead of writing to the console (screen), the DOS program (R.exe) writes the output to the indicated file.

To Install R on a Windows Web Server

Figure 17. R console window



```
R Console
File Edit Misc Packages Windows Help

R version 2.10.0 (2009-10-26)
Copyright (C) 2009 The R Foundation for Statistical Computing
ISBN 3-900051-07-0

R is free software and comes with ABSOLUTELY NO WARRANTY.
You are welcome to redistribute it under certain conditions.
Type 'license()' or 'licence()' for distribution details.

Natural language support but running in an English locale

R is a collaborative project with many contributors.
Type 'contributors()' for more information and
'citation()' on how to cite R or R packages in publications.

Type 'demo()' for some demos, 'help()' for on-line help, or
'help.start()' for an HTML browser interface to help.
Type 'q()' to quit R.

Loading required package: rcom
Loading required package: rscproxy
> |
```

1. Download the desired version of R from <http://cran.r-project.org>.
2. Follow the instructions that come with the R download and install R on the Web server (requires admin privileges).
3. Make sure R runs:
 - a. Open Windows File Explorer.
 - b. Navigate to the R installation bin folder (e.g., C:\Program Files\R\R-2.9.0\bin).
 - c. Run RGui.EXE.
 - d. You should see the screen similar to **Figure 17**.
 - e. Click the Windows “X” icon to close RGui.exe. Do not save the workspace.
4. Grant full permissions to the R folder to the ASPNET Windows user account:
 - a. Open Windows File Explorer.
 - b. Navigate to the R installation folder (e.g., C:\Program Files\R\R-2.9.0).
 - c. Right-click on the folder and click Properties.
 - d. Select the Security tab.
 - e. Click Add.
 - f. Click Locations.
 - g. Select the top node, which is the machine name, then click OK.
 - h. In the “Enter the objects names to select” box, enter ASPNET.
 - i. Click Check Names. The ASPNET that was entered should expand to (machine name)\ASPNET. If it does, click OK. If it does not, you may be running a newer version

of .NET or IIS that does not have the ASPNET user account. Consult Microsoft help for information.

- j. Select ASP.NET Machine Account from the list of group or user names.
 - k. Check the “Allow” checkbox next to Full Control.
 - l. Click OK.
 - m. The ASPNET account should now have permission to access the R folder.
5. Update the web.config line to point to the location of the R bin folder:
<add key=“REXEPath” value=“C:\Program Files\R\R-2.10.0\bin”/>

The Web site code sets the PATH environment variable based on this setting.

Running R on Web

Risk assessment was performed using the BRCAPRO package running in the R statistical programming application. A subject’s family cancer history data are collected through various pages on the Web site and are stored in a SQL database. When the Calculate button is clicked on the Web site, the following programmatic operations occur:

1. The filename base (not including extension) for the seven files that are created during the Calculate operation is determined. Each time the Calculate operation is run, a unique filename base is used. The filename for the first time Calculate is run is the Patient Code (e.g., “DRFTW”). Each subsequent Calculation operation appends a sequential number in parenthesis after the Patient Code (e.g., DRFTW(1), DRFTW(2), DRFTW(3), etc.)
2. The following seven files are created in the brcadata folder. Table 2 describes each file type in more detail.
 - (filename base).CSV
 - (filename base).TXT
 - (filename base).BAT
 - (filename base).R
 - (filename base).ERR
 - (filename base).PDF
 - (filename base)_Provider.PDF
3. The Web site code then starts a new Windows process to run the Windows command line interpreter (a “DOS box”), with a Window style of Hidden and runs the following command:
`R --vanilla --no-restore <(basefilename).R >(basefilename).TXT`

This command runs R.EXE with the command line switches “—vanilla” and “—no-restore.” It redirects stdin from the latest .R file and redirects stdout to a .TXT file. stderr is redirected to a .ERR file.

4. After R runs, it returns to the Web site code and the two output PDF files are generated.

Table 2. Files generated during the calculate operation

File Extension	Description
.CSV	Comma-Separated Value plain text file that contains the family cancer history data for the subject. This file is an input file for the BRCAPRO algorithm. This file contains the following fields/columns: <ul style="list-style-type: none">• ID• Gender• FatherID• MotherID• AffectedBreast• AffectedOvary• AgeBreast• AgeOvary• AgeBreastContralateral• Oophorectomy• AgeOophorectomy
.TXT	Plain text file that contains the user interface text that was generated by R. This would be the text that the R user would see if the package was run in the R program with a user interface. The contents of this file are read by the BRCA code to extract the raw BRCA probability value. This value is then compared to .01 to determine the risk category (at risk/not at risk).
.BAT	Contains a record of the DOS command line command that is used. This file is not used in the DOS command line; it is only created for reference.
.R	Contains the main R script to be run by R. For more detail on the R scripts in this file, see the section called R Script .
.ERR	Plain text file that contains the DOS screen output text. This is what would be seen when the DOS command line version of R is run.
*.PDF	PDF file of Patient Action Plan.
*_Provider.PDF	PDF file of output for providers.

Issues Running R on a Web Server

The R application accesses the Windows Registry; therefore, it will not be allowed to run in some shared environments for security reasons. RTI enforces a minimum of Medium Trust on its shared Web servers, so R could not run in a shared environment. In addition to requiring access to the Registry, the R program also needed to be installed on the Web server. Again, because of security reasons, this was not allowed. We had to configure a dedicated VM to be used as the Web server for BRCA.

R Script. The main R script file (*.R) contains the following R command line commands:

1. **library (BayesMendel)** —Loads the BayesMendel package into R as a resource. Any other packages on which BayesMendel depends are automatically loaded by R.
2. **data (BRCAPenet.metaDSL.2008, death.othercauses, compriskSurv, BRCAbaseline.race.2008, CBRCAPenet.metaDSL.2009)** —Loads a number of data files used by BRCAPRO.
3. **familydata = read.csv ('C:\\Applications\\brca\\htdocs\\prod\\brcadata\\GUSMX.CSV')** —Loads the main family data into an R variable called familydata.

4. `oophorectomy <- data.frame(familydata[,10], familydata[,11])`—Loads two columns from the familydata variable into an R variable called oophorectomy.
5. `dimnames(oophorectomy)[[2]] <- c("Oophorectomy", "AgeOophorectomy")`—Names the fields in the Oophorectomy variable. BRCAPRO requires the fields to be named a certain way.
6. `BRCAPRO(familydata, counselee.id=7, allef.type="nonAJ", race="White", oophorectomy = oophorectomy)`—Runs the main BRCAPRO algorithm code in R.
7. `q()`—Stops R and returns to the command prompt.

Appendix A. Requirements Traceability Matrix

Requirements	Release Version	Trace to Design Spec
FEAT110: Login The system will allow a user to login with unique credentials consisting of a user name and password.	1.1	UC11
FEAT111: Remember Login The system will allow a user the option of storing their login information in a cookie with a 2-week duration on the user's personal computer.	1.1	UC11
FEAT120: Security Roles The education module must be capable of displaying role-specific content.	1.1	UC12, UC11
FEAT121: Navigation The system must provide a means to navigate through various educational components with preconditions determining access to each component. For example, a response to a decision point question may determine access to additional educational components. Users must be able to navigate to previously viewed sections of material.	1.1	UC12, UC11, UC21, UC22, UC23, UC24, UC25
FEAT210: Bulk Add Family Members The system must provide a method for adding multiple family members at one time and uniquely identifying the family members for the patient without providing PII.	1.1	UC21, UC11, UC12
FEAT211: Add/Edit/Delete Family Members The system must provide a method for adding/editing/deleting single instances of family members once the initial family tree has been created.	1.1	UC21, UC11, UC12
FEAT212: Account for Duplicate Patient-Provided Identifiers The system must provide a method for allowing patients to add the same set of initials to more than one type of family member.	1.1	UC21, UC11, UC12
FEAT220: Update Family Cancer History Data The system will provide a method for updating the cancer history for each member of the family tree identified by the patient. Family members for whom no data are entered will be ignored during the calculation.	1.1	UC22, UC11, UC12
FEAT221: Generate Pedigree The system will generate a graphical pedigree representing the inputs collected during the Family Tree Building and Family Cancer History processes.	1.1	UC22, UC11, UC12
FEAT230: Provide Decision Point for Calculating BRCA Risk The system will provide a yes/no question to confirm that the patient wants to calculate her BRCA mutation risk probability. If "no" is selected, the system will collect an explanation.	1.1	UC23, UC11, UC12
FEAT231: Run BRCAPRO Algorithm The system will use the patient-provided data to run the BRCAPRO algorithm using the R statistical engine. The results will be displayed on the screen to the user in the form of "Increased Risk" and "NOT at Increased Risk" along with the date the algorithm was last run for the patient.	1.1	UC23, UC11, UC12

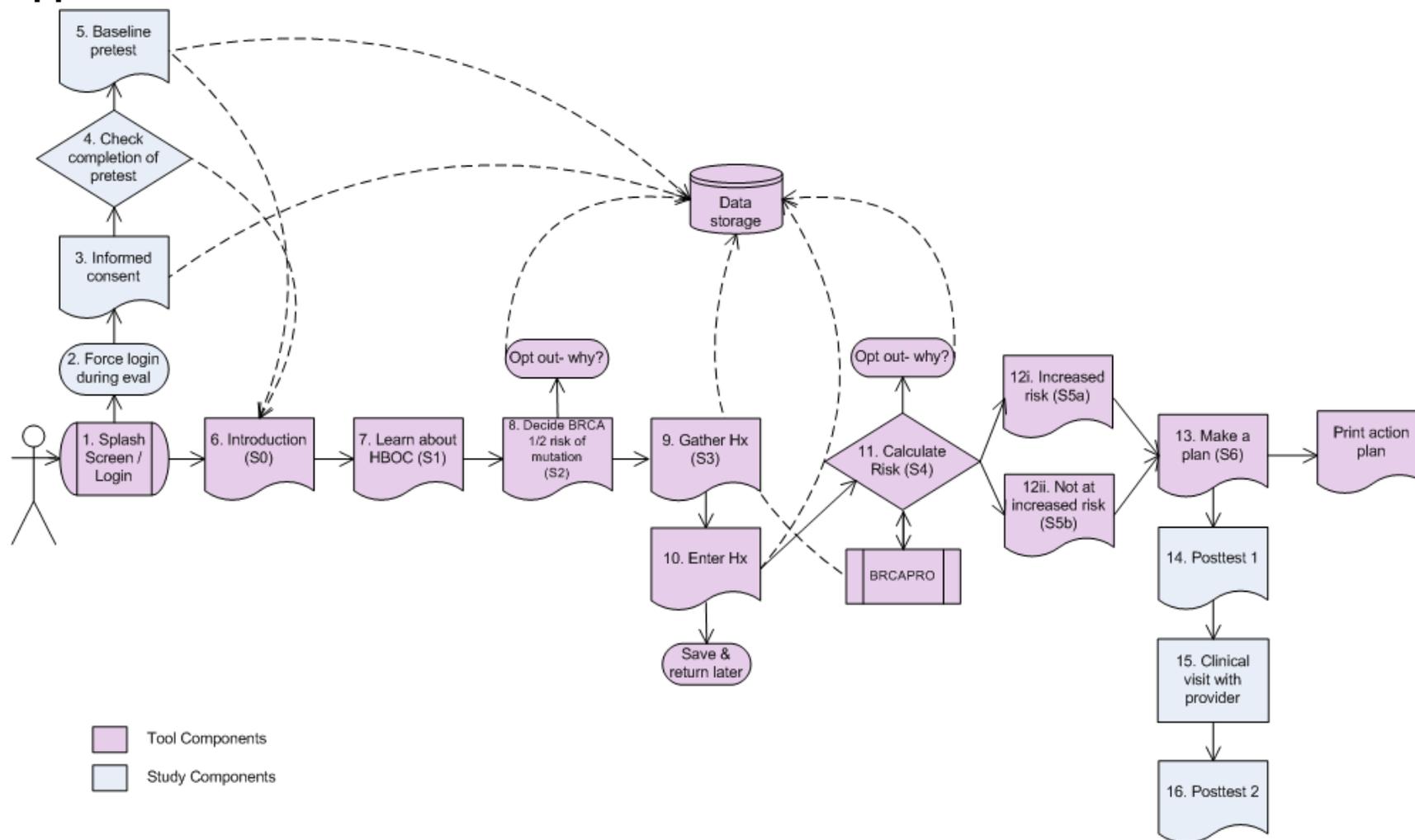
Effective Health Care Program Research Report Number 30

Requirements	Release Version	Trace to Design Spec
<p>FEAT240: Question List They system will allow a user to create a question list from predetermined lists of questions, based on her risk result. This question list will include open text boxes for each category to allow the user to type free-form questions to be included in the resulting question list. “Increased Risk” patients will have the following categories:</p> <ol style="list-style-type: none"> 1. Selecting questions to ask your doctor 2. Questions about genetic testing for BRCA1 or BRCA2 3. Questions about the test itself 4. Questions about the results 5. Questions about family implications 6. Questions about family history 7. Other questions <p>“NOT at Increased Risk” patients will have the following category:</p> <ol style="list-style-type: none"> 1. Selecting questions to ask your doctor 	1.1	UC24, UC11, UC12
<p>FEAT241: Report Output The system will dynamically generate a PDF report that includes the following:</p> <ol style="list-style-type: none"> 1. BRCAPRO Result of “Increased Risk” or “NOT at Increased Risk” 2. Family pedigree—graphical representation suitable for sharing with a genetic counselor 3. Family tree with cancer history in tabular format 4. Patient selected/provided questions from question list 	1.1	UC24, UC11, UC12
<p>FEAT310: View Patient List The system will display a patient list for providers and site coordinators immediately upon logging into the system. The patient list will be context aware and display only the patients for the user’s practice/site. The list displays the following for clinicians:</p> <ol style="list-style-type: none"> 1. User name (clickable link) 2. Patient ID 3. Appointment date/time 4. Provider name 5. Results as “Increased risk” or “Not at Increased Risk” 6. Risk results PDF (clickable link) <p>The list displays the following for site coordinators:</p> <ol style="list-style-type: none"> 1. User name 2. Patient ID 3. Appointment date/time 4. Provider name 5. Results date 6. Risk results PDF (clickable link) 7. Edit (clickable link) 	1.1	UC31, UC11

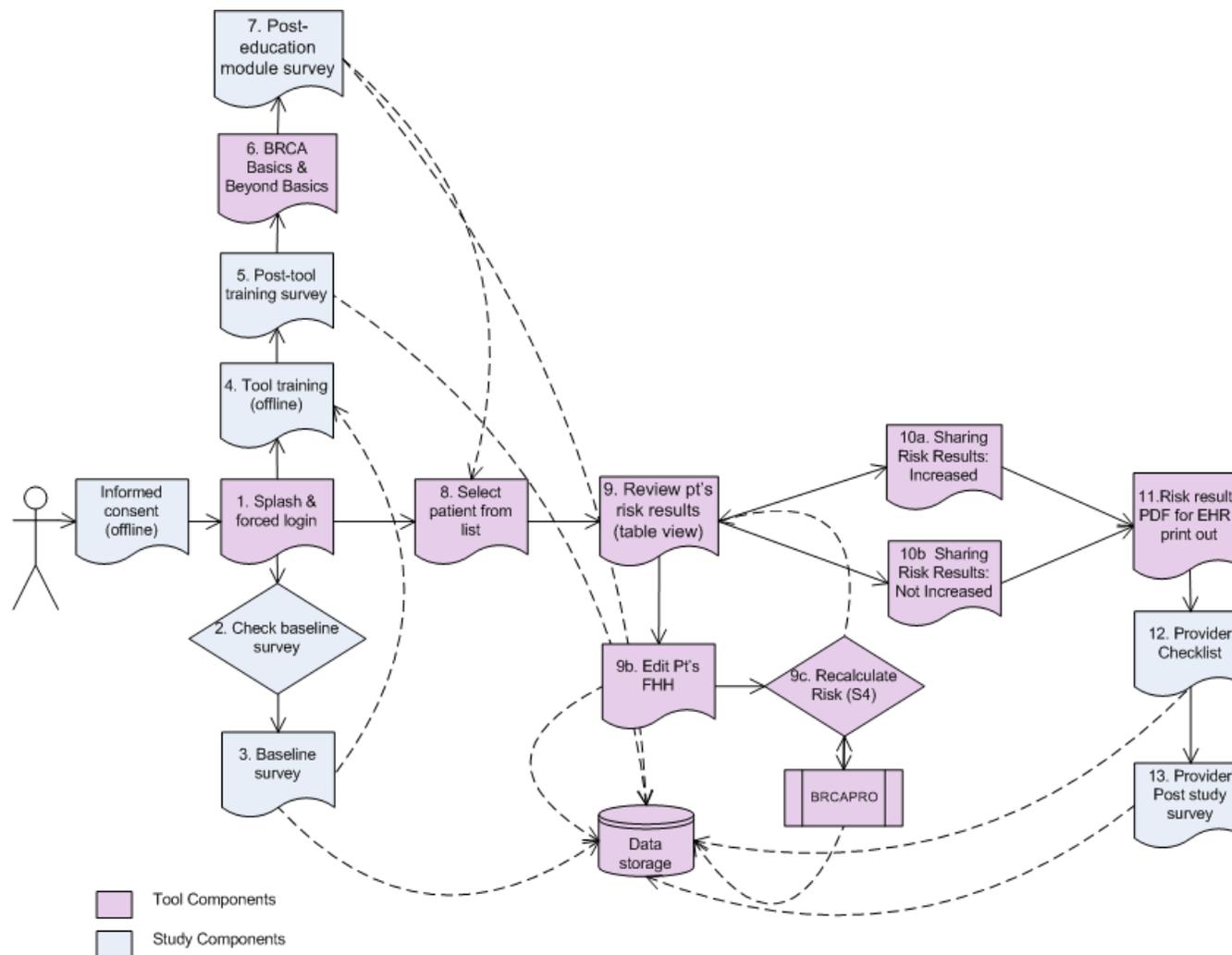
Effective Health Care Program Research Report Number 30

Requirements	Release Version	Trace to Design Spec
<p>FEAT311: Sorting The system will allow a user to sort the list in ascending or descending order by clicking on the following column headings:</p> <ol style="list-style-type: none"> 1. User name 2. Patient ID 3. Appointment date/time 4. Provider name 5. Results/results date 	1.1	UC31, UC11
<p>FEAT320: Clinician Results Report The system will display generate a PDF patient report for clinicians that includes</p> <ol style="list-style-type: none"> 1. User name 2. Risk result as “Increased Risk” or “Not at Increased Risk” 3. Mutation probability score as generated by BRCAPRO 4. Tips for talking with your patient (contextually related to risk result) 5. Family tree in tabular form with cancer history 6. Graphical pedigree with symbols relevant to cancer history 	1.1	UC32, UC11, UC31
<p>FEAT410: Run Tool as Patient The system will allow a clinician to select an individual patient from the patient list and have the patient interface display with notification that the clinician is running the patient tool as that patient. A link will be provided to allow the clinician to return to the Patient List. The clinician will be able to interact with the patient tool, just as the patient, to add/edit/delete family members, update cancer history, and run the BRCAPRO risk calculation.</p>	1.1	UC41, UC11, UC31, UC12, UC21, UC22, UC23
<p>FEAT510: Edit Patient List Information The system will allow a site coordinator to edit certain Patient List information for patients that are assigned to the site coordinator’s practice/site. The information that can be edited is as follows:</p> <ol style="list-style-type: none"> 1. Patient ID 2. Appointment date/time 3. Provider name 	1.1	UC51, UC11, UC31

Appendix B. Patient Web Tool Evaluation Workflow



Appendix C. Provider Web Tool Evaluation Workflow



Appendix D. Patient List

Patient List

Patients that have been assigned a Username from your site are listed below.

