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A decision aid for additional findings in genomic sequencing: Development and pilot testing

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ABSTRACT

Objective: To describe the development of a web-based, patient-facing decision aid to support patients and research participants to make an informed, values-based decision about whether to receive additional results from genomic sequencing.
Methods: We developed the decision aid following the multi-step process described in the International Patient Decision Aids Standards. This utilized literature review, focus groups, and alpha testing with research participants undergoing clinical genomic sequencing.
Results: The decision aid, the Optional Results Choice Aid (ORCA), includes a seven-question "values clarification exercise," illustrative patient quotes, and summative guidance for the user. The decision aid was found to be highly readable, acceptable and relevant in alpha testing.
Conclusion: We developed a decision aid to support informed, values-based decision making for patients and research participants considering whether to receive additional results from genomic sequencing. ORCA is being implemented in the NHGRI-funded Cancer Health Assessment Reaching Many (CHARM) study, where we are measuring informed values-choice congruence.
Practice implications: ORCA was designed to support patients and research participants to make an informed, values-based decision about whether to receive additional results from genomic sequencing.

1. Introduction

In March 2013, the American College of Medical Genetics (ACMG) published a policy statement advocating the return of medically actionable additional findings (often referred to as secondary or incidental findings) for patients receiving genomic sequencing. [1] ACMG Working Group on Incidental Findings in Clinical Exome and Genome Sequencing recommended that laboratories seek and report additional findings in genes where preventative measures and/or treatments were available would likely result in medical benefit for the patients and families of patients undergoing clinical sequencing [1]. However, concerns arose that this recommendation did not respect patient autonomy, also known as the "right not to know." [2–4] Therefore, in November 2014, the policy was revised to allow patients to choose to opt out of receiving the additional findings of their genomic sequencing [5]. Clinicians and researchers need tools that encourage individuals to make informed choices about whether or not to receive these additional findings.

Previous studies have shown that when given the choice, most people choose to receive all additional findings [6–8]. When asked about their considerations regarding choices about medically actionable additional findings, many adults report feeling that it is better to have this information than not. However, they also report valuing the opportunity to choose whether or not to receive additional findings [7]. Although decisional conflict about receiving medically actionable findings is generally low, there is greater decisional conflict among patient populations with lower education and health literacy levels and with lower self-efficacy in coping with positive findings [8].

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Effective decision making as defined by the multi-dimensional model of informed choice (MMIC) identifies three key dimensions: knowledge, values, and the extent to which the choice made reflects values [9]. Receiving additional findings from genomic sequencing is not a familiar health care decision to most; an effective decision aid for this choice may promote informed, value-based decisions by informing patients about additional findings, assessing their related values, and guiding them toward a choice that matches their values [10].

As genomic sequencing becomes more routine, decision aids for additional findings may improve the efficiency and effectiveness of genetic counseling [11–13]. We are aware of three such decision aids: Genomics ADViSER, DECIDE and the decision aid used in the Baby Beyond Hearing study [14–16]. The latter two are both designed for parents choosing to receive additional findings for their children [15,16]. Genomics ADViSER is targeted towards adults but was evaluated in a cohort making a hypothetical decision rather than an actual decision [17].

Here we describe the design of the Optional Results Choice Aid (ORCA), a web-based, patient-facing decision aid about the option to receive medically actionable additional findings from genomic sequencing that is accessible to adults with low literacy. We designed this tool as part of the ongoing NHGRI-funded Cancer Health Assessments Reaching Many (CHARM) study in which research participants who are at risk of a hereditary cancer syndrome undergo genomic sequencing and are given the option to receive additional medically actionable findings. This decision aid was designed to support informed, values-based decision making, meaning that the user has sufficient relevant knowledge and makes a choice that is congruent with their values.

2. Methods

2.1. Study setting

CHARM is a clinically embedded study at Kaiser Permanente Northwest (KPNW), an integrated health plan serving an all-insured population in Oregon and southwest Washington, and Denver Health, a safety net health care system serving patients with and without insurance in Colorado. CHARM is focused on identifying ways to reduce health disparities in genomic sequencing for hereditary cancer risk. Patients who are at risk for a hereditary cancer syndrome based on personal or family history of cancer, or who lack sufficient family history information to determine risk are recruited. Eligible participants complete a multi-step online education and study consent process that includes offering participants the choice to receive additional findings. ORCA is being implemented at the point of making this decision.

The KPNW IRB approved this study. All collaborating IRBs (see acknowledgements for full list) ceded to KPNW except for Dana Farber Cancer Institute which reviewed and approved the study separately.