If you are a PROVIDER, you will see the patient's calculated BRCA risk probability once calculated by the patient. You may click on View Output for the PDF output of the patient's pedigree and results. Once you have completed the visit with the patient, click on the Checklist icon to record information about the patient interaction.

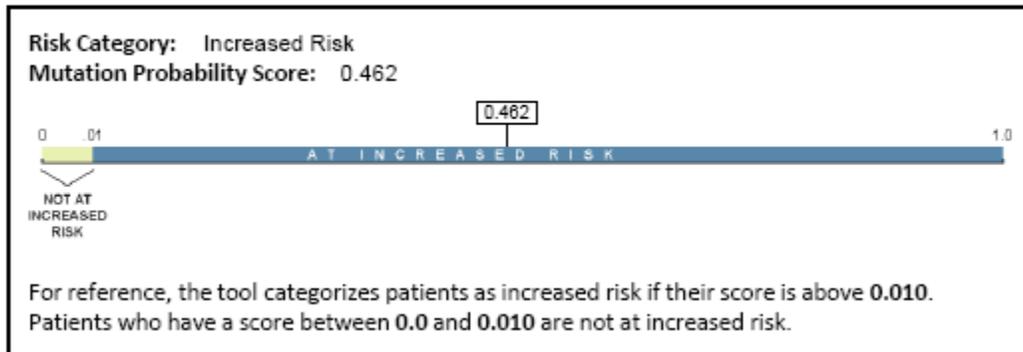
If you are a SITE ADMINISTRATOR, you will be able to see important dates of progression as the patient makes her way through the tool. You will also be able to EDIT information in this table to add the patient's appointment date as well as the patient's initials and year of birth to be used as a visual identifier for the provider.

Click here to view the [User Guide](#).

USERNAME	Patient ID	Appt Date/Time	Provider Name	Results	Risk Results PDF	Checklist	Checklist Date
DIGXE	RTI1	4/12/2010 12:00:00 AM	Dr A				
DVAYM	INC RISK	4/15/2010 2:00:00 PM	Dr. Smith	★ Increased Risk			
DTMZX	LOW RISK	4/15/2010 3:00:00 PM	Dr. Jones	★ Not at Increased Risk			
DHHVY							
DIJZT							
DXOVU							
DJWSH							
DXQOI							
DWQTO							
DGVCV							
DDHDG							
DGXVI							
DAUJZ							
DOOFZ							
DILSQ							
DSQBW							
DGLXX							
DJAQZ							

Appendix E. Patient Risk Results

Your Patient's Risk Result and Family History



Appendix F. Family History Summary

Username: DVAYM

Family History Summary – Data Supplied

Relationship to Patient	Initials	Gender	Age (now or at death)	Breast Cancer	Age at Diagnosis	Ovarian Cancer	Age at Diagnosis	Ovaries Removed	Age Ovaries Removed
Paternal Grandfather		Male	90						
Paternal Grandmother		Female	38	uni	37				
Maternal Grandfather		Male	77						
Maternal Grandmother		Female	83	uni	62				
Father		Male	65						
Mother		Female	60					Yes	45
You		Female	24						
Sister	CS	Female	30			Yes	28		
Brother	DS	Male	35						
Maternal Aunt	EA	Female	54						
Maternal Uncle	HA	Male	63						
Maternal Female Cousin	GA	Female	25						
Maternal Male Cousin	FA	Male	20						
Maternal Female Cousin	JA	Female	23						
Maternal Male Cousin	IA	Male	24						
Paternal Aunt	GS	Female	60					Yes	36
Paternal Uncle	JS	Male	63						
Paternal Female Cousin	IS	Female	42						
Paternal Male Cousin	HS	Male	40						
Paternal Female Cousin	LS	Female	30	uni	30				
Paternal Male Cousin	KS	Male	28						

Appendix G. Pedigree

Username: DVAYM

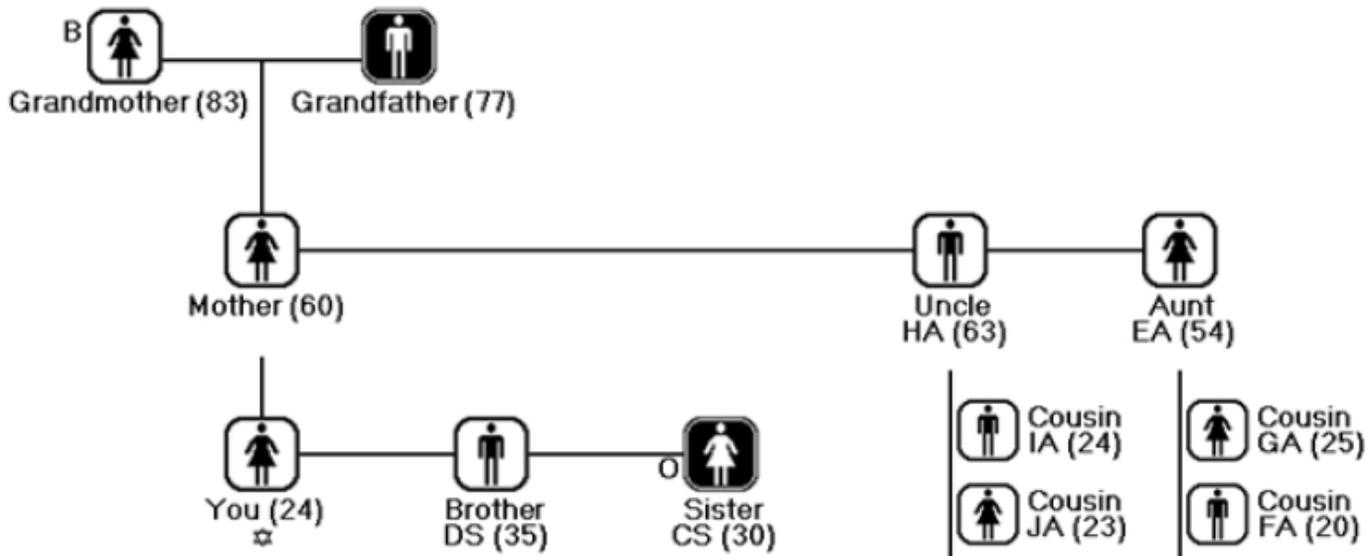
Mother's Side Family Tree

LEGEND

B = Unilateral Breast Cancer (1 breast)
B2 = Bilateral Breast Cancer (both breasts)
Ovarian Cancer

Gender: Male (M), Female (F)
Relationship: (age)

Other: Deceased (star), Half-Sibling (H), No Data Provided (N)



Appendix K. Risk Assessment and Accuracy Testing Results

Introduction

Cancer in the Family calculates the probability a person carries a BRCA1 or BRCA2 mutation using the BayesMendel software implementation of BRCAPRO with the permission of the developers. BRCAPRO is a statistical model originally developed at Duke University under the leadership of Don Berry and Giovanni Parmigiani. RTI chose this model and associated software because it was freely available and can be adapted to specific populations. The use of BayesMendel also allows for extension of *Cancer in the Family* in the future to other inherited cancer syndromes.

Cancer in the Family is designed to predict risk in women without breast cancer. A woman enters her family's history of breast cancer in the tool, which stores it in a database. When the woman clicks the Calculate button, the BayesMendel software calculates the probability that the woman carries a BRCA1 or BRCA2 mutation. The tool then compares the calculated probability to the high-risk cutoff value programmed in the tool (currently 0.01) and determines if she is high risk or low risk. Risk is classified in two levels to reflect the clinical options available: referral for genetic counseling and possibly testing, or routine care. The tool then displays the appropriate messages for her risk level and produces the appropriate reports for her and her physician. *Cancer in the Family* only uses the family history information. It does not collect or use information on breast cancer tumor characteristics.

Data Requirements

To calculate a risk score, BRCAPRO needs the following data for the individual for whom the risk is to be calculated: age, race, Jewish ancestry, history of breast or ovarian cancer, and whether the individual has had an oophorectomy. If the individual has had either type of cancer, BRCAPRO gathers the age of diagnosis and, if breast cancer, whether it was unilateral or bilateral. In addition, the BRCAPRO calculation needs cancer history for the following family members: parents, siblings, half-siblings, children, nieces and nephews, maternal grandparents, paternal grandparents, maternal aunts and uncles, paternal aunts and uncles, maternal cousins, and paternal cousins. For each individual, BRCAPRO collection information on whether they are living or dead; if living, current age (if deceased, age of death); and history of breast and/or ovarian cancer. If the family member has had breast cancer, BRCAPRO also collects the age of diagnosis and whether it was unilateral or bilateral breast cancer. If a relative has had ovarian cancer, BRCAPRO collects the age of diagnosis. BRCAPRO also incorporates whether female relatives have had an oophorectomy into the calculation.

Accuracy Testing: Plans and Methods for Testing

Original Plan

We originally planned to test the accuracy of the CDS tools and the clinical algorithms in two stages. For the first stage of testing, we planned to create a small sample ($n = 100$) of hypothetical cases for the CDS tool and assess how accurately the tool classified the cases. For the BRCA tools, we planned to classify the hypothetical cases by their expected risk of BRCA1 or BRCA2 mutations and their appropriateness for genetic testing. We then would enter the hypothetical case information into the tools and obtain risk estimates from the tool. We planned to determine the accuracy of the congruence between pretesting case assignment and tool recommendations using chi-square analysis. Based on evidence reports, we anticipated that a successful tool would classify 70 percent of cases accurately.

We planned to conduct a more extensive second stage of testing using approximately 1,000 existing cases from one or more of the following data sources: the Cancer Genetics Network, Breast Cancer and Colon Cancer Registry, Utah Population Database, and a previous study on BRCA gene mutations conducted by our Johns Hopkins consultant. (Chen, 2006 #102) . In addition to assessing the correlation between the tool risk calculation and recommendations, we also planned to assess how well the tool recommendations aligned with actual practice. The planned procedures for the second-stage testing were similar to that of the first stage of testing—classify the cases, enter the case into the CDS tools, and analyze congruence between pretesting case outcomes and tool recommendations.

Modifications to Accuracy Testing Plan

We identified several existing tools to identify women at high risk of BRCA1 and BRCA2 mutations, but no one tool was clearly best for use in a primary care population. After discussion with AHRQ, we decided to incorporate BRCAPRO into our CDS tools. Three considerations guided this decision: (1) The literature indicates that computer-based algorithms are better at identifying high-risk women than clinical guidelines (McClain, 2008; Palomaki, 2006). (2) BRCAPRO was developed in a U.S. population and would be expected to require less modification than risk algorithms developed in Europe. (3) One of the developers of BRCAPRO serves as a consultant to this project and is willing to modify the risk algorithm to maximize its performance in primary care.

We modified our accuracy testing plans because of our decision to incorporate BRCAPRO into the CDS tool and the data available to be used in testing. We identified two data sets for testing: the 2005 California Health Interview Survey (CHIS) and the Breast Cancer Family Registry (BCFR). The CHIS has data on the respondent's personal history of breast cancer and cancer family history and was used to estimate the proportion of the general population that would be classified as high risk for a specified risk cutoff. We used the BCFR, which has data on cancer family history and genetic test results, to determine how well BRCAPRO classifies families with respect to their BRCA1 or BRCA2 mutation status. After this testing was completed, we used hypothetical cases to ensure the CDS tool gave the same risk estimates as the stand-alone version of BRCAPRO, to examine risk estimates for specific types of family histories, and to examine the effect of updates to BRCAPRO.

Proportion Identified as High Risk

We estimated the proportion of women in primary care who would be identified at high risk of being mutation carriers with data from the 2005 CHIS, a population-based survey of the noninstitutionalized adult population of California. The 2005 CHIS included a detailed cancer family history module for respondents between 18 and 65. The module asked about the cancer history of the respondent and their first and second degree relatives, including type of cancer and whether the cancer was diagnosed before or after age 50. To calculate risks in BRCAPRO, we imputed the current age of family members as a function of the respondent's age. We imputed the age at cancer diagnosis for family members as a random number from a uniform distribution. If the cancer diagnosis occurred before age 50 years, we set the lower bound of the distribution at 25 and the upper bound at 50 or the family member's estimated age, whichever was lower. If the cancer diagnosis occurred after age 50, the lower bound of the distribution was 50, and the upper bound was the current estimated age or their age at death.

We estimated the probability of carrying a mutation in BRCA 1 or BRCA2 for each CHIS respondent. The risk estimation procedure results in a continuous distribution of probabilities between 0 and 1. We examined four potential values for the cutoff between "not high risk" and "high risk":

0.01, 0.02, 0.05, and 0.10. Although a cutoff of 0.10 has been used in the past, several TEP members felt this missed too many women with mutations. Therefore, we evaluated lower cutoffs as well. The ideal cutoff minimizes both false positive and false negative tests.

We calculated the percentage of the California population that would have been referred for genetic counseling using each cutoff. We also determined the percentage of the California population that would have been referred for genetic counseling using the U.S. Preventative Services Task Force (U.S. Preventive Services Task Force U.S. Preventive Services Task Force, #440) criteria for referral. We used kappa statistics to determine the agreement between the BRCAPRO and USPSTF identification of women as high risk.

Sensitivity and Specificity of BRCAPRO

We assessed the sensitivity of BRCAPRO in identifying people with a BRCA mutation as high risk, the proportion of people in the general population classified as high risk, and the proportion of BRCA families correctly classified by risk status. We initially planned to calculate an estimated risk for each family member. We limited the risk calculation to one member of each family because of the large number of families available (~7,000) and the limited resources of the project.

We used data from the BCFR, a set of registries of families with multiple cases of breast or ovarian cancer, to examine the sensitivity and specificity of BRCAPRO using different cutoffs. The BCFR data include extensive family histories and, when available, genetic test results for BRCA1 and BRCA2 mutations. We calculated the risk for the first listed member of each family (considered the consultant) using BRCAPRO. We then classified each consultant by their screening and genetic testing results and calculated the sensitivity and specificity. We conducted these analyses overall and by type of recruitment (population or clinic based), individual registry, sensitivity and specificity of the genetic test, and consultant age and race. The genetic testing sensitivity was defined as 90 percent if gene sequencing was done and as 60 to 70 percent if only screening for known or founder mutations was done. We excluded unclassified variants when calculating the presented sensitivity and specificity. Unclassified variants may or may not be deleterious. Since families with nondeleterious mutations would not have a high-risk family history, the sensitivity and specificity estimates for BRCAPRO could be biased if these cases were included. Sensitivity and specificity treating unclassified variants as positive or as negative test results are included in the appendix.

We had planned to compare the predictive value of BRCAPRO at each cutoff using sensitivity and specificity classification tables, the generalized *R*-squared statistic, and a receiver operating characteristic (ROC) chart. After calculating the proportion of the population expected to be at high risk, the range of potential cutoff values was limited to between 1 percent and 10 percent. Given the narrow range of potential values, classification tables provided sufficient information for our purposes.

Agreement between CDS Tool and BRCAPRO

We constructed 100 hypothetical families for testing the CDS tool (Table 1). Each family consisted of a female consultant and the following family members: mother, father, maternal and paternal grandparents, sister, brother, son, daughter, maternal aunt and uncle, and paternal aunt and uncle. Cancer histories and ages were varied to reflect a range of expected risk levels. In addition to these cases, other cases were constructed to test specific aspects of the tool or estimation as needed.

Table 1. Summary of hypothetical data expected and actual risk classification

Target risk (range)	Characteristics	Families #	Distribution of risks			
			VL	A	M	HR
Original cases						
Very low (<0.0001)	≤ 2 breast cancer cases; no diagnosis ≤ age 60	12	3	2	6	1
Average (0.001–0.0001)	2–4 cases of breast or ovarian cancer; no diagnosis before age 40; ≤ 1 diagnosis before age 60	15	0	7	6	2
Moderate risk (0.01–0.001)	Multiple family members with breast cancer, or male breast cancer but not female breast cancer	30	0	3	12	15
High risk (>0.01)	At least one USPSTF criteria for referral.	43	0	2	7	34

Note: VL = Very low, A = Average, M = Moderate, and HR = High risk

Results of Accuracy Testing

Burden—How Many High-Risk People Are There?

Based on a 0.01 cutoff, 1.1 percent of the population was classified as high risk of being a mutation carrier (Table 2). Using a cutoff of 0.10, 0.3 percent of respondents were classified as high risk. In contrast, the USPSTF guidelines classified 3.0 percent of the California population as high risk. BRCAPRO classification agreed with the USPSTF guidelines most often when the cutoff was 0.01. These results suggest that USPSTF guidelines classify too many people as at high risk of being a mutation carrier. One reason that USPSTF guidelines overclassify people as high risk is that BRCAPRO adjusts a respondent’s risk for years lived cancer free, while the USPSTF guidelines do not (Figure 1).

Table 2. Referral for genetic counseling in general population age 18–65 at various cutpoints based on risk calculated from BRCAPRO and USPSTF Guidelines. California Health Interview Survey Data, 2005

USPSTF Guidelines BRCAPRO screening cutpoint	Percentage of population referred 3%	Agreement of risk classification between USPSTF and BRCAPRO kappa statistic (95% C.I.)
1%	1.1%	0.39 (0.35, 0.42)
2%	0.7%	0.30 (0.27, 0.36)
5%	0.4%	0.21 (0.18, 0.24)
10%	0.3%	0.15 (0.12, 0.18)

The prevalence of BRCA1 and BRCA2 mutations differ by ancestry. The most striking difference is the tenfold increase in prevalence among people with Ashkenazi Jewish ancestry compared to non-Jewish Caucasians (Rubinstein, 2004). The mutation prevalence is lower among those with Asian ancestry (John, 2007), which is reflected in the smaller proportion of Asian-Americans classified as high risk by either BRCAPRO or the USPSTF guidelines (Figure 2).

The CHIS data are unique in providing detailed cancer family history data on a large defined population, but the data do have some limitations. The data do not include exact age of family members at the time of the survey or their age at diagnosis. Because the risk of cancer increases with

age, the procedure we used for imputing this information (described above) underestimates age at cancer diagnosis on average. Since younger age at diagnosis is associated with an increased risk of having a BRCA mutation, we may have slightly overestimated the probability of carrying a BRCA mutation.

Figure 1. Percentage high risk at selected cut points, by race

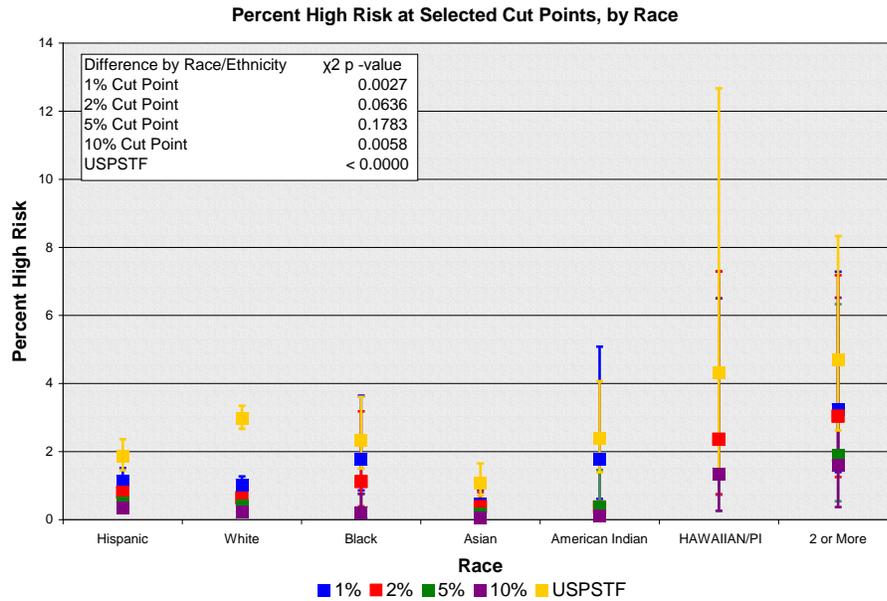
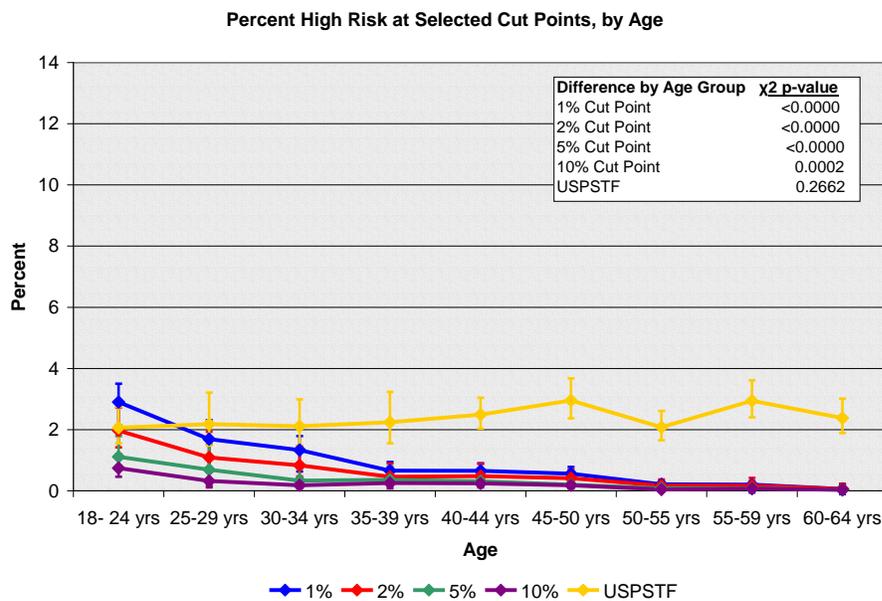


Figure 2. Percentage high risk at selected cut points, by age



Sensitivity and Specificity of BRCAPRO. The mutation prevalence among families with genetic testing enrolled in the two population-based North American sites was 20 percent, including unclassified variants and 8 percent excluding unclassified variants (Table 3). Among families who had gene sequencing for both BRCA1 and BRCA2, sensitivity ranged from 84 percent using a 0.10 cutoff to 96 percent using a 0.01 cutoff. Specificity ranged from 30 percent using a 0.01 cutoff to 80 percent using a 0.10 cutoff. No discernable pattern was found in the sensitivity and specificity when examined by consultant age. The specificity among black and white consultants was similar (Table 4). The sensitivity appeared somewhat higher among black consultants, but many fewer black consultants were tested. Differences in the mutation prevalence were apparent, however. Black consultants had a much larger proportion of unclassified variants than white women, which is consistent with the published literature (Haffty, 2006).

The BCFR data allowed us to compare the estimated risks with the actual genetic test results, but the data do have some limitations. Recruitment criteria differed by site. Some sites selected eligible woman from all breast cancer cases within the recruitment area, while others recruited families from high-risk cancer genetics clinics. Even the population-based sites used eligibility criteria that selected women with characteristics associated with an increased likelihood of carrying a BRCA1 or BRCA2 mutation. These populations have higher mutation prevalence than would be expected in primary care and may have more highly penetrant mutations. The sensitivity and specificity of BRCAPRO may be lower in a primary care population.

Another limitation was the variability in the thoroughness of the mutation testing. Not all families had full sequencing of both BRCA1 and BRCA2. Some were tested for Ashkenazi Jewish founder mutations, and others were tested for mutations in only one gene. Obviously, the sensitivity of the mutation testing affects the calculated sensitivity and specificity of BRCAPRO. When possible, we limited the analysis to families with full sequencing of both genes, but this substantially reduced the sample size of the analysis.

Table 3. Sensitivity and specificity of BRCA^{PRO} screening by sensitivity of mutation identification among families enrolled in North American sites with population-based recruiting. Breast cancer family registry data

Genetic testing sensitivity	Total	Mutation prevalence		Risk determination ^a	High risk			Low risk			Sensitivity ^b	Specificity ^c
		All	Without unclassified		1 Unclassified mutation	2 Deleterious mutation	3 No mutation	4 Unclassified mutation	5 Deleterious mutation	6 No mutation		
All	3427	0.199	0.081	0.01	209	271	1858	193	8	417	0.971	0.183
				0.02	145	264	1427	257	15	1301	0.946	0.477
				0.05	72	243	889	330	36	1857	0.871	0.676
				0.10	44	230	576	358	49	2170	0.824	0.790
				NCI	156	230	1700	247	60	1131	0.793	0.400
90%	588	0.197	0.087	0.01	43	49	331	22	2	141	0.961	0.299
				0.02	32	49	253	33	2	219	0.961	0.464
				0.05	13	45	146	52	6	326	0.882	0.691
				0.10	7	43	93	58	8	379	0.843	0.803

^a Risk determination is either the cutoff level for high risk used in BRCA^{PRO} (first four rows) or the family history criteria recommended by the National Cancer Institute and the U.S. Preventative Services Task Force.

^b Sensitivity = Column 2 / (Column 2 + Column 5)

^c Specificity = Column 6 / (Column 3 + Column 6)

Table 4. Sensitivity and specificity of BRCA^{PRO} Screening with any sensitivity of mutation identification, by race. Breast cancer family registry data

Genetic testing sensitivity	Mutation prevalence				High risk			Low risk			Sensitivity ^b	Specificity ^c
	Total	All	Without unclassified	Risk determination ^a	1	2	3	4	5	6		
					Unclassified mutation	Deleterious mutation	No mutation	Unclassified mutation	Deleterious mutation	No mutation		
White	1461	0.113	0.076	1%	28	93	483	26	18	813	0.838	0.627
				2%	17	86	313	37	25	983	0.775	0.758
				5%	12	79	199	42	32	1097	0.712	0.846
				10%	8	76	122	46	35	1174	0.685	0.906
Black	75	0.320	0.027	1%	11	2	20	11	0	31	1.000	0.608
				2%	7	2	15	15	0	36	1.000	0.706
				5%	6	2	8	16	0	43	1.000	0.843
				10%	4	2	5	18	0	46	1.000	0.902

^a Risk determination is the cutoff level for high risk.

^b Sensitivity = Column 2 / (Column 2 + Column 5)

^c Specificity = Column 6 / (Column 3 + Column 6)

BRCAPRO could not calculate a risk for 1.9 percent (140/7,200) of the families because there were multiple connections between the maternal and paternal family lines. The current version of our tool is focused on parent and child relationships and does not collect marriage information. This strategy avoids the problem with multiple matings between separate familial lines and reduces the identifiability of the family history data. For some families, however, it excludes relevant information that could affect the patient’s mutation risk.

Comparison with USPSTF Guidelines. BRCAPRO is clearly a better screening method than the USPSTF guidelines. As discussed above, the USPSTF guidelines classify approximately 3 times more people as high risk than BRCAPRO does at the lowest considered cutoff (0.01) (Table 5). At the same time, the sensitivity of the guidelines was lower than that of BRCAPRO at the highest risk cutoff (0.10), 0.793 vs. 0.824, respectively. The specificity of the USPSTF guidelines, 0.400, was also lower than that of BRCAPRO at all but the lowest cutoff value. With a 0.01 cutoff, BRCAPRO had a specificity of 0.183, lower than that of the USPSTF guidelines, but with a cutoff of 0.02, the specificity of BRCAPRO was higher than that of the guidelines, 0.477.

Table 5. Hypothetical high-risk families discrepant between USPSTF Preventative Services Guidelines and BRCAPRO risk estimate

High-risk family history characteristic	Estimated risk
1 male case breast cancer at < 60 years old	0.0006
1 male case of breast cancer at age < 60	0.0014
1 male case of breast cancer at age < 60	0.0084
Ashkenazi Jewish. 1 case at < 40 years	0.0010
Ashkenazi Jewish. 1 case at < 40 years, no other cases in family	0.0047
Ashkenazi Jewish. >1 case diagnosed ages 40 - 60	0.0059
≥ 1 case with both breast and ovarian cancer	0.0041
≥2 cases breast cancer at < 50 years on the same side of the family	0.0044
≥2 cases breast cancer at < 50 years on the same side of the family	0.0053

Of 43 hypothetical families that met the USPSTF high-risk criteria, for only 10 was their BRCAPRO estimated risk greater than or equal to 0.10, and 9 families had a BRCAPRO calculated risk below 0.01 (Table 1 and Table 5). One-third of the hypothetical families with multiple family members with breast or ovarian cancer that did not meet the USPSTF criteria had a calculated risk above 0.10 and one-half had a risk above 0.01. The high-risk family histories and the calculated risk for the 9 families that met the USPSTF criteria for referral that were not identified as high risk by BRCAPRO are shown in Table 5. The estimated risk for a case of male breast cancer in the family was approximately 10 times higher than the risk associated with a female case with the same characteristics (data not shown). Four cases of contralateral breast cancer also initially had lower than expected risks. Further investigation revealed this was caused by incorrect data entry.

Agreement between Cancer in the Family and External BRCAPRO Run in SAS. We compared the risk estimates for the 100 hypothetical families from our *Cancer in the Family* tool with those from BRCAPRO to ensure the results were the same. We also manually entered the family history for 20 families into the tool interface. We developed six additional cases to test the effect of race following a BRCAPRO upgrade that included race-specific prevalence estimates. Following

iterative testing and correction of errors, the estimates from the CDS tools and from BRCAPRO agreed to at least the fourth decimal place.

Definition of High Risk. In our preliminary testing and evaluation of the tool, we used a high-risk cutoff value of 0.01. This value has a very high sensitivity, 0.97, but has a low specificity, 0.18. Based on the results of the analyses discussed above, we should consider using a risk cutoff value of 0.02. This value results in a slightly lower sensitivity, 0.95, but much better specificity, 0.48. At this level, approximately 1 in 143 primary care patients would be referred for genetic counseling.

Further evaluation of the performance of this tool in primary care is needed. We need a sample of primary care patients to complete the tool and have genetic testing to determine how accurately the tool classifies primary care patients by their risk status.

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Appendix L. Cognitive Testing of Instruments Report

BRCA Cognitive Testing Summary

Round 2: Patient Surveys

July 14, 2009

Claudia Squire, Doug Rupert, and Susana Peinado

Participant Demographics

Table 1 provides the participant demographic information for the seven participants completing an interview in round 2. Participants were recruited by a professional recruiting company in Raleigh, North Carolina.

Table 1. Participant Demographics for Round 2—Patient Survey Testing

	Age	Education	Race	Breast or Ovarian Family Cancer History	Diagnosed with Cancer
Participant 1	54	HS	White	Breast cancer	No
Participant 2	50	College	White	Ovarian cancer	No
Participant 3	39	Some college	White	Breast cancer	No
Participant 4	29	College	White	Breast cancer	No
Participant 5	59	Some college	White	Breast cancer	No
Participant 6	58	High school	White	Breast cancer	No
Participant 7	40	High school	Hispanic	Neither	No

General Comments:

- Participants liked the 5-point answer scales and thought there was a meaningful difference between the response options. One participant described the scale as being broken down into 20 percent chunks (i.e., 1 = 0–20 percent, 2 = 21–40 percent, etc.), which helped her select the best answer choice. Two other participants used words to describe the numbers (i.e., 2 = somewhat comfortable, 3 = neutral, 4 = comfortable). A third participant wasn't able to describe what the different points meant, but was able to use the scale appropriately.
- Women had no difficulty understanding the concept of family cancer history.

Baseline Survey:

- Question 5 – One participant was confused by this question. She had to read the question more than once before realizing that she could check two answers.
- *Recommendation: If space is not an issue, consider asking about breast and ovarian cancer separately. It is generally preferable to avoid double-barreled questions.*
- Question 6 – This question was repetitive to the two participants who had indicated in Q5 that they didn't have any friends or family who had breast or ovarian cancer.
- *Recommendation: Consider a skip pattern so only respondents who have a friend/family member with breast/ovarian cancer are asked this question.*
- Question 8 – Two out of three participants said that it would be easy to gather their family's cancer history from some relatives, but harder to get it from other relatives. However, they were both able to choose an answer category that accurately reflected their situation. The third participant said it would be very easy for her because she would only need to talk with one person who would provide the information on the rest of the family. One participant said her answer to this question could change completely if her mother died because then she would lose all contact with that side of the family, but currently it was easy. The other participant perceived this scale to be "flipped." It was not what she expected. She expected a scale that went from Very easy to Very difficult. She said this confused her because when the scales are all uniform, she can breeze through a questionnaire, but when they are not she has to stop or she may accidentally answer incorrectly.
- Questions 9 & 10 – One participant perceived these questions to be linked, like a two-part version of the same question.
- Question 11 – One participant had had a hysterectomy and, consequently, felt the likelihood of developing ovarian cancer was "impossible." She didn't feel like the existing answer choices (5-point scale + "Don't Know") were sufficient. This was also an issue for one of the participants that I interviewed. When answering Q10, she also pointed out that her sister has had her breasts removed due to a strong family history of breast cancer, and therefore, couldn't get breast cancer. This is likely much more rare than women who have had hysterectomies. One participant wanted to select "Don't know," which actually is an option on the interviewer version of the survey, but apparently has been removed from the participant version.
- *Recommendation: Since hysterectomies aren't uncommon among our target population, we may want to address this issue via a skip pattern or other approach.*
- Question 13 - "Don't know" has been removed as an option from the participant version of the survey.
- Question 15 – The participant who had a hysterectomy suggested asking about breast and ovarian cancer separately. However, she was able to choose an answer category that she felt accurately reflected her feelings, so unless this was an issue with other participants, it doesn't seem necessary. Also of interest, after reading the summary document about the tool, this participant asked several questions about how the tool would work for someone like her who couldn't get ovarian cancer. One participant said she did not know the statistics necessary to answer this question, so she selected 3 because to her that meant there was a 50/50 chance. The other participant wanted a "Don't know" response option for this question, but she decided to

choose 1 because she was being optimistic about her sister-in-law, who has Stage 4 breast cancer.

- Genes and Cancer Section (Q 17-27) – Neither participant was knowledgeable about BRCA mutations, so neither knew the answers to Q 17-27. However, the women dealt with this differently. One woman chose to guess on the questions (i.e., “I don’t know, but I’ll guess ‘True’ ”); the other woman felt compelled to select Don’t Know. Of the three participants, none were familiar with BRCA mutations. Participants answered Don’t Know for many questions, but were able to answer other questions in this series based on knowledge (Who can get breast cancer?) or inference (A woman who has a BRCA1 or BRCA2 gene mutation is at greater risk for breast and/or ovarian cancer). Findings were the same with the final two participants. Neither was familiar with or knowledgeable about BRCA mutations. One said she felt guilty if she couldn’t provide an answer, so she tried to guess rather than selecting “Don’t know.”
- *Recommendation: This may or may not be an issue, depending on our analysis plan. We may want to regroup and think about how we wish to conceptualize “Don’t know” responses during analysis. If we consider “don’t know” and incorrect answer choices as the same thing, then I think we’re okay. However, if we consider “don’t know” as somewhere between a right answer and a wrong answer, then this may cause problems in our analysis.*
- *Recommendation: We also might want to consider providing a simple and brief definition of a BRCA mutation. (For example: “One type of gene mutation is called BRCA. BRCA mutations can cause hereditary breast or ovarian cancer.”) Because it’s very unlikely that any participant will know what a BRCA mutation is prior to using the tool, we might artificially depress the baseline knowledge scores if we don’t provide some explanation. Whatever text we add to explain mutations needs to be accurate, and should be run by Nedra. I would change the example to something like this, but an expert is a better person to edit this: “Everyone has BRCA1 and BRCA2 genes. However, some people can have mutations in their BRCA1 and BRCA2 genes, which are passed down in their family and can cause breast and ovarian cancer.”*
- Question 18 – This question asks whether breast cancer is MUCH more common than ovarian cancer. While this didn’t come up in any of my interviews, it seems like there could be confusion over “much.” For example, how is “much” defined.
- *Recommendation: Consider dropping “much” and ask whether breast cancer is more common than ovarian cancer.*
- Question 24 – One participant may have missed the subtle difference between “all of your relatives” and “only blood relatives.” Perhaps if the option read: all of your relatives (including relatives related to you by adoption or through marriage), then she would be more likely to select “only blood relatives.”
- Question 30 – This question states there is no REAL reason to get any type of genetic test. Is it necessary to say “real”?
- *Recommendation: Consider dropping “real” from the sentence.*
- Question 33 – Participants had a little difficulty understanding the connection between this question and a BRCA mutation. One participant said it would be easy to handle learning she had a greater chance of getting cancer. But when asked how easy or difficult it would be to learn she had a gene mutation, the participant said “Ah, that might be more difficult.”

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- Question 35 – Women had trouble answering this question. They felt it was very likely their doctor’s office would share the genetic test result with their health insurance company. However, they weren’t sure whether to conceptualize this as a violation of privacy.
- Question 36 – Participants weren’t sure whether this question asked about health insurance coverage of (a) the genetic test or (b) cancer treatment.
- Talking with Your Doctor Section (Q 37-43) – There were a few issues with this section:
 - Both participants seemed unable to make meaningful distinctions between the individual questions. If they were confident in their ability to ask or share one thing (e.g., chance of getting cancer), they were just as confident in their ability to do everything else (e.g., ask about GT, ask for explanation, etc.). This might be legitimate, but I got the sense that they answering about their interpersonal skills in general—rather than their ability to raise a particular topic with their physician. While the participants that I interviewed responded differently to these questions based on their ease with the topic, one had difficulty with the concept of how “confident” she was. When probed about changing the question to “how comfortable” they were, all three preferred that term. The findings were the same with the final two interviews. Although participants read each question out loud, little distinction was made between the questions. Both participants said they had no problem talking with their doctor and asking questions.
 - *Recommendation: We might avoid this issue by asking how “comfortable” people are doing X, rather than how “confident they are in their ability” to do X. Would rephrasing the question that way still result in a measure of self-efficacy, which is I believe what we’re trying to measure with these questions? But, I wonder how many participants will be less than confident and whether this measure will be changed at all by using the tool.*
 - Q42 – One participant referenced her willingness to follow her doctor’s advice, rather than her ability to do so.
 - Both participants seemed to view these questions as having either/or answer choices. They were either confident or not; they avoided using the answer scales.
- Talking with your doctor section – Two participants had difficulty with this series because the doctors they say most often weren’t primary physicians or OB/GYNs (one was an orthopedist and one was an allergy doc). Both felt like these topics were more appropriate for OB/GYNs.
- Q40 and Q41 – One participant was confused by these two questions: “Who is sharing the opinion?”
- *Recommendation: It seemed like this participant had forgotten the stem question (which was on the other page. If the questions in this section are broken up, it would be good to include the stem at the top of the second page.*
- Question 52 – Add “Check all that apply” because someone could do more than one.

Post-test #1 Survey:

- Question 8 – One respondent suggested asking about “your decision” as opposed to “the decision.”