2.2. Multi-step framework

ORCA was developed using the framework described by Coulter et al. and put forth by the International Patient Decision Aids Standards (IPDAS) collaboration, which consists of five steps: (1) defining the scope, (2) design, (3) prototype development, (4) alpha testing and steering committee review, and (5) beta testing (Fig. 1) [18]. Here we focus on the first four steps; beta testing is occurring as a randomized controlled trial and will be reported separately.

2.2.1. Defining the scope

Consistent with the IPDAS framework for defining scope, the ORCA decision aid supports a target audience of low-literacy adults undergoing genomic sequencing to make a choice about receiving additional findings. Key information about additional findings was developed by the CHARM team and patient advisory committee (PAC), which included community members with an interest in the study (Table 1). In addition, we planned to include three additional components in the decision aid: a values clarification exercise, patient quotes, and summative guidance [19–21]. We also planned a comprehension assessment administered in a survey after using the decision aid to test understanding of key information about additional findings [22]. Beginning in November 2019, the randomized controlled trial, with the decision aid used in one arm and web-based information used in the other arm, compared achievement of "informed values-choice congruence" [22].

2.2.1.1. Literature review. Through literature review, ASF and EGL identified constructs (i.e., themes we wished to evaluate) relevant to the consideration of receiving additional findings. These were divided into subjective considerations such as individual priorities and personal or family circumstances ('values constructs') and information pertinent to making the decision about receiving additional findings ('knowledge constructs'). The PubMed search tool was used with the following keywords: 'incidental findings,' 'secondary findings', 'additional findings', accompanied by 'genomic sequencing' or 'exome sequencing' and was limited to articles in English. The PubMed related article search function was also used to find additional relevant articles [23]. In total, 15 qualitative studies evaluated the perspectives of patients and

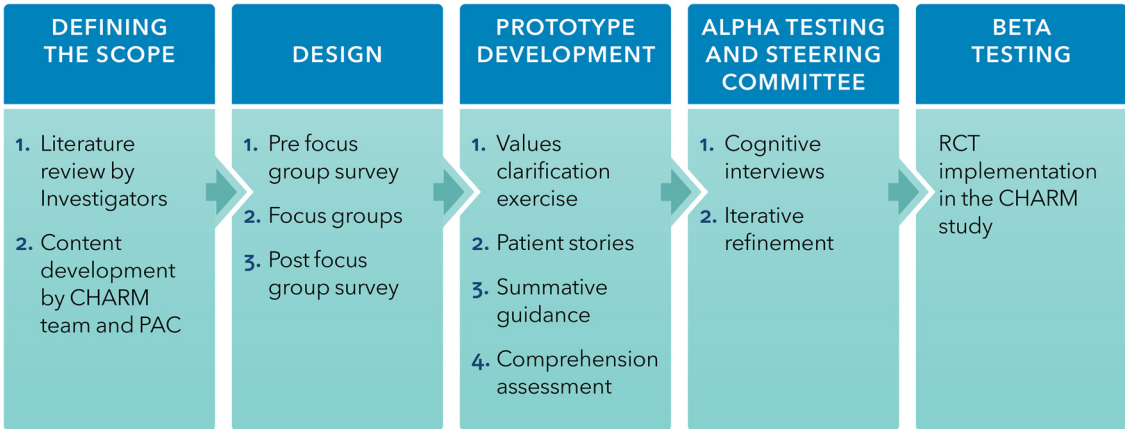

Fig. 1. Multi-step Framework for Development. PAC = patient advisory committee.

Table 1
Description of groups involved in decision aid development.

Group Title	Group Description
CHARM team	A multidisciplinary group of over 30 researchers and clinicians in genetics, genetic counseling, oncology, medical anthropology, primary care medicine and bioethics
CHARM Patient Advisory Committee (PAC)	A representative group of 17 health system members (patients) from both study settings who helped develop study materials prior to recruitment of participants. Two PAC members were interviewed for feedback about the decision aid.
Focus groups	A subset of 8 members of the CHARM team who participated in a modified Delphi method of surveys and focus groups. It included genetic counselors, geneticists, genetic researchers and ethicists
Multidisciplinary Steering Committee	A subset of 13 CHARM team members who oversaw the development and implementation of the decision aid portion of the CHARM study and included clinical geneticists, genetic counselors, a primary care internist with decision aid design experience, medical anthropologists, a biostatistician, bioethicist and programmer/web designer.
CHARM study participants	967 health system members (patients) at both study sites who had enrolled to participate in the CHARM study. Eleven were recruited for cognitive interviews during the alpha testing step.

research participants, healthcare providers, and the general population about values or information relevant to receiving additional findings; from these, we extracted an exhaustive list of 14 values constructs and 19 knowledge constructs. After eliminating constructs pertaining to receiving carrier findings, non-medically actionable findings, or other categories of additional findings, the list was narrowed to 8 values constructs and 10 knowledge constructs (Table 2).