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- Question 14 – One respondent had trouble answering this question. She said it would be easy to ask some relatives, but harder to ask others. She was able to choose an answer that averaged the two.
- Question 15 – Consider dropping “in your opinion” since it is not used in other questions.
- Question 18 – One participant wasn’t sure if the question was asking about how difficult the process was or how difficult it was emotionally to enter their family history.
- Question 29 – Women may not always answer this question like the others because, while they would take their doctor’s opinion and advice into account, they may feel the need to make decisions themselves.

Post-test #2 Survey:

- Question 16 – How will this question work? Will the scales for each item be generated by the program?
- Question 18 – Add an open-ended response? (Other: _____)

Appendix M. Study Protocol and Surveys

Overview of Patient Evaluation

The patient evaluation consists of the following:

1. a pretest prior to the use of the *Cancer in the Family* tool
2. a posttest after using the *Cancer in the Family* tool at home and prior to their appointment with their provider
3. a posttest after completing their appointment with their provider

Patients received a \$10 gift card to Amazon.com (delivered electronically) for completing each of the three surveys and a \$25 gift card from the sites after completing their appointment with their provider.

Patient recruitment. Recruitment was handled by a study site coordinator at each of the three study sites. Women who were eligible to participate in the evaluation

- had a well-women appointment scheduled with a provider who was participating in the study within the field period (April 19 to June 11, 2010),
- were between the ages of 21 and 60,
- were fluent in English,
- had no personal cancer history, and
- had residential access to a computer and the Internet.

Site coordinators were encouraged to review potential participants' cancer history in the EMR to avoid making recruitment calls to patients who had a documented history of cancer.

Recruitment of potential participants was to take place approximately 1 month prior to a patient's schedule appointment to give study participants enough time to complete the surveys, use the tool, gather and enter their cancer family history, and calculate their risk.

Recruitment tracking database. Sites managed their recruitment efforts through a database that contained fields for each patient's name, phone number, mailing address, and other contact information. Sites documented each call attempt and its outcome in the database. As site coordinators reached potential participants, they documented whether patients were interested in the study and whether they met the eligibility criteria. If an individual was ineligible or declined, sites documented the reason for ineligibility or refusal. Site coordinators made at least four attempts to reach a potential participant before deeming the patient "unable to be reached."

Introducing the study to potential participants. Site coordinators contacted participants by phone and explained the background of the study, its purpose and requirements, and asked the participants several questions to verify eligibility. Once a participant verbally agreed over the phone to participate, sites mailed a preprinted patient enrollment packet containing a welcome letter, a "How-To" instruction sheet on getting started with the tool, a flowchart depicting the patient's steps through the study (see Figure M-1), and a consent form explaining the purpose of the study and the patient's responsibilities. Patients' responsibilities and suggested dates for completing each task can be found in Table M-1.

Figure M-1. Cancer in the Family patient flowchart

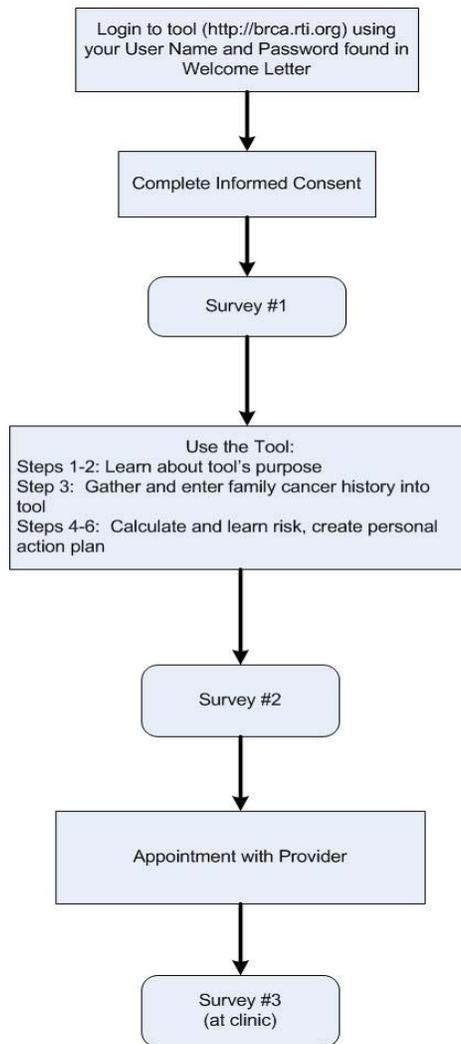


Table M-1. Patient responsibilities listed in the patient welcome letter

Responsibility	Suggested Date for Completion
Log into tool. Complete informed consent and survey #1.	Within 2–3 days of receiving packet
Learn about tool's purpose (Steps 1–2).	Within 5 days of receiving packet
Collect and enter family cancer history into tool (Step 3).	Within 7–10 days of receiving packet
Calculate and learn risk. Create your personal action plan (Steps 4–6). Complete survey #2.	3–5 days before appointment
Attend your clinic appointment. Complete survey #3 (right after appointment).	Day of appointment

Patients' use of cancer in the family and surveys. After receiving the welcome packet, patients were encouraged to log on to the tool using their username and password, which were included in the welcome letter. After logging on, the online informed consent form was displayed. Patients completed the consent form online and then were directed to the online pretest survey. After completing the pretest, participants were instructed to go through Steps 1 and 2 of the tool. In Step 3, patients could decide if they wanted to gather and record their family's cancer history. The welcome letter instructed them to complete this task within 7 to 10 days of receiving the packet and prior to their appointment with their provider.

After participants entered in their family structure, the *Cancer in the Family* tool produced a worksheet that participants could use to record their cancer family history as they talked to their relatives. After entering in their cancer family history data, participants were asked whether they wanted to calculate their risk of having a BRCA mutation. For those who chose to learn their risk, the *Cancer in the Family* tool calculated and presented their risk to them and also provided additional explanation of their risk result (either increased risk or not at increased risk). In Step 6, the tool helped participants select questions they wanted to ask their provider. These questions, plus their risk result, were assembled into a pdf document that participants were encouraged to save, print, and bring to their appointment with their provider to discuss. The posttest 1 survey was activated 1 week prior to participants' scheduled appointment with their provider.

Patients attended their scheduled appointment with their providers and were asked to complete posttest 2 on a computer at the clinic site prior to their departure. If patients did not have time to complete the posttest 2 survey, they were allowed to complete it at home. Site coordinators tracked completion rates and called those participants who did not complete their survey.

Monitoring patients' progress through the study. Site coordinators had a tool that allowed them to check whether participants had logged onto *Cancer in the Family*, completed the consent, completed each of the three surveys, and calculated their risk. If patients were not progressing through these steps in the scheduled time period, site coordinators called to encourage them to complete their surveys and use the tool. Coordinators also called to remind patients of their scheduled appointment with the provider.

Site coordinators made the first follow-up call several days after the enrollment packets were mailed to ensure patients received the packet and were able to log onto the tool. If the patient has not logged onto the tool, the site coordinator encouraged patients to begin using the tool because it can take several weeks to collect a family's history of cancer.

To ensure that providers knew when a study patient was coming in for an appointment, site coordinator flagged the patient's medical record. On the day of the appointment, the site coordinator printed the patient's risk result summary for the provider.

RTI and site coordinators also conducted weekly calls in which problems or issues with patient compliance were discussed.

Overview of Provider Evaluation

The provider evaluation consists of the following:

1. a pretest prior to the use of the *Cancer in the Family* tool
2. a posttest after providers received training on the study protocol and the *Cancer in the Family* tool
3. a posttest after providers had an opportunity to explore the tool for about a week
4. a poststudy survey at the conclusion of the field test

In addition, providers were asked to complete a postencounter checklist for each study participant to document the findings of the risk assessment and whether they referred the patient for genetic counseling. Providers received a \$25 gift card to Amazon.com for completing each of the four surveys.

Introducing the study to providers. Similar to the patient enrollment packets, providers received a packet containing a welcome letter, a flyer describing the study, a “How-To” instruction sheet on getting started with the tool, a flowchart depicting the provider’s steps throughout the study (see Figure M-2), and a consent form (two copies) explaining the purpose of the study and the provider’s responsibilities. Site coordinators were responsible for ensuring providers signed a hard copy of the consent form.

To ensure there was no duplication of usernames and passwords, site coordinators used the same process for assigning passwords to providers as they did for the patients. Unique usernames and passwords were created for providers and preprinted on the welcome letter. When sites enrolled a provider, they hand wrote the provider’s name on the welcome letter and recorded the provider’s name with their username in the secure database.

Surveys. After signing the consent form, providers completed a baseline survey that gathered information on their knowledge, attitudes, and opinions about BRCA screening and decision aids. After completing the baseline survey, providers participated in a training led by an RTI staff member that covered the purpose of the study, the information generated by the tool, and advantages to using the tool. The training also described how to use the tool from the perspective of the provider, the patient, and the site coordinator. Providers then completed the posttraining survey, which measured providers’ opinions about the tool after they had learned about it and asked for feedback on the training.

Providers were given 1 week to review the educational content on the tool and begin familiarizing themselves with the tool. After providers reviewed the tool, they completed a third survey that assessed their knowledge of BRCA mutations and opinions about clinical decision support tools. The provider’s final step in the study process was to complete the poststudy survey.

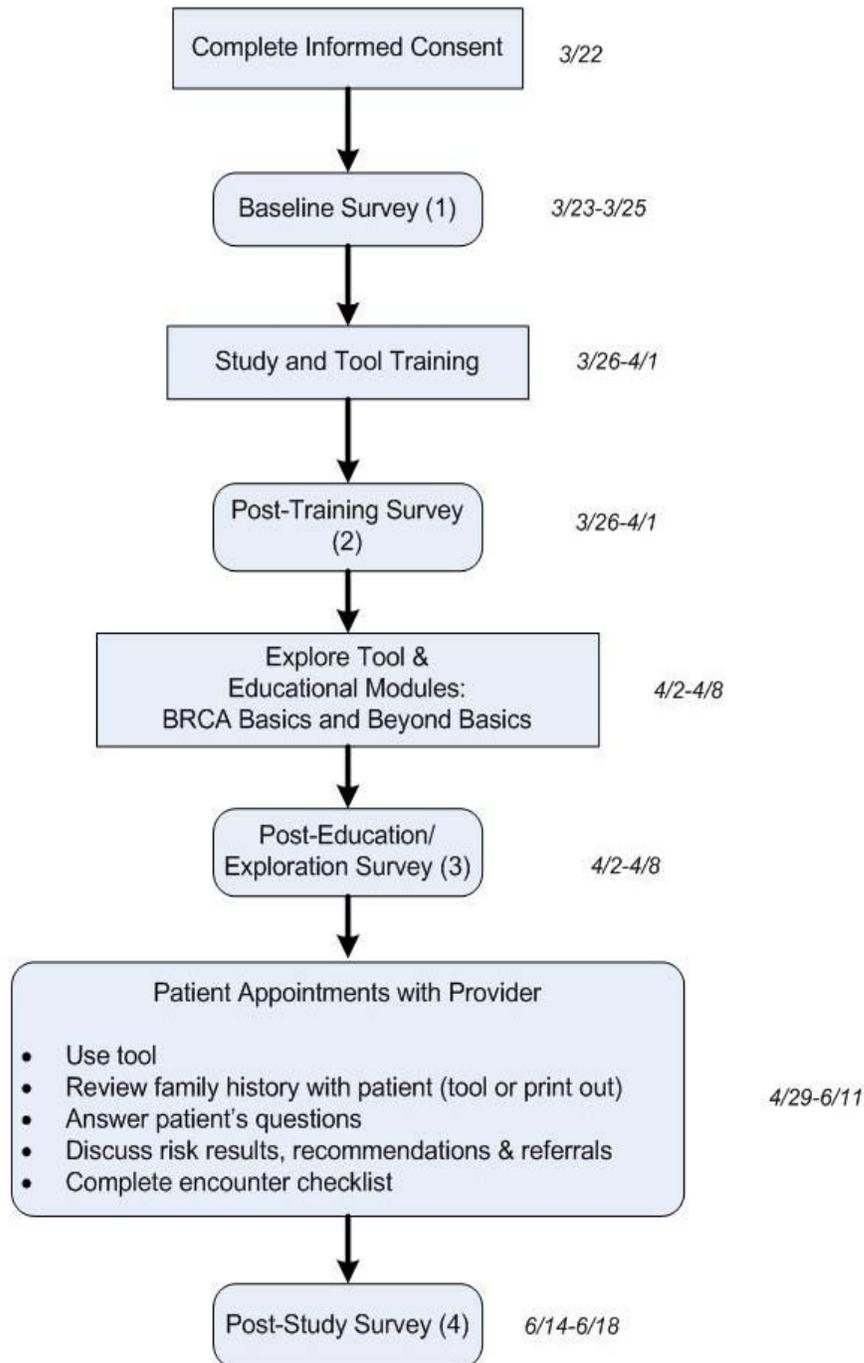
To document the patient encounter, providers completed a checklist that asks about their use of the tool, interaction with the patient, and whether they made a referral to genetic counseling.

To assess the strengths and weaknesses of the study protocol, providers were asked to record questions, problems, and feedback about the study in a diary. The providers were asked to complete the diaries once a week, so that the site coordinator could give them to RTI with the weekly study reports.

Providers’ use of the tool with patients. Providers’ had three ways to access a patient’s risk assessment results: the patient could bring her printout from the tool, the site coordinator could print the results of the risk assessment and distribute it to the provider, and the provider could log into the *Cancer in the Family* and view the risk assessment results during the appointment.

The protocol called for the provider and patient to discuss the risk results, the patient’s family history of cancer, and any questions that the patient had during the patient’s appointment. If they were logged into *Cancer in the Family*,

Figure M-2. Cancer in the Family provider flowchart



providers could view and edit a patient’s family history. According to the protocol, the appointment offered the patient and provider a chance to review the prerecorded questions on the patient’s risk results as well as any additional questions the patient may have. If the patient was at increased risk, the provider was to discuss the risks of hereditary breast and ovarian cancer and recommendations for screening. As directed by the U.S. Preventive Services Task Force guidelines, providers were directed to refer patients at increased risk for having a BRCA

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mutation to a genetic counselor for further evaluation. If a patient was not at increased risk, the provider was to review the patient's history of cancer screening and discuss with her when she should receive each type of screening.

GENES AND GENETIC TESTING

Your body is made up of tiny cells, and each cell contains genes (sometimes called DNA). Genes can affect a person's blood type, hair color, eye color, and other things, including the chances of getting certain illnesses. You get half of your genes from your mother and the other half from your father. Certain changes in genes may cause medical problems, such as cancer.

A gene test or **genetic test** looks at a person's gene information. The test looks to see if the genes are normal or have changes that are called **mutations**.

19. Have you ever had a genetic test for any reason?

- Yes
- No
- Don't know

GENES AND CANCER

Next, we are interested in what you already know about breast cancer, ovarian cancer, and two gene mutations called BRCA1 and BRCA2. If you don't know the answer, it's okay to answer "don't know."

20. Which one of the following statements is true?

- Very few people have a BRCA mutation
- Almost everyone will have a BRCA mutation at some point
- All women can get a BRCA mutation
- Don't know

21. Breast cancer is more common than ovarian cancer.

- True
- False
- Don't know

22. Who can get breast cancer?

- All women
- Only women who have a BRCA mutation
- Only women with a mother who had breast cancer
- Don't know

23. Who can get ovarian cancer?

- All women
- Only women who have a BRCA mutation
- Only women with a mother who had ovarian cancer
- Don't know

24. A woman who does not have a BRCA1 or BRCA2 gene mutation can still get cancer.

- True

- False
- Don't know

25. A woman who has a BRCA1 or BRCA2 gene mutation...

- Will definitely get breast or ovarian cancer
- Is at lower risk for breast or ovarian cancer
- Is at greater risk for breast and/or ovarian cancer
- Don't know

26. Your chances of having a BRCA1 or BRCA2 gene mutation is based on...

- Whether your mother had breast and/or ovarian cancer
- Your entire family history of all diseases
- Your entire family history of breast and ovarian cancer
- Don't know

27. A family cancer history should include: (Choose one answer).

- All of your relatives
- Only blood relatives
- Only relatives that are alive
- Don't know

28. About 1 in 10 women have a BRCA 1 or BRCA 2 gene mutation.

- True
- False
- Don't know

29. A BRCA genetic test cannot tell you...

- If you have a BRCA1 or BRCA2 mutation
- If you will get breast and/or ovarian cancer
- If you have a greater chance of getting breast and ovarian cancer
- Don't know

A genetic counselor is a health care professional who can help you understand if your genes make you more likely to get an illness.

30. If you see a genetic counselor, you must get a genetic test.

- True
- False
- Don't know

YOUR UNDERSTANDING OF BRCA MUTATIONS AND GENETIC TESTING

31. To me, having a BRCA1 or BRCA2 gene mutation would be no big deal.

Strongly disagree (1) _____ *Strongly agree (5)*

- 1
- 2
- 3
- 4
- 5
- Don't know

For question 39, please say how much you agree or disagree with the statement.

39. I am concerned that if I were to get a genetic test that my health insurance coverage would not cover the genetic test.

Not at all concerned (1) _____ - _____ *Very concerned (5)*

1 2 3 4 5

Don't know

TALKING WITH YOUR DOCTOR

This section is about talking with your doctor. Please think of your OB/GYN or main doctor.

How confident are you in your ability to...

40. Ask your doctor questions?

Not at all confident (1) _____ - _____ *Very confident (5)*

1 2 3 4 5

41. Ask your doctor questions about genetic testing?

Not at all confident (1) _____ - _____ *Very confident (5)*

1 2 3 4 5

42. Decide whether or not you want to learn your risk of having a BRCA mutation?

Not at all confident (1) _____ - _____ *Very confident (5)*

1 2 3 4 5

43. Make decisions about your medical care with your doctor?

Not at all confident (1) _____ - _____ *Very confident (5)*

1 2 3 4 5

ABOUT YOU (DEMOGRAPHICS)

44. What year were you born? _____

45. What is your current marital status?

Married or living as married

Not married

46. What is the highest grade of school you completed?

Never attended school

Elementary / middle school (Grade 1 to 8)

- Some high school (Grade 9 to 11)
- High school (Grade 12 or GED)
- Some college or technical school (College 1-3 years)
- College (College 4 years or more)
- Graduate degree (MS, PhD, MBA, etc.)

47. Are you Hispanic or Latino?

- Yes
- No

48. What is your race?

PLEASE SELECT ONE OR MORE.

- American Indian or Alaskan Native
- Asian
- Native Hawaiian or other Pacific Islander
- Black or African American
- White

49. For statistical purposes, we need to ask a question regarding family income. What is your yearly household income?

- Less than \$20,000
- \$20,000-\$39,999
- \$40,000-\$59,999
- \$60,000-\$79,999
- \$80,000-\$99,999
- \$100,000 or more
- Don't know → SKIP NEXT QUESTION

50. How many people (adults and children) are supported by this income? _____

51. Did someone help you complete this survey?

- Yes → GO TO NEXT QUESTION
- No → SKIP TO QUESTION 57

52. How did that person help you?

CHECK ALL THAT APPLY.

- Read the questions to me
- Explained the questions to me
- Entered the answers I gave
- Answered some or all of the questions for me
- Translated the questions into my language
- Helped in some other way, please specify: _____

53. Are you currently covered by health insurance or some other kind of health care plan?

- Yes → GO TO NEXT QUESTION
- No → SKIP TO END OF SURVEY

54. What kind of health insurance or health care plan or coverage do you have?

CHECK ALL THAT APPLY.

- Private or employer health insurance plan
- Medicaid
- Medicare
- Military Health Care/VA
- Other, please specify: _____

Thank you for taking part in this study. The purpose of this survey is to learn how people feel about genetic testing and breast and ovarian cancer. The information you provide is very important. It will help to improve an educational tool we are developing for patients like you. If you truly do not know the answer to a question, then it is okay to check the box that says “Don’t know.”

NOTE: THESE QUESTIONS MAY BE REORDERED SO THEY ARE NOT IN EXACTLY THE SAME ORDER AS THE PRETEST.

YOUR UNDERSTANDING OF BREAST AND OVARIAN CANCER

1. **Would you say your chance of getting breast cancer in your lifetime is...**

Very low (1) _____ - _____ *Very high (5)*
1 2 3 4 5

2. **Would you say your chance of getting ovarian cancer in your lifetime is...**

Very low (1) _____ - _____ *Very high (5)*
1 2 3 4 5

N/A, I no longer have ovaries

For questions 3-6, please say how much you agree or disagree with each statement.

3. **Almost all women who get breast cancer die from the disease.**

Strongly disagree (1) _____ - _____ *Strongly agree (5)*
1 2 3 4 5

4. **Almost all women who get ovarian cancer die from the disease.**

Strongly disagree (1) _____ - _____ *Strongly agree (5)*
1 2 3 4 5

5. **I would like to know my chances of getting breast cancer.**

Strongly disagree (1) _____ - _____ *Strongly agree (5)*
1 2 3 4 5

Don't know

Public reporting burden for this collection of information is estimated to average 30 minutes per response, the estimated time required to complete the survey. An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to: AHRQ Reports Clearance Officer Attention: PRA, Paperwork Reduction Project (0935-0124) AHRQ, 540 Gaither Road, Room # 5036, Rockville, MD 20850.

6. I would like to know my chances of getting breast cancer.

Strongly disagree (1) - *Strongly agree (5)*

1 2 3 4 5

Don't know

7. Would you say your chance of having a BRCA1 or BRCA2 mutation is...

Very low (1) - *Very high (5)*

1 2 3 4 5

Don't know

GENES AND CANCER

Next, we are interested in what you have learned about breast cancer, ovarian cancer, and BRCA1 and BRCA2 mutations. If you don't know the answer, it's okay to answer "don't know."

8. Which one of the following statements is true?

- Very few people have a BRCA mutation
- Almost everyone will have a BRCA mutation at some point
- All women can get a BRCA mutation
- Don't know

9. Breast cancer is more common than ovarian cancer.

- True
- False
- Don't know

10. Who can get breast cancer?

- All women
- Only women who have a BRCA mutation
- Only women with a mother who had breast cancer
- Don't know

11. Who can get ovarian cancer?

- All women
- Only women who have a BRCA mutation
- Only women with a mother who had ovarian cancer
- Don't know

12. A woman who does not have a BRCA1 or BRCA2 gene mutation can still get cancer.

- True
- False
- Don't know

13. A woman who has a BRCA1 or BRCA2 gene mutation...

- Will definitely get breast or ovarian cancer
- Is at lower risk for breast or ovarian cancer
- Is at greater risk for breast and/or ovarian cancer
- Don't know

14. Your chances of having a BRCA1 or BRCA2 gene mutation is based on...

- Whether your mother had breast and/or ovarian cancer
- Your entire family history of all diseases
- Your entire family history of breast and ovarian cancer
- Don't know

15. A family cancer history should include: (Choose one answer).

- All of your relatives
- Only blood relatives
- Only relatives that are alive
- Don't know

16. About 1 in 10 women have a BRCA 1 or BRCA 2 gene mutation.

- True
- False
- Don't know

17. A BRCA genetic test cannot tell you...

- If you have a BRCA1 or BRCA2 mutation
- If you will get breast and/or ovarian cancer
- If you have a greater chance of getting breast and ovarian cancer
- Don't know

A genetic counselor is a health care professional who can help you understand if your genes make you more likely to get an illness.

18. If you see a genetic counselor, you must get a genetic test.

- True
- False
- Don't know

YOUR UNDERSTANDING OF BRCA MUTATIONS AND GENETIC TESTING

19. To me, having a BRCA1 or BRCA2 gene mutation would be no big deal.

Strongly disagree (1) _____ - _____ *Strongly agree (5)*

- 1 2 3 4 5
- Don't know

For question 27, please say how much you agree or disagree with the statement.

27. I am concerned that if I were to get a genetic test that my health insurance coverage would not cover the genetic test.

Not at all concerned (1) - *Very concerned (5)*

1 2 3 4 5

Don't know

YOUR RISK OF BRCA MUTATION

28. According to the tool, what is your risk of having a BRCA mutation?

- Increased risk → GO TO QUESTION 29
- Average risk → SKIP TO QUESTION 30
- I chose not to calculate my risk → SKIP TO NEXT SECTION – USE OF TOOL
- Don't remember → SKIP TO NEXT SECTION – USE OF TOOL

29. You said that the tool indicated you are at increased risk for a BRCA mutation. Before using the tool, were you aware that you were at increased risk?

- Yes
- No

30. How accurate do you think your BRCA risk assessment results are?

Not at all accurate (1) - *Very accurate (5)*

1 2 3 4 5

31. Did you print out the results of your risk assessment?

- Yes → GO TO NEXT QUESTION
- No → SKIP TO QUESTION 32
- Don't remember → SKIP TO QUESTION 32

32. Where did you print the risk assessment results?

- My home
- My work
- A friend's home
- Doctor's office / clinic
- Public facility (i.e., library)
- Don't remember

➤ QUESTIONS 33 – 37 ARE ASKED ONLY OF THOSE WHO SAY INCREASED OR AVERAGE RISK FOR Q28

Now that you have learned your risk of having a BRCA mutation...

33. How worried are you about getting breast cancer?

Not at all (1) _____ - _____ *A lot (5)*
1 2 3 4 5

34. How worried are you about getting ovarian cancer?

Not at all (1) _____ - _____ *A lot (5)*
1 2 3 4 5

N/A, I no longer have ovaries

35. How satisfied are you with your decision to learn your risk of having a BRCA mutation?

Not at all satisfied (1) _____ - _____ *Very satisfied (5)*
1 2 3 4 5

36. How easy or difficult will it be to decide whether or not you will have a genetic test?

Very easy (1) _____ - _____ *Very difficult (5)*
1 2 3 4 5

37. If you had to make a decision today, how likely is it that you would decide to be tested for BRCA 1 and BRCA 2 mutations?

Not at all likely (1) _____ - _____ *Very likely (5)*
1 2 3 4 5

YOUR USE OF THE TOOL

Finally, we'd like to ask you some questions about how you used the tool.

Family History

38. How effective was the tool at helping you understand how to gather your family's cancer history?

Not at all effective (1) _____ - _____ *Very effective (5)*
1 2 3 4 5

39. Did you ask any of your family members about their cancer history?

- Yes → GO TO NEXT QUESTION
- No → SKIP TO QUESTION 46

40. Did you use the worksheet provided by the tool for collecting your family history?

- Yes → GO TO NEXT QUESTION
- No → SKIP TO QUESTION 44
- Don't know → SKIP TO QUESTION 44

41. How easy or difficult was it to ask your relatives about their history of cancer?

Very easy (1) - Very difficult (5)
1 2 3 4 5

42. In your opinion, how useful was the worksheet for collecting your family's cancer history?

Not at all useful (1) - Very useful (5)
1 2 3 4 5

43. How easy or difficult was it to use the worksheet?

Very easy (1) - Very difficult (5)
1 2 3 4 5

44. Did you enter your family's cancer history into the tool?

- Yes – I entered my family's complete cancer history → GO TO NEXT QUESTION
- Yes – I entered some or most of my family's cancer history → GO TO NEXT QUESTION
- No - Did not enter any history → SKIP TO QUESTION 46

45. How easy or difficult was it to enter your family history into the tool?

Very easy (1) - Very difficult (5)
1 2 3 4 5

Educational Content

46. How effective was the tool in helping you understand what BRCA mutations are?

Not at all effective (1) - Very effective (5)
1 2 3 4 5

47. How effective was the tool in helping you understand the advantages and disadvantages of learning your risk for BRCA mutations?

Not at all effective (1) - Very effective (5)
1 2 3 4 5

QUESTION 48 IS ASKED ONLY OF THOSE WHO SAY INCREASED OR AVERAGE RISK FOR Q28

48. How effective was the tool in helping you understand the results of your BRCA risk assessment?

19. Overall, how satisfied were you with your participation in the conversation with your doctor?

Not at all satisfied (1) - *Extremely satisfied (5)*
1 2 3 4 5

20. If you had a genetic test, how confident are you that the result would be kept private by your doctor's office?

Not at all confident (1) - *Very confident (5)*
1 2 3 4 5

Don't know

21. I am concerned that if I were to get a genetic test that my health insurance coverage would not cover it.

Not at all concerned (1) - *Very concerned (5)*
1 2 3 4 5

Don't know

Additional Comments

Is there anything else that you would like to share with us about your participation in this study?

PROVIDER PRE STUDY SURVEY

Thank you for participating in this evaluation. The purpose of this survey is to learn about your background, your experience with and opinions about decision support tools, and how you feel about BRCA screening. The information you provide is very important and will help us assess the effectiveness of the clinical decision support tool and educational module.

BACKGROUND INFORMATION

1. What type of primary care provider are you?

- Primary Care Physician
- Obstetrician/Gynecology
- Physicians Assistant
- Internal Medicine
- Other _____

2. Do you have any specialties?

- Yes → If yes, please specify: _____
- No

3. How long have you been a primary care physician?

_____ years and _____ months

4. How long have you been with your current employer?

_____ years and _____ months

5. How long have you been with your current clinic?

_____ years and _____ months

6. Have you ever had any type of training (including CME courses) on hereditary breast and ovarian cancer or BRCA testing?

- Yes → IF YES: How long ago did you participate? _____ years
- No

ATTITUDES TOWARD AND EXPERIENCE WITH BRCA SCREENING AND GENETIC TESTING

7. In a primary care setting such as yours, how important do you think it is to screen all women for BRCA mutations?

Not at all important (1) - Very important (5)
1 2 3 4 5

8. In primary care, how low or high a priority is screening patients for BRCA mutations?

Extremely low priority (1) - Extremely high priority (5)
1 2 3 4 5

For questions 9 and 10, please indicate how much you agree or disagree with each statement.

9. It is not worth screening or testing women for BRCA mutations unless they have had a cancer diagnosis.

Strongly disagree (1) - Strongly agree (5)
1 2 3 4 5

10. Even if I did screen patients for BRCA mutations, they probably would not see a genetic counselor if I gave them a referral.

Strongly disagree (1) - Strongly agree (5)
1 2 3 4 5

11. In the past 12 months, how many patients did you recommend get any type of genetic testing?

_____ patients

12. In the past 12 months, how many patients did you refer to a genetic counselor for any reason?

_____ patients

13. In the past 12 months, for how many patients did you order a BRCA genetic test?

_____ patients

BRCA CDS PROVIDER EDUCATIONAL PRETEST QUESTIONS

The next few questions are about your understanding of hereditary breast and ovarian cancer as well as BRCA mutations. If you do not know the answer to a question, please just choose the answer that you think is best.

14. In the past 12 months, from how many patients did you gather a complete cancer family history?

_____ patients

15. Each year, more than 192,000 American women learn they have breast cancer. Approximately how many of these cases have a hereditary form of the disease?

- A. 1 – 5%
- B. 5 – 10%
- C. 10 – 15%
- D. 15 – 20%

16. Specific gene alterations have been identified in different ethnic groups. Which of the following groups has a higher frequency of BRCA mutations? (Select all that apply).

- A. Hispanic women
- B. African American women
- C. Ashkenazi Jewish women
- D. Indo-European women

17. Hereditary breast and ovarian cancer (HBOC) syndrome is characterized by which of the following features in a family. (Select all that apply).

- A. An early age of onset of breast cancer
- B. Family history of both breast and ovarian cancer
- C. An autosomal dominant pattern of inheritance
- D. More aggressive tumor growth

18. Based on the U.S. Preventive Services Task Force (USPSTF) recommendations, which one of the following groups should be referred for genetic counseling and possible BRCA testing? (Select all that apply).

- A. All women with a first-degree female relative with breast cancer
- B. All women older than 40 years
- C. Women of Ashkenazi Jewish origin
- D. Women with a strong family history of breast cancer or ovarian cancer

19. In order to assess a patient’s risk of having a BRCA mutation, physicians should document family history of which cancer types?
- A. Breast cancer
 - B. Ovarian cancer
 - C. Colorectal cancer
 - D. Pancreatic cancer
20. Each offspring of an individual with a BRCA1 or BRCA2 mutation has what percentage chance of inheriting the mutation?
- A. 25%
 - B. 50%
 - C. 75%
 - D. 100%
21. For every 100 women with a BRCA mutation, ___ will develop breast cancer and ___ will develop ovarian cancer by the age of 70.
- A. 30, 50
 - B. 50, 30
 - C. 80, 50
 - D. 90, 40
 - E. 7, 1
22. True or False: BRCA mutations can be inherited from *both* the mother and the father’s side of the family.
- True
 - False
23. True or False: The USPSTF recommends that women with an increased risk for BRCA mutations, based on family history, be referred for genetic counseling and possible BRCA testing.
- True
 - False
24. True or False: The USPSTF recommends that women with an increased risk for BRCA mutations, based on family history, receive a mammogram every three years.
- True
 - False

Don't know

51. Do you consider yourself to be an early adopter, late adopter, or somewhere in between when it comes to incorporating new technology into your practice?

Early adopter (1) - Late adopter (5)

1

2

3

DEMOGRAPHIC INFORMATION

52. What year were you born? _____

53. Are you Hispanic or Latino?

Yes

No

Don't know

54. What gender do you currently identify as?

Male

Female

55. Which of these groups best describes you?

CHECK ALL THAT APPLY.

White

Black/African American

American Indian or Alaska Native (American Indian includes North American, Central American, and South American Indians)

Native Hawaiian

Other Pacific Islander

Asian

Other, please specify: _____

ADMINISTERED AFTER THE EDUCATIONAL MODULE IS COMPLETED

Thank you for completing the educational module. This survey is to assess what you may have learned from the module. Thank you for taking the time to answer this short set of questions.

BRCA CDS PROVIDER POST-EDUCATION SURVEY

1. **Each year, more than 192,000 American women learn they have breast cancer. Approximately how many of these cases have a hereditary form of the disease? (BRCA Basics, Section 1)**
 - A. 1 – 5%
 - B. 5 – 10%
 - C. 10 – 15%
 - D. 15 – 20%

2. **Specific gene alterations have been identified in different ethnic groups. Which of the following groups has a higher frequency of BRCA mutations? (Select all that apply). Beyond BRCA Basics: Genetics of Breast and Ovarian Cancer.**
 - A. Hispanic women
 - B. African American women
 - C. Ashkenazi Jewish women
 - D. Indo-European women

3. **Hereditary breast ovarian and cancer (HBOC) syndrome is characterized by which of the following features in a family? (Select all that apply).**
 - A. An early age of onset of breast cancer (BRCA Basics, Section 1)
 - B. Family history of both breast and ovarian cancer (Beyond Basics, BRCA Screening in Primary Care)
 - C. An autosomal dominant pattern of inheritance (Beyond Basics, BRCA Screening in Primary Care) (I recommend changing this to “increased risk of metastasis”)
 - D. More aggressive tumor growth

4. **Based on the U.S. Preventive Services Task Force (USPSTF) recommendations, which one of the following groups should be referred for genetic counseling and possible BRCA testing? (Select all that apply).**
 - A. All women with a first-degree female relative with breast cancer
 - B. All women older than 40 years
 - C. Women of Ashkenazi Jewish origin
 - D. Women with a strong family history of breast cancer or ovarian cancer

5. In order to assess a patient's risk of having a BRCA mutation, physicians should document family history of which cancer types?
- A. Breast cancer
 - B. Ovarian cancer
 - C. Colorectal cancer
 - D. Pancreatic cancer
6. Each offspring of an individual with a BRCA1 or BRCA2 mutation has what percentage chance of inheriting the mutation?
- A. 25%
 - B. 50%
 - C. 75%
 - D. 100%
7. For every 100 women with a BRCA mutation, ___ will develop breast cancer and ___ will develop ovarian cancer by the age of 70.
- A. 30, 50
 - B. 50, 30
 - C. 80, 50
 - D. 90, 40
 - E. 7, 1
8. True or False: BRCA mutations can be inherited from *both* the mother and the father's side of the family. ([Beyond Basics, Genetics of Breast Cancer and Ovarian Cancer](#))
- True
 - False
9. True or False: The USPSTF recommends that women with an increased risk for BRCA mutations, based on family history, be referred for genetic counseling and possible BRCA testing. [BRCA Basics, Section 1](#)
- True
 - False
10. True or False: The USPSTF recommends that women with an increased risk for BRCA mutations, based on family history, receive a mammogram every three years.
- True
 - False

PROVIDER POST-STUDY SURVEY

Thank you for participating in this evaluation. The purpose of this final survey is to learn about your experience with the BRCA clinical decision support tool and your attitudes toward BRCA testing and decision support tools in general. We'll also ask for your feedback on the methods used in this evaluation.

ATTITUDES TOWARD AND EXPERIENCE WITH BRCA SCREENING AND GENETIC TESTING

1. In a primary care setting such as yours, how important do you think it is to screen all women for BRCA mutations?

Not at all important (1) - Extremely important (5)

1 2 3 4 5

2. In primary care how low or high a priority is screening patients for BRCA mutations?

Extremely low priority (1) - Extremely high priority (5)

1 2 3 4 5

ATTITUDES TOWARD DECISION AIDS (GENERAL)

Please indicate how much you agree or disagree with the following statements:

3. It is not worth screening or testing women for BRCA mutations unless they have had a cancer diagnosis.

Strongly disagree (1) - Strongly agree (5)

1 2 3 4 5

4. Even if I did screen patients for BRCA mutations, they probably would not see a genetic counselor if I gave them a referral.

Strongly disagree (1) - Strongly agree (5)

1 2 3 4 5

PROVIDER CHECKLIST
Effective Health Care Program Research Report Number 30
Complete immediately after your encounter with each patient

This patient's risk for having a BRCA mutation was:

- Not at increased risk
- Increased risk
- N/A: Assessment not run

When did you use the tool to review this patient's risk results:

- Before patient's appointment
- During patient's appointment
- N/A: did not use tool

Did you refer this patient for genetic counseling?

- Yes
- No

What other referrals did you provide to this patient?

- Mammography
- Pap test
- Colorectal cancer screening
- Other: _____

During the patient's visit, which of the following did you do with the patient?

- Reviewed cancer family history
- Updated cancer family history after review
- Explained risk result
- Addressed questions
- Checked understanding

[SKIP PATTERNS]

[If patient not at increased risk, but referral given: Pop up question]: You indicated the patient was not at increased risk but that you referred her to genetic counseling. Why did you decide to refer this patient to genetic counseling?

[If patient at increased risk, but no referral given: Pop up question]: You indicated the patient was at increased risk but that you did not refer her to genetic counseling. Why did you decide not to refer this patient to genetic counseling?

CHARACTERISTICS OF PRACTICE

Name of Site: _____

1. **Which of the following categories best describes this main primary care practice location (i.e., the practice location where you spend the most hours per week)?**

CHECK ONE BOX.

- Physician-owned practice
- Large medical group or health care system (non-university)
- Group or staff model HMO
- University hospital or clinic
- Hospital or clinic not associated with a university (including community health clinics)
- Other (specify):

2. **How many physicians are in this main primary care practice location?**

CHECK ONE BOX.

- 1
- 2 – 5
- 6 – 15
- 16 – 49
- 50 – 99
- 100 +

3. **How many nurse practitioners and/or physician's assistants are in your main primary care practice location?**

Insert number above

4. **During a typical week, approximately how many patients are seen in this primary care practice location?**

CHECK ONE BOX.

- 25 or fewer
- 26 – 50
- 51 – 75
- 76 – 100
- 101 – 125
- 126 or more

5. **Approximately what percentage of patients in this primary care practice are female?
(Your best estimate is fine.)**

_____ %

6. Approximately what percent of female patients in this main primary care practice are:

(Your best estimate is fine.)

less than 18 years..... %

18 – 39 years %

40 – 64 years %

65 + years %

TOTAL 100%

7. Approximately what percent of patients in this primary care practice location are:

(Your best estimate is fine.)

CHECK ONE BOX ON EACH LINE.	0 – 5%	6 – 25%	26 – 50%	51 – 75%	76 – 100%	Don't know
Uninsured	<input type="checkbox"/>					
Insured by Medicaid	<input type="checkbox"/>					

8. Approximately what percent of your patients in this main primary care practice are:

(Your best estimate is fine.)

CHECK ONE BOX ON EACH LINE.	0 – 5%	6 – 25%	26 – 50%	51 – 75%	76 – 100%	Don't know
White	<input type="checkbox"/>					
Black or African American	<input type="checkbox"/>					
Asian	<input type="checkbox"/>					
Native Hawaiian or Other Pacific Islander	<input type="checkbox"/>					
Hispanic or Latino	<input type="checkbox"/>					
American Indian or Alaska Native	<input type="checkbox"/>					

Appendix N. Site Training

Evaluation of the *Cancer in the Family* Clinical Decision Support Tool

Site Training

March 2010

www.rti.org



Study Purpose

Evaluate a Web-based clinical decision support (CDS) tool. The tool helps patients and providers assess a woman's risk of hereditary breast and ovarian cancer.

2



Cancer in the Family Tool

- Estimates a woman's risk of having BRCA1 or BRCA2 gene mutation.
- BRCA mutations increase risk of breast and ovarian cancer. Cancer may occur earlier, more aggressive.
- Uses family cancer history to calculate risk.
- Assigns women into one of two risk categories:
 - Increased risk
 - Not at increased risk

3



Cancer in the Family Tool

Advantages

- Patient-driven tool
- Patient family tree / cancer history record
- Identify high risk women, refer to genetic counseling
- Discourage genetic testing for low-risk women
- Shared decision about genetic testing
- EMR documentation

4



Accessing Tool

Patient Access

- Web login at home or other personal computer
- Password-protected site

Provider Access

- Web login at clinic, office, or exam rooms
- Password-protected site
- Access to patients at their clinic only

<http://brca.rti.org>

5



Accessing Tool

Data Storage and Security

- Family history and risk results stored on secure RTI servers
- No personally identifying information, only initials
- Study-specific patient and provider IDs

6



Tool Login Screen



Could you have a gene causing Hereditary Breast and Ovarian Cancer?



Welcome

Login

User Name:

Password:

Remember Login

Welcome

Welcome to the Cancer in the Family Education and Risk Assessment Tool.

This tool provides information about hereditary breast and ovarian cancer (HBOC) and is designed for patients and their doctors to use together. This tool can help patients gather their family's cancer history and use it to assess their risk for HBOC.

Please enter your user name and password to begin.

Take a Tour

Take a video tour of the **Cancer in the Family** tool to find out what to expect from and how to work with this website.

IMPORTANT DISCLAIMER: The information provided on or through this web site does not constitute medical advice, and should not be used for diagnosing or treating a health or medical condition. The information, including but not limited to risk profiles, is provided for information purposes only, and any use of or reliance on the information is solely at the user's own risk. Users of this web site should consult their physicians in regard to diagnosis and treatment of any symptoms or conditions requiring medical attention. RTI International ("RTI") makes no warranties or representations as to the accuracy or completeness of the information provided here, and RTI will not be liable for any claim or damages related in any way to any of the information provided on or through this web site, irrespective of cause or legal theory.

Patient Interface



Could you have a gene causing Hereditary Breast and Ovarian Cancer?



[Home](#)
[Additional Resources](#)
[Glossary](#)
[Logout](#)

INTRODUCTION

STEP 1: LEARN

STEP 2: DECIDE

STEP 3: GATHER >

STEP 4: CALCULATE

STEP 5: KNOW

STEP 6: PLAN

INTRODUCTION

Welcome to the Cancer in the Family Education and Risk Assessment Tool.

The purpose of this tool is to help you:

- Learn about hereditary breast and ovarian cancer.
- Learn if your family's history of cancer increases your chances of getting breast or ovarian cancer.
- Discuss your risk with your doctor.

This tool will help you and your doctor decide if you should see a genetic counselor and if you should consider having a test to find out if you have the changed gene that can increase your chances of getting **breast cancer** or **ovarian cancer**.

This tool will NOT tell you exactly what your chances are of getting breast cancer or ovarian cancer. Knowing if you have an increased chance of having a gene mutation that can cause breast or ovarian cancer can inform the decisions you make about your health.

HELPFUL HINT

DO NOT USE THE BROWSER BACK AND FORWARD BUTTONS TO NAVIGATE. If you accidentally click the browser back button, you can return to your location by clicking on the browser Refresh button and then clicking Retry.

Take a Tour

Take a video tour of the **Cancer in the Family** tool to find out what to expect from and how to work with this website.



Patient Interface



Could you have a gene causing Hereditary Breast and Ovarian Cancer?



[Home](#)
[Additional Resources](#)
[Glossary](#)
[Logout](#)

INTRODUCTION

STEP 1: LEARN

STEP 2: DECIDE

STEP 3: GATHER

- Enter Your Cancer History
- Enter Your Family Tree
- View Your Family Cancer History Worksheet
- Enter Mother's Side Cancer History
- View Mother's Side Cancer History
- Enter Father's Side Cancer History
- View Father's Side Cancer History

STEP 4: CALCULATE

STEP 5: KNOW

STEP 6: PLAN

STEP 3: GATHER YOUR FAMILY'S HISTORY OF CANCER

This tool will help you gather your family's history of cancer by taking you through these steps:

- A. Enter your own history of breast and ovarian cancer into the tool.
- B. Create your family tree.
- C. Print your personalized family history worksheet and gather your family's history of breast and ovarian cancer.
- D. Enter your family's cancer history into the tool.

Your health information and your family's history of cancer will be used to calculate your risk of having a BRCA mutation.

Each of these steps is described below. Please read through these steps and then use the menu on the left-side to go through each of these steps.

A. Enter Your Cancer History

To begin, you'll be asked to enter some basic information about you and your personal cancer history. The program uses this information to help calculate your risk. Use the menu item on the left side called Enter Your Cancer History.

B. Create Your Family Tree

Take a Tour
Take a video tour of the Cancer in the Family tool.

Patient Interface



Could you have a gene causing Hereditary Breast and Ovarian Cancer?



[Home](#)
[Additional Resources](#)
[Glossary](#)
[Logout](#)

INTRODUCTION

STEP 1: LEARN

STEP 2: DECIDE

STEP 3: GATHER

- Enter Your Cancer History
- Enter Your Family Tree
- Your Children
- Your Siblings**
- Your Nieces and Nephews
- Your Maternal Aunts and Uncles
- Your Maternal Cousins
- Your Paternal Aunts and Uncles
- Your Paternal Cousins
- View Your Family Cancer History Worksheet
- Enter Mother's Side Cancer History
- View Mother's Side Cancer History
- Enter Father's Side Cancer History
- View Father's Side Cancer History

STEP 4: CALCULATE

STEP 5: KNOW

CREATE YOUR FAMILY TREE - SIBLINGS

For each relationship, please enter in the number of family members you have and the initials of each family member. Be sure to SAVE the information before moving on to the next page.

Full Siblings
Full siblings are sisters and brothers who have the same mother and father as you.

How many Full-Sisters do you have? Initials:

How many Full-Brothers do you have? Initials:

Maternal Half-Siblings
Maternal half-siblings are half-brothers and half-sisters who have the same mother as you, but not the same father.

How many Maternal Half-Sisters have?

Patient Interface

Your Maternal Cousins
Your Paternal Aunts and Uncles
Your Paternal Cousins
View Your Family Cancer History Worksheet
[Enter Mother's Side Cancer History](#)
View Mother's Side Cancer History
Enter Father's Side Cancer History
View Father's Side Cancer History

STEP 4: CALCULATE
STEP 5: KNOW
STEP 6: PLAN

Take a Tour
Take a video tour of the **Cancer in the Family** tool to find out what to expect from and how to work with this website.

Please enter as much information as you know for each person.

The bar above each family member is shaded gray when information has not yet been saved. When you save information, the bar changes from gray to pink for female family members and from gray to blue for male family members

Don't forget to hit **SAVE** or **SAVE ALL** after entering each family member's information

NOTE: Need to delete or add a family member? Simply navigate to the **Create Your Family Tree** section using the left hand menu, choose the type of family member you wish to add or delete. Adjust the number for that type of family member and press save.

memo on the next menu slide or the to come back to pick up where you off.

Save All

Grandfather

Still living? No Yes Age at death: (years)

Ever diagnosed with breast cancer? No Yes

Save

Grandmother

Still living? No Yes Age now: (years)

Ever diagnosed with breast cancer? No Yes

Age when first diagnosed: (years)

Was cancer in both breasts? No Yes

Ever diagnosed with ovarian cancer? No Yes

Ovaries removed? No Yes

Save

Patient Interface

Worksheet

```

graph TD
    G83[Grandmother 83] --- G77[Grandfather 77]
    G83 --- M60[Mother 60]
    G77 --- M60
    M60 --- U63[Uncle HA 63]
    M60 --- A54[Aunt EA 54]
    M60 --- Y24[You 24]
    M60 --- B35[Brother DS 35]
    M60 --- S30[Sister CS 30]
    U63 --- C24[Cousin IA 24]
    U63 --- C23[Cousin JA 23]
    A54 --- C25[Cousin GA 25]
    A54 --- C20[Cousin FA 20]
    
```

LEGEND

B = Unilateral Breast Cancer (1 breast)
B2 = Bilateral Breast Cancer (both breasts)
Ovarian Cancer

Gender: Male (M), Female (F)
Relation/Status (Age): You (48), Deceased, Half-Sibling, No Data Provided

Jewish Ancestry

the y tool to ect from th this

Patient Interface

STEP 2: DECIDE

STEP 3: GATHER

- Enter Your Cancer History
- Enter Your Family Tree
 - Your Children
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 - Your Maternal Cousins
 - Your Paternal Aunts and Uncles
 - Your Paternal Cousins
- View Your Family Cancer History Worksheet
- Enter Mother's Side Cancer History
- View Mother's Side Cancer History
- Enter Father's Side Cancer History
- View Father's Side Cancer History

STEP 4: CALCULATE

STEP 5: KNOW

STEP 6: PLAN

cancer, you can find out your chances of having a BRCA1 or BRCA2 gene mutation.

If you would like to review the pros and cons of knowing your chances of having a BRCA1 or BRCA2 gene mutation, [return to Step 2](#).

If you still have questions, you can:

- Review the information in this tool again
- [Click here](#) for other places to get information
- Talk to your doctor

While the tool will calculate your risk based on any number of family members, the more information you enter into the tool about each of your family members, the better the result.

You have entered cancer history information for **21** out of **21** family members.

DECISION POINT:

Would you like to have the tool calculate your chances of having a BRCA1 or BRCA2 gene mutation now? Please click Yes or No to continue.

Yes No

Calculate Chances of BRCA Mutation

Your Results

You are at **Increased Risk** for breast cancer.

The last BRCA risk calculation was run on 3/18/2010 4:09:50 PM. If you make any changes to your or your family's cancer history data, be sure to re-calculate the risk.

Take a Tour

Take a video tour of the **Cancer in the Family** tool to find out what to expect from and how to work with this website.

Patient Interface



Could you have a gene causing Hereditary Breast and Ovarian Cancer?



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 - Your Maternal Cousins
 - Your Paternal Aunts and Uncles
 - Your Paternal Cousins
- View Your Family Cancer History Worksheet
- Enter Mother's Side Cancer History
- View Mother's Side Cancer History
- Enter Father's Side Cancer History
- View Father's Side Cancer History

STEP 4: CALCULATE

STEP 6: PLAN FOR YOUR VISIT WITH THE DOCTOR

In this step, you will create an action plan for talking to your doctor about your risk of having a BRCA1 or BRCA2 gene mutation.

How that I know my chances of having a BRCA1 or BRCA2 gene mutation, what should I do next?

This step will help you create an action plan based on your chances for having a BRCA1 or BRCA2 gene mutation. You can print this action plan when you are done.

Your action plan should focus on:

- Talking about the results of this tool with your doctor.
- Getting your questions answered.
- Deciding whether to see a genetic counselor.

To help make your action plan, you can first learn more about:



Provider Interface



Could you have a gene causing Hereditary Breast and Ovarian Cancer?



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Sharing Results - NOT at Increased Risk

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Patient List

Patients that have been assigned a Username from your site are listed below.

If you are a PROVIDER, you will see the patient's calculated BRCA risk probability once calculated by the patient. You may click on View Output for the PDF output of the patient's pedigree and results. Once you have completed the visit with the patient, click on the Checklist icon to record information about the patient interaction.

If you are a SITE ADMINISTRATOR, you will be able to see important dates of progression as the patient makes her way through the tool. You will also be able to EDIT information in this table to add the patient's appointment date as well as the patient's initials and year of birth to be used as a visual identifier for the provider.

Click here to view the [User Guide](#).

USERNAME	Patient ID	Appt Date/Time	Provider Name	Results	Risk Results PDF	Checklist	Checklist Date
DJGXE	RTI1	4/12/2010 12:00:00 AM	Dr A				
DVAYM	INC RISK	4/15/2010 2:00:00 PM	Dr. Smith	★ Increased Risk			
DTMZK	LOW RISK	4/15/2010 3:00:00 PM	Dr. Jones	★ Not at Increased Risk			
DHHVY							
DIJZT							
DXOVU							
DIWSH							
DXQQI							
DIWQO							

Provider Interface



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BRCA Basics

Click on each heading to learn more.

- [Importance of BRCA Screening in Primary Care](#)
- [Primary Care Provider's Role](#)
- [How this Tool Uses Cancer Family History to Calculate BRCA Carrier Risk](#)
- [Next Steps for Cancer Screening After Risk Is Calculated](#)



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Adobe Reader Plug-In

Provider Interface



Could you have a gene causing Hereditary Breast and Ovarian Cancer?



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Beyond The Basics: Additional Resources and Information

Click on each heading to learn more.

- [Information on the Genetics of Breast Cancer and Ovarian Cancer](#)
- [Information on How This Tool Will Use Cancer Family History to Calculate BRCA Carrier Risk](#)
- [What You and Your Patients Need to Know About Genetic Discrimination](#)
- [Why Should I Refer My Patients Who Are At Increased Risk of HBOC to a Genetic Counselor?](#)
- [The Shared Decision-Making Process](#)
- [Information on Preventive Treatments That Are Available for BRCA Mutation Carriers](#)
- [View Risk Examples](#)
- [Additional Web Links](#)



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Could you have a gene causing Hereditary Breast and Ovarian Cancer?



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Sharing Results - Increased Risk

For more detailed information, click on the headings below.

1. Review your patient's family history and confirm it is complete and accurate
2. Explain what it means to be at "increased risk"
3. Discuss recommendations and next steps
4. Referral to genetic counseling
5. Review your patient's medical record
6. Address questions from your patient
7. Check patient understanding

[Additional Resources](#)



- Try to speak slowly
- Focus ideas and concepts using simple, conversational

Provider Interface



Could you have a gene causing Hereditary Breast and Ovarian Cancer?

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[Sharing Results - NOT at Increased Risk](#)
[Referen](#)

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Sharing Results - Increased Risk

For more detailed information, click on the headings below.

- Review your patient's family history and confirm it is complete and accurate**
 - Review your patient's family history they entered in the webtool.
 - Confirm that there are no missing pieces of information, outstanding questions, or new information that needs to be entered.
 - If any changes are made to the cancer family history, rerun the *BRC4PRO* algorithm to display your patient's most current risk results.
- Explain what it means to be at "increased risk"**

Explain to patient:

"Based on the information you provided about your family's history of cancer, your chance of having a BRCA1 or BRCA2 mutation is higher than it is for most people in the United States. At least 1 in 100 women with a family history of cancer like yours has a BRCA1 or BRCA2 mutation."

What being at "increased risk" **DOES NOT** mean:



Site Coordinator Interface



Could you have a gene causing Hereditary Breast and Ovarian Cancer?



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Patient List

Patients that have been assigned a Username from your site are listed below.

If you are a PROVIDER, you will see the patient's calculated BRCA risk probability once calculated by the patient. You may click on View Output for the PDF output of the patient's pedigree and results. Once you have completed the visit with the patient, click on the Checklist icon to record information about the patient interaction.

If you are a SITE ADMINISTRATOR, you will be able to see important dates of progression as the patient makes her way through the tool. You will also be able to EDIT information in this table to add the patient's appointment date as well as the patient's initials and year of birth to be used as a visual identifier for the provider.

Click here to view the [User Guide](#).

USERNAME	Patient ID	Appt Date/Time	Provider Name	Last Login Date	Baseline Survey Date	Post-test 1 Survey Date	Post-test 2 Survey Date	Results Date	Checklist Date
DIGXE	RT11	4/12/2010 12:00:00 AM	Dr A	3/11/2010					Edit
DVAYM	INC RISK	4/15/2010 2:00:00 PM	Dr. Smith	3/19/2010				3/18/2010	Edit
DTMZC	LOW RISK	4/15/2010 3:00:00 PM	Dr. Jones	3/18/2010				3/18/2010	Edit
DHHVY				3/11/2010					Edit
DIJZT				3/11/2010					Edit
DXOVU				3/11/2010					Edit
DJWSH				3/11/2010					Edit

Site Coordinator Interface



**Cancer
IN THE
FAMILY**

*Could you have a gene causing
Hereditary Breast and Ovarian Cancer?*



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Patient List

Patients that have been assigned a Username from your site are listed below.

If you are a PROVIDER, you will see the patient's calculated BRCA risk probability once calculated by the patient. You may click on View Output for the PDF output of the patient's pedigree and results. Once you have completed the visit with the patient, click on the Checklist icon to record information about the patient interaction.

If you are a SITE ADMINISTRATOR, you will be able to see important dates of progression as the patient makes her way through the tool. You will also be able to EDIT information in this table to add the patient's appointment date as well as the patient's initials and year of birth to be used as a visual identifier for the provider.

Click here to view the [User Guide](#).

USERNAME	Patient ID	Appt Date/Time	Provider Name	Last Login Date	Baseline Survey Date	Post-test 1 Survey Date	Post-test 2 Survey Date	Results Date	Checklist Date		
DIGXE	RT11	4/12/2010 12:00:00 AM	Dr A	3/11/2010						Edit	
DVAYM	INC RISK	4/15/2010 2:00:00 PM	Dr. Smith	3/19/2010				3/18/2010		Edit	
Patient ID:		<input type="text" value="INC RISK"/>									
Appt Date/Time:		<input type="text" value="4/15/2010 2:00:00 PM"/>									
Provider Name:		<input type="text" value="Dr. Smith"/>									
Update Cancel											
DTHZY	LOW	4/15/2010	Dr. Jones	3/18/2010				3/18/2010		Edit	

Appendix O. Provider Training

Evaluation of the *Cancer in the Family* Clinical Decision Support Tool

Primary Care Provider Training
Spring 2010

www.rti.org



Study Purpose

Evaluate a Web-based clinical decision support (CDS) tool. The tool helps patients and providers assess a woman's risk of hereditary breast and ovarian cancer.

2



Training Purpose

I. *Cancer in the Family* Tool and Functionality

- Tool Overview
- Accessing Tool
- Patient Interface
- Provider Interface

II. Pilot Testing Overview

III. Provider Role / Responsibilities

3



**I. *Cancer in the Family* Tool
and Functionality**

4



Cancer in the Family Tool

- Estimates a woman's risk of having BRCA1 or BRCA2 gene mutation.
- BRCA mutations increase risk of breast and ovarian cancer. Cancer may occur earlier, more aggressive.
- Uses family cancer history to calculate risk.
- Assigns women into one of two risk categories:
 - Increased risk
 - Not at increased risk

5



Cancer in the Family Tool

Advantages

- Patient-driven tool
- Patient family tree / cancer history record
- Identify high risk women, refer to genetic counseling
- Discourage genetic testing for low-risk women
- Shared decision about genetic testing
- EMR documentation

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Accessing Tool

Patient Access

- Web login at home or other personal computer
- Password-protected site

Provider Access

- Web login at clinic, office, or exam rooms
- Password-protected site
- Access to patients at your clinic only

<http://brca.rti.org>

7



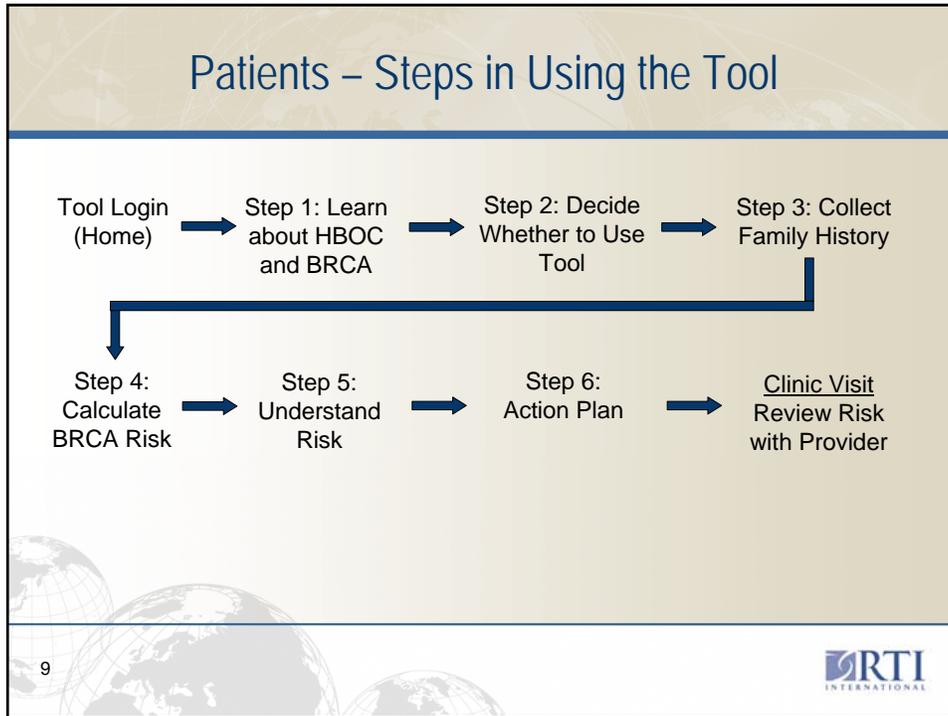
Accessing Tool

Data Storage and Security

- Family history and risk results stored on secure RTI servers
- No personally identifying information, only initials
- Study-specific patient and provider IDs

8





Login Screen



Could you have a gene causing Hereditary Breast and Ovarian Cancer?



Welcome

Login

User Name:

Password:

Remember Login

Welcome

Welcome to the Cancer in the Family Education and Risk Assessment Tool.

This tool provides information about hereditary breast and ovarian cancer (HBOC) and is designed for patients and their doctors to use together. This tool can help patients gather their family's cancer history and use it to assess their risk for HBOC.

Please enter your user name and password to begin.

Take a Tour

Take a video tour of the **Cancer in the Family** tool to find out what to expect from and how to work with this website.

IMPORTANT DISCLAIMER: The information provided on or through this web site does not constitute medical advice, and should not be used for diagnosing or treating a health or medical condition. The information, including but not limited to risk profiles, is provided for information purposes only, and any use of or reliance on the information is solely at the user's own risk. Users of this web site should consult their physicians in regard to diagnosis and treatment of any symptoms or conditions requiring medical attention. RTI International ("RTI") makes no warranties or representations as to the accuracy or completeness of the information provided here, and RTI will not be liable for any claim or damages related in any way to any of the information provided on or through this web site, irrespective of cause or legal theory.

Patient Interface – Introduction



Could you have a gene causing Hereditary Breast and Ovarian Cancer?



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INTRODUCTION

Welcome to the Cancer in the Family Education and Risk Assessment Tool.

The purpose of this tool is to help you:

- Learn about hereditary breast and ovarian cancer.
- Learn if your family's history of cancer increases your chances of getting breast or ovarian cancer.
- Discuss your risk with your doctor.

HELPFUL HINT

DO NOT USE THE BROWSER BACK AND FORWARD BUTTONS TO NAVIGATE. If you accidentally click the browser back button, you can return to your location by clicking on the browser Refresh button and then clicking Retry.

Take a Tour

Take a video tour of the Cancer in the Family tool to find out what to expect from and how to work with this website.



This tool will help you and your doctor decide if you should see a genetic counselor and if you should consider having a test to find out if you have the changed gene that can increase your chances of getting [breast cancer](#) or [ovarian cancer](#).

This tool will NOT tell you exactly what your chances are of getting breast cancer or ovarian cancer. Knowing if you have an increased chance of having a gene mutation that can cause breast or ovarian cancer can inform the decisions you make about your health.



Patient Interface – Step 1: Learn



Could you have a gene causing Hereditary Breast and Ovarian Cancer?



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STEP 1: LEARN ABOUT HOW BREAST AND OVARIAN CANCER CAN RUN IN FAMILIES

In this step, you will learn about how breast and ovarian cancer can run in families.

Who can get breast or ovarian cancer?

Any woman can get breast cancer or ovarian cancer. But your chances of getting these cancers may be higher if these cancers run in your family.

Being prone to getting inherited breast or ovarian cancer is called [Hereditary Breast and Ovarian Cancer \(HBOC\)](#) syndrome. Typically, individuals with HBOC may have a few family members related by blood who have had breast or ovarian cancer, especially at a young age.

How can I find out if breast or ovarian cancer runs in my family?

Finding out who has had cancer in your family lets you and your doctor see if certain types of cancer tend to run in your family.

The history of cancer in your family applies only to your blood relatives. So that does not include people who are related to you only through marriage or adoption.

This tool will help you find out who in your family has had breast or ovarian cancer.

When these cancers seem to run in a family, they may be caused by a problem with a gene.

What are genes?



Patient Interface – Step 3: Gather



Could you have a gene causing Hereditary Breast and Ovarian Cancer?



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Enter Your Family Tree

View Your Family Cancer History Worksheet

Enter Mother's Side Cancer History

View Mother's Side Cancer History

Enter Father's Side Cancer History

View Father's Side Cancer History

STEP 4: CALCULATE

STEP 5: KNOW

STEP 6: PLAN

STEP 3: GATHER YOUR FAMILY'S HISTORY OF CANCER

This tool will help you gather your family's history of cancer by taking you through these steps:

- A. Enter your own history of breast and ovarian cancer into the tool.
- B. Create your family tree.
- C. Print your personalized family history worksheet and gather your family's history of breast and ovarian cancer.
- D. Enter your family's cancer history into the tool.

Your health information and your family's history of cancer will be used to calculate your risk of having a BRCA mutation.

Each of these steps is described below. Please read through these steps and then use the menu on the left-side to go through each of these steps.

A. Enter Your Cancer History

To begin, you'll be asked to enter some basic information about you and your personal cancer history. The program uses this information to help calculate your risk. Use the menu item on the left side called Enter Your Cancer History.

B. Create Your Family Tree

Take a Tour
Take a video tour of the Cancer in the Family tool.

Patient Interface – Step 3: Gather



Could you have a gene causing Hereditary Breast and Ovarian Cancer?



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Enter Your Cancer History

Enter Your Family Tree

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Your Siblings

Your Nieces and Nephews

Your Maternal Aunts and Uncles

Your Maternal Cousins

Your Paternal Aunts and Uncles

Your Paternal Cousins

View Your Family Cancer History Worksheet

Enter Mother's Side Cancer History

View Mother's Side Cancer History

Enter Father's Side Cancer History

View Father's Side Cancer History

STEP 4: CALCULATE

STEP 5: KNOW

CREATE YOUR FAMILY TREE - SIBLINGS

For each relationship, please enter in the number of family members you have and the initials of each family member. Be sure to SAVE the information before moving on to the next page.

Full Siblings
Full siblings are sisters and brothers who have the same mother and father as you.

How many Full-Sisters do you have? Initials:

How many Full-Brothers do you have? Initials:

Maternal Half-Siblings
Maternal half-siblings are half-brothers and half-sisters who have the same mother as you, but not the same father.

How many Maternal Half-Sisters have?

Patient Interface – Step 3: Gather

Your Maternal Cousins
Your Paternal Aunts and Uncles
Your Paternal Cousins
View Your Family Cancer History Worksheet
[Enter Mother's Side Cancer History](#)
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Enter Father's Side Cancer History
View Father's Side Cancer History

STEP 4: CALCULATE
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Take a Tour
Take a video tour of the **Cancer in the Family** tool to find out what to expect from and how to work with this website.

Please enter as much information as you know for each person.

The bar above each family member is shaded gray when information has not yet been saved. When you save information, the bar changes from gray to pink for female family members and from gray to blue for male family members

Don't forget to hit **SAVE** or **SAVE ALL** after entering each family member's information

NOTE: Need to delete or add a family member? Simply navigate to the **Create Your Family Tree** section using the left hand menu, choose the type of family member you wish to add or delete. Adjust the number for that type of family member and press save.

menu on the left hand side or the top to come back to pick up where you left off.

Save All

Grandfather

Still living? No Yes Age at death: (years)

Ever diagnosed with breast cancer? No Yes

Save

Grandmother

Still living? No Yes Age now: (years)

Ever diagnosed with breast cancer? No Yes

Age when first diagnosed: (years)

Was cancer in both breasts? No Yes

Ever diagnosed with ovarian cancer? No Yes

Ovaries removed? No Yes

Save

Patient Interface – Step 3: Gather

Worksheet

```

graph TD
    G83[Grandmother 83] --- G77[Grandfather 77]
    G83 --- M60[Mother 60]
    G77 --- M60
    M60 --- U63[Uncle HA 63]
    M60 --- A54[Aunt EA 54]
    M60 --- Y24[You 24]
    M60 --- B35[Brother DS 35]
    M60 --- S30[Sister CS 30]
    U63 --- C24[Cousin IA 24]
    U63 --- C23[Cousin JA 23]
    A54 --- C25[Cousin GA 25]
    A54 --- C20[Cousin FA 20]
    
```

LEGEND

B = Unilateral Breast Cancer (1 breast)
B2 = Bilateral Breast Cancer (both breasts)
Ovarian Cancer

Gender: Male (M), Female (F)
Religion/Ethnicity (Age): Jewish, Hispanic, etc.

Icons: Deceased (D), Half-Sibling (HS), No Data Provided (ND)

the Family tool to expect from this

Patient Interface – Step 4: Calculate



Could you have a gene causing Hereditary Breast and Ovarian Cancer?



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STEP 4: CALCULATE YOUR RISK

Now that you entered your family's history of cancer, you can find out your chances of having a BRCA1 or BRCA2 gene mutation.

If you would like to review the pros and cons of knowing your chances of having a BRCA1 or BRCA2 gene mutation, [return to Step 2](#).

If you still have questions, you can:

- Review the information in this tool again
- Click [here](#) for other places to get information
- Talk to your doctor

While the tool will calculate your risk based on any number of family members, the more information you enter into the tool about each of your family members, the better the result.

It appears that you have not yet entered your family members.

[Click here to enter family members.](#)

DECISION POINT:

Would you like to have the tool calculate your chances of having a BRCA1 or BRCA2 gene mutation now? Please click Yes or No to continue.

Yes No

[Calculate Chances of BRCA Mutation](#)

Your Results

You are at **increased risk** for having a BRCA gene mutation.

The last BRCA risk calculation was run on 04/24/2019 20:31:27. If you make any changes to your or your family's cancer history data, be sure to re-calculate the risk.

Previous
Next



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Patient Interface – Step 5: Know



Could you have a gene causing Hereditary Breast and Ovarian Cancer?



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STEP 5: KNOW WHAT YOUR RISK OF HAVING A BRCA MUTATION MEANS TO YOU AND YOUR FAMILY

What does it mean to be at "increased risk" of a BRCA1 or BRCA2 gene mutation?

Based on the information you entered in the tool about your family's history of cancer, your chances of having a BRCA1 or BRCA2 gene mutation are higher than for most women in the U.S. At least 1 in 100 women with a family history of cancer like yours has a BRCA1 or BRCA2 gene mutation.

Being at "**increased risk**" for a BRCA1 or BRCA2 gene mutation:

- Means that you **MAY** have a higher chance of getting breast or ovarian cancer than other women.



Patient Interface – Step 6: Plan



Could you have a gene causing Hereditary Breast and Ovarian Cancer?



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- Your Paternal Cousins
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- Enter Mother's Side Cancer History
- View Mother's Side Cancer History
- Enter Father's Side Cancer History
- View Father's Side Cancer History

STEP 4: CALCULATE

STEP 6: PLAN FOR YOUR VISIT WITH THE DOCTOR

In this step, you will create an action plan for talking to your doctor about your risk of having a BRCA1 or BRCA2 gene mutation.

Now that I know my chances of having a BRCA1 or BRCA2 gene mutation, what should I do next?

This step will help you create an action plan based on your chances for having a BRCA1 or BRCA2 gene mutation. You can print this action plan when you are done.

Your action plan should focus on:

- Talking about the results of this tool with your doctor.
- Getting your questions answered.
- Deciding whether to see a genetic counselor.

To help make your action plan, you can first learn more about:



Patient Interface – Action Plan

CANCER IN THE FAMILY

COULD YOU HAVE A GENE CAUSING HEREDITARY BREAST AND OVARIAN CANCER?

Your Action Plan

Your Risk Result

You may be at increased risk for having a BRCA mutation

Now that you know your chances of having a BRCA1 or BRCA2 mutation, you should talk to your primary care provider about next steps.

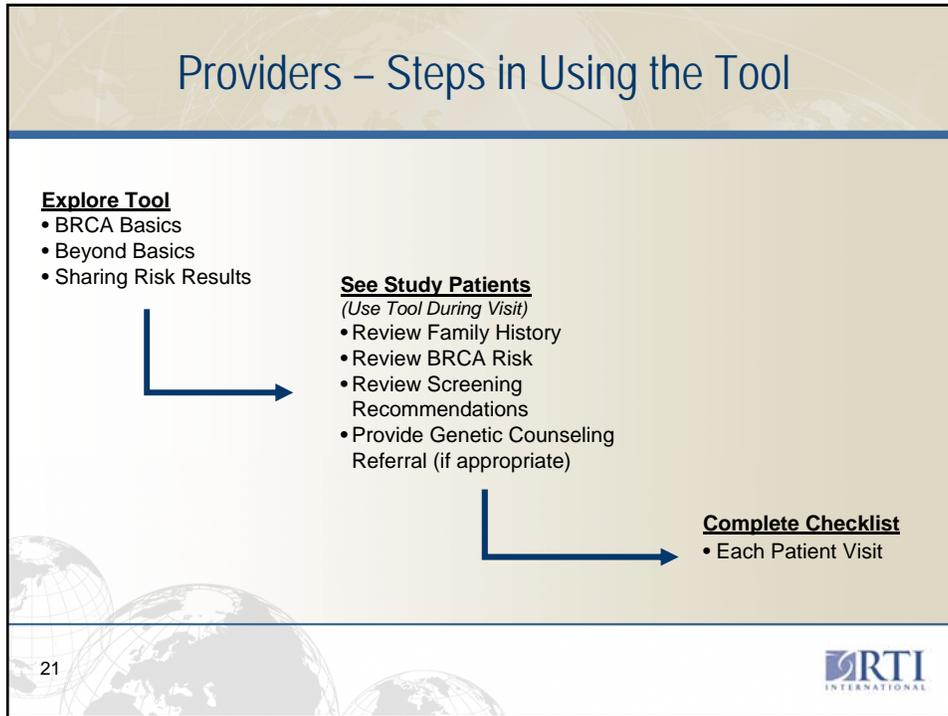
This printout is your action plan. It provides tips on talking to your doctor, lists the questions you want to ask your doctor, and depicts your family tree and family cancer history. Bring this printout to your next appointment and share it with your doctor.

Remember, this tool simply tells you your chances of having a BRCA1 or BRCA2 mutation. It cannot tell if you actually have a mutation, and it cannot tell if you have cancer. You and your doctor should discuss your family history and decide together if genetic testing makes sense.

Tips for Talking to Your Doctor

Here are some suggestions for talking to your doctor about your family cancer history.

1. **Give information.**
Tell your doctor what you know about your family's history of cancer. Don't wait to be asked.



Provider Interface – Patient List

Could you have a gene causing Hereditary Breast and Ovarian Cancer?

Home
BRCA Basics
Beyond Basics
Sharing Results - Increased Risk
Sharing Results - NOT at Increased Risk

References
Additional Resources
Glossary
Logout

Patient List

Patients that have been assigned a Username from your site are listed below.

If you are a PROVIDER, you will see the patient's calculated BRCA risk probability once calculated by the patient. You may click on View Output for the PDF output of the patient's pedigree and results. Once you have completed the visit with the patient, click on the Checklist icon to record information about the patient interaction.

If you are a SITE ADMINISTRATOR, you will be able to see important dates of progression as the patient makes her way through the tool. You will also be able to EDIT information in this table to add the patient's appointment date as well as the patient's initials and year of birth to be used as a visual identifier for the provider.

Click here to view the [User Guide](#).

USERNAME	Patient ID	Appt Date/Time	Provider Name	Results	Risk Results PDF	Checklist	Checklist Date
DJGXE	RTII	4/12/2010 12:00:00 AM	Dr A				
DVAYM	INC RISK	4/15/2010 2:00:00 PM	Dr. Smith	★ Increased Risk			
DTMZK	LOW RISK	4/15/2010 3:00:00 PM	Dr. Jones	★ Not at Increased Risk			
DHHVY							
DIUZT							
DXOVU							
DIWSH							
DXQOI							
DIWOTO							

Provider Interface – *BRCA Basics*



Could you have a gene causing Hereditary Breast and Ovarian Cancer?



Home	BRCA Basics	Beyond Basics	Sharing Results - Increased Risk	Sharing Results - NOT at Increased Risk
References	Additional Resources	Glossary	Logout	

BRCA Basics

Click on each heading to learn more.

- [Importance of BRCA Screening in Primary Care](#)
- [Primary Care Provider's Role](#)
- [How this Tool Uses Cancer Family History to Calculate *BRCA* Carrier Risk](#)
- [Next Steps for Cancer Screening After Risk Is Calculated](#)



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Provider Interface – *Beyond Basics*



Could you have a gene causing Hereditary Breast and Ovarian Cancer?



Home	BRCA Basics	Beyond Basics	Sharing Results - Increased Risk	Sharing Results - NOT at Increased Risk
References	Additional Resources	Glossary	Logout	

Beyond The Basics: Additional Resources and Information

Click on each heading to learn more.

- [Information on the Genetics of Breast Cancer and Ovarian Cancer](#)
- [Information on How This Tool Will Use Cancer Family History to Calculate *BRCA* Carrier Risk](#)
- [What You and Your Patients Need to Know About Genetic Discrimination](#)
- [Why Should I Refer My Patients Who Are At Increased Risk of HBOC to a Genetic Counselor?](#)
- [The Shared Decision-Making Process](#)
- [Information on Preventive Treatments That Are Available for *BRCA* Mutation Carriers](#)
- [View Risk Examples](#)
- [Additional Web Links](#)



Provider Interface – Sharing Results



Could you have a gene causing Hereditary Breast and Ovarian Cancer?



Home	BRCA Basics	Beyond Basics	Sharing Results - Increased Risk	Sharing Results - NOT at Increased Risk
References	Additional Resources	Glossary	Logout	

Sharing Results - Increased Risk

For more detailed information, click on the headings below.

1. Review your patient's family history and confirm it is complete and accurate
2. Explain what it means to be at "increased risk"
3. Discuss recommendations and next steps
4. Referral to genetic counseling
5. Review your patient's medical record
6. Address questions from your patient
7. Check patient understanding

[Additional Resources](#)



Provider Interface – Sharing Results



Could you have a gene causing Hereditary Breast and Ovarian Cancer?



Home	BRCA Basics	Beyond Basics	Sharing Results - Increased Risk	Sharing Results - NOT at Increased Risk	Referen
Glossary	Logout				

Sharing Results - Increased Risk

For more detailed information, click on the headings below.

1. Review your patient's family history and confirm it is complete and accurate
 - Review your patient's family history they entered in the webtool.
 - Confirm that there are no missing pieces of information, outstanding questions, or new information that needs to be entered.
 - If any changes are made to the cancer family history, rerun the BRCAPRO algorithm to display your patient's most current risk results.
2. Explain what it means to be at "increased risk"

Explain to patient:

"Based on the information you provided about your family's history of cancer, your chance of having a BRCA1 or BRCA2 mutation is higher than it is for most people in the United States. At least 1 in 100 women with a family history of cancer like yours has a BRCA1 or BRCA2 mutation."

What being at "increased risk" DOES NOT mean:

Provider Interface – Additional Resources



Could you have a gene causing Hereditary Breast and Ovarian Cancer?



Home	BRCA Basics	Beyond Basics	Sharing Results - Increased Risk	Sharing Results - NOT at Increased Risk
References	Additional Resources	Glossary	Logout	

Additional Resources

Click here for more information on the **genetics of breast and ovarian cancer**:
<http://www.cancer.gov/cancertopics/pdq/genetics/breast-and-ovarian/HealthProfessional/page1>

Click here for more information on **GINA**:
<http://www.genome.gov/Pages/PolicyEthics/GeneticDiscrimination/GINAInfoDoc.pdf>

Click here for more information on **Shared Decision Making in Healthcare**:
<http://www.informedmedicaldecisions.org/>

Click here for more information on **chemoprevention**:
<http://www.ahrq.gov/clinic/3rduspstf/breastchemo/breastchemorr.pdf>

Click here for more information on **prophylactic surgeries**:
<http://www.ahrq.gov/clinic/uspstf05/brcagen/brcagenrs.pdf>

For additional information on **preventive treatments**, click on this link for the National Cancer Institute FactSheet on BRCA1 and BRCA2 Cancer Risk and Genetic Testing:
<http://www.cancer.gov/cancertopics/factsheet/Risk/BRCA>

Mammography

- The USPTF indicates that women who are at increased risk for breast cancer (including those with a family history of breast cancer) are likely to benefit from regular mammography and that routine screening can begin in their 40s.

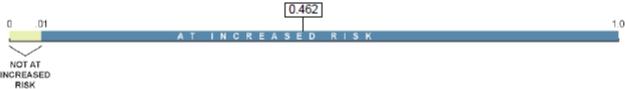
Provider Interface – Patient Risk Results

Username: DVAYM

CANCER IN THE FAMILY: COULD YOU HAVE A GENE CAUSING HEREDITARY BREAST AND OVARIAN CANCER?

Your Patient's Risk Result and Family History

Risk Category: Increased Risk
Mutation Probability Score: 0.462



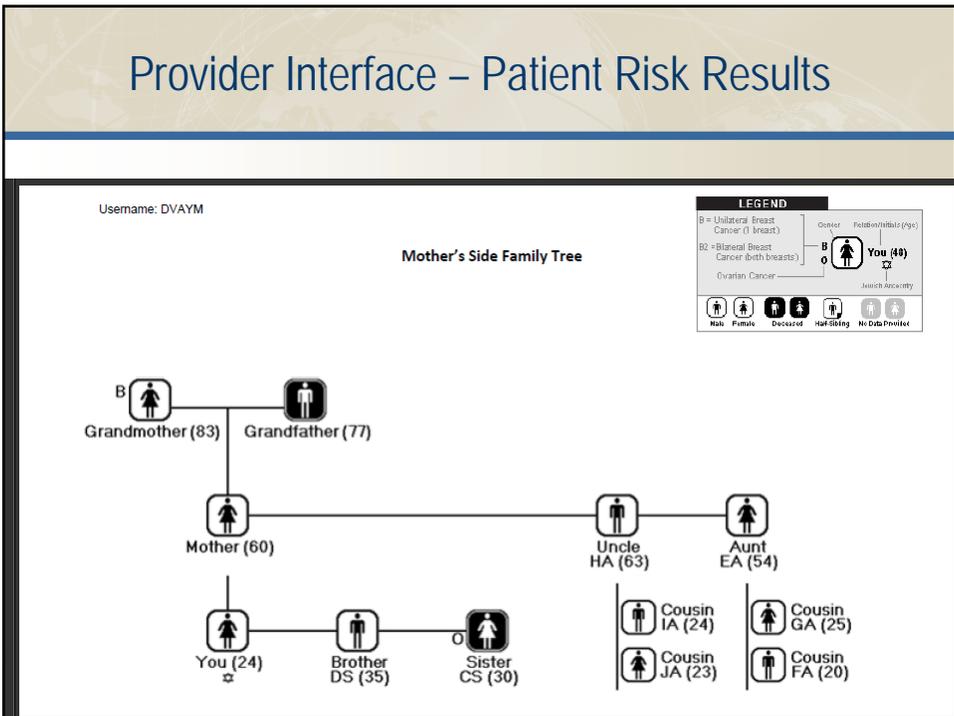
For reference, the tool categorizes patients as increased risk if their score is above **0.01**. Patients who have a score between **0.0** and **0.01** are not at increased risk.

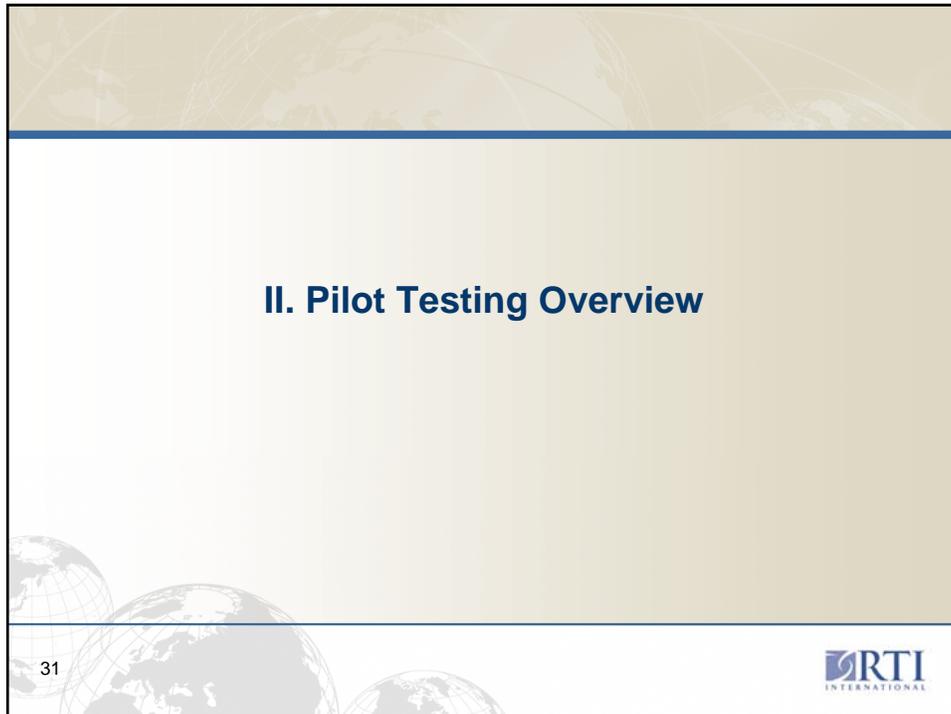
This printout is a summary of the patient's risk result and family history. The following pages provide a table and pedigree of the patient's family members, their history of cancer, and their life status.

Provider Interface – Patient Risk Results

Family History Summary – Data Supplied

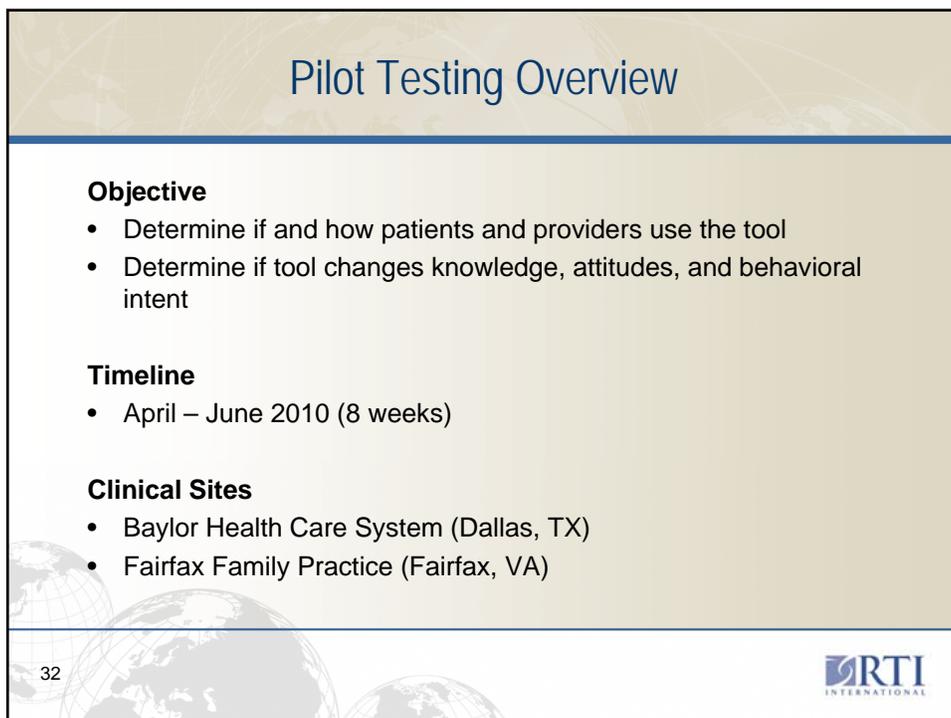
Relationship to Patient	Initials	Gender	Age (now or at death)	Breast Cancer	Age at Diagnosis	Ovarian Cancer	Age at Diagnosis	Ovaries Removed	Age Ovaries Removed
Paternal Grandfather		Male	90						
Paternal Grandmother		Female	38	uni	37				
Maternal Grandfather		Male	77						
Maternal Grandmother		Female	83	uni	62				
Father		Male	65						
Mother		Female	60					Yes	45
You		Female	24						
Sister	CS	Female	30			Yes	28		
Brother	DS	Male	35						
Maternal Aunt	EA	Female	54						
Maternal Uncle	HA	Male	63						
Maternal Female Cousin	GA	Female	25						
Maternal Male Cousin	FA	Male	20						
Maternal Female Cousin	JA	Female	23						
Maternal Male Cousin	IA	Male	24						
Paternal Aunt	GS	Female	60					Yes	36
Paternal Uncle	JS	Male	63						
Paternal Female Cousin	IS	Female	42						
Paternal Male Cousin	HS	Male	40						
Paternal Female Cousin	LS	Female	30	uni	30				
Paternal Male Cousin	KS	Male	28						





II. Pilot Testing Overview

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Pilot Testing Overview

Objective

- Determine if and how patients and providers use the tool
- Determine if tool changes knowledge, attitudes, and behavioral intent

Timeline

- April – June 2010 (8 weeks)

Clinical Sites

- Baylor Health Care System (Dallas, TX)
- Fairfax Family Practice (Fairfax, VA)

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Pilot Testing Participants

Patient Participants

- Women with scheduled annual exams
- Age 21-60, English fluency
- No personal cancer history
- Residential access to computer / Web

Provider Participants

- Primary care provider
- Scheduled to see patients during pilot
- Number of providers involved varies by site

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Site Coordinators

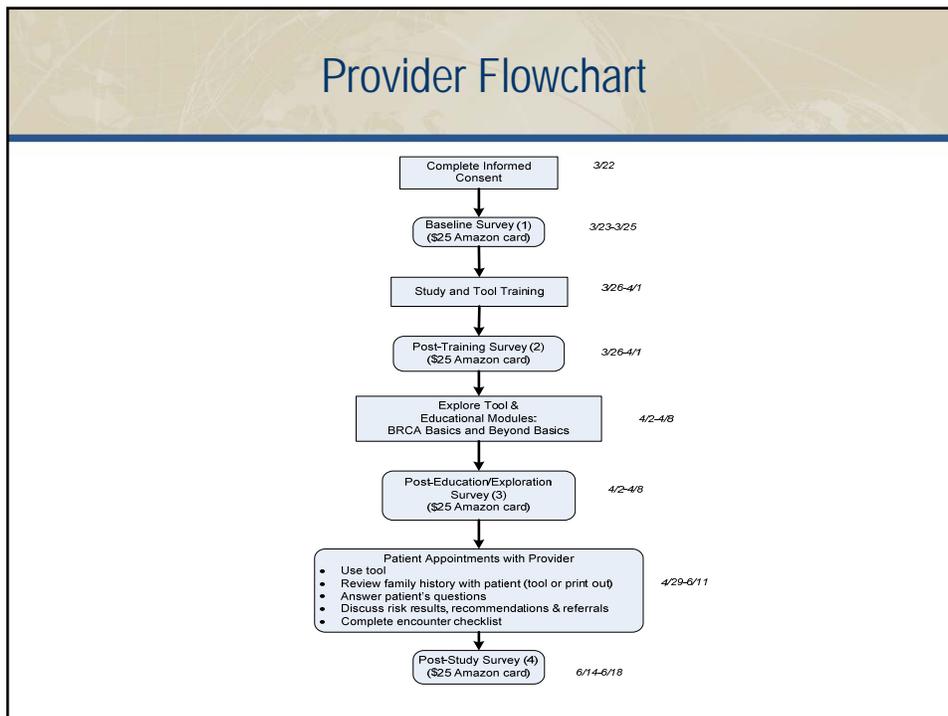
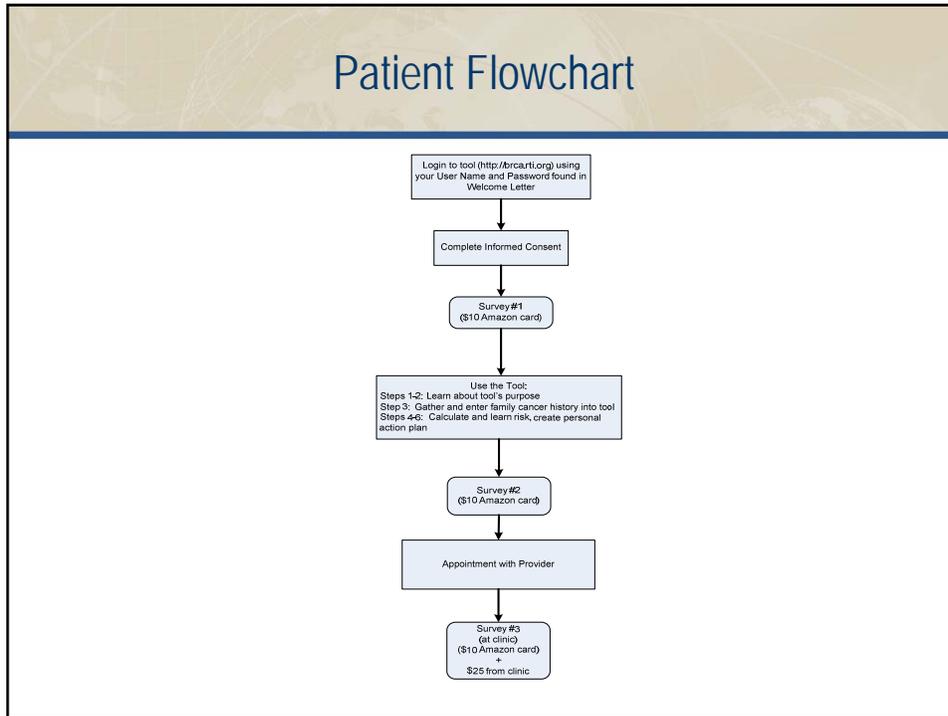
Site coordinators are here to help!

Coordinator Responsibilities

- Identify and recruit patient participants
- Track patient progress, ensure tool usage
- Reminder calls to patients
- Help providers navigate study protocol

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III. Provider Role / Responsibilities

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Provider Role

To help patients understand the meaning and implications of their risk assessment results

- Review family cancer history
- Discuss risk for BRCA mutation
 - Increased risk vs. Not at increased risk
 - Risk of BRCA mutation vs. Risk of cancer
- Recommend cancer prevention and screening
- Refer to genetic counseling (if appropriate)

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Initial Responsibilities

- Login
- Complete baseline survey
- Complete study training & post training survey
- Explore tool
 - BRCA Basics
 - Beyond Basics
 - Sharing Risk Results
 - Sample Cases
- Complete post-education survey
- Complete provider diary weekly

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Clinic Visit Responsibilities

- Login
- Select patient record
- Assess patient tool use
- Review (or edit) family history
- Review (or re-calculate) risk result
- Discuss family history and BRCA risk with patient
- Offer recommendations and referrals
 - Screening
 - Genetic counseling
- Complete visit checklist
- Save patient results in EMR (optional)

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Provider Interface – Visit Checklist



**Cancer
IN THE
FAMILY**

*Could you have a gene causing
Hereditary Breast and Ovarian Cancer?*



Home	BRCA Basics	Beyond Basics	Sharing Results - Increased Risk	Sharing Results - NOT at Increased Risk
References	Additional Resources	Glossary	Logout	

Provider Checklist

This patient's risk for having a BRCA mutation was:

Not at Increased Risk Increased Risk N/A: Assessment not run

When did you use the tool to review this patient's risk results?

before patient's appointment during patient's appointment N/A: did not use tool

Did you refer this patient for genetic counseling?

Yes No

What other referrals did you provide to this patient?

Mammography Pap test Colorectal cancer screening

Other, please specify:

During the patient's visit, which of the following did you do with the patient?

Provider Diary

- Utility of the Tool (e.g., features/content)
- Effect on Workflow
- Review of Risk Results
- Challenges
- Facilitators
- Patients' Responses to Tool
- Effect of Tool on Communication with Patients



Key Contacts

Study Protocol / Patient Appointments

BAYLOR HEALTH CARE SYSTEM

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