2.2.2. Design

2.2.2.1. Obtaining expert consensus. To develop a consensus among the CHARM team, we used a modified Delphi method to gather feedback (Table 1). Neither PAC members nor study participants were included in the focus groups due to time constraints. This approach consisted of an initial ("pre-focus-group") survey, followed by two semi-structured focus groups (one each on values and knowledge constructs), and finally, a second ("post-focus-group") survey [24]. The purpose was to finalize the list of value and knowledge constructs most important and relevant to decision aid users and refine user-facing language representing each of the constructs [25]. In the pre-focus group survey, team members were asked to assess the importance of each construct on a 4-point scale (Supplement 1). During the focus groups, members reviewed the survey results, eliminated constructs rated as less important, and refined language.

2.2.2.2. Validation of values clarification exercise and comprehension assessment. In the post-focus group surveys, we asked the eight focus group members to rate the clarity and relevance of the user-facing language representing the underlying construct. Each statement for the values clarification exercise and question for the comprehension assessment was rated using a 4-point scale (Supplement 1).

2.2.3. Prototype development

The design steps above resulted in the values clarification exercise and comprehension assessment. The decision aid prototype incorporated the key information that had been developed by the CHARM team and patient advisory committee and refined in the expert consensus process, and the values clarification exercise, as well as illustrative quotes and summative guidance, described in the next section. All content was text-based, written at a fourth grade reading level in English, with no audio or video component [26]. The comprehension assessment questions were administered separately from the decision aid.

2.2.3.1. Drafting of patient quotes and summative guidance. Previous studies of decision aids have demonstrated that research participants considering additional findings want to hear stories and patient quotes illustrating how other patients made this choice [15]. Accordingly, ASF and EGL drafted patient quotes, adapted from those located in the literature review of

Table 2
Constructs Assessed for Consensus.

Values Constructs	Consensus Range 0–4 points where 4 = very important
Desiring as much information as possible	3.5
Providing risk information to blood relatives	3.25
Being unwilling or unable to have additional tests or medications	3.25
Anxiety about test results showing a higher chance for a health problem	3
Worrying that results could adversely affect lifestyle	2.75
Desiring to monitor or treat potential health problems	2.5
Feeling comfortable with additional doctors' visits	2
Worrying about an effect on insurability	2
Knowledge Constructs	**Consensus Range 0–4 points where 4 = very important**
All conditions tested for are considered medically actionable	4
Negative test results do not mean a "clean bill of health"	3.75
A positive result indicates an increased genetic risk, not a clinical diagnosis	3.5
Negative results do not rule out a genetic condition	3.5
Relatives can be tested if there is an additional finding	3
These findings are typically incidental, and patients are asymptomatic	2.5
A law protects against discrimination based on genetic test results for health insurance but not life or disability insurance.	2.25
These results are separate from the primary findings.	2.25
Most people will have one or less additional results	2
Most conditions are inherited in a dominant pattern (i.e., first degree relatives have a 50 % chance of having the same genetic risk, if found).	1

patient stakeholder qualitative studies, to illustrate reasons for and against receiving additional findings (Box 1) [4]. Guidance, in the setting of a web-based patient decision aid, refers to an automated summary of the user's values [21]. We drafted summative guidance to provide feedback to users about how their responses to the values clarification exercise reflected their attitude towards receiving additional findings (Box 2). Feedback about the quotes and summative guidance was solicited during the focus groups as well but no significant changes were made.

2.2.4. Alpha testing and steering committee review

To further refine the prototype decision aid and comprehension assessment questions, we conducted semi-structured cognitive interviews initially with two CHARM PAC members followed by eleven CHARM study participants (Table 1) [18]. The goals of these interviews were to assess the content for *readability* (clarity of the text), *relevance* (importance of content to the individual experiences of participants), and *acceptability* (word choice and phrasing experienced as inoffensive and relatively easy to answer). The iterative process of revising the decision aid and the questions repeatedly over the series of interviews was overseen by a multidisciplinary steering committee consisting of 13 CHARM team members (Table 1).

2.2.4.1. CHARM study participant identification and recruitment. The first two interviews were with two members of the CHARM patient advisory committee, and additional interviews were with CHARM study participants (Table 1). Study participants were eligible for an interview if they spoke English and had already completed CHARM study enrollment and consent (including choosing whether or not to receive additional findings) but had not yet received results. Eligible participants were contacted by email, followed by a phone call, and were offered a gift card as compensation for their time. Those who agreed to participate received the decision aid and comprehension assessment via email, then participated in a 45 – 60-minute phone interview.

2.2.4.2. Data collection. We developed an interview guide that focused on relevance, readability, and acceptability (Supplement 2) of both the decision aid and comprehension assessment questions. One of three interviewers (ASF, EGL and IG) conducted eleven interviews between July and August 2019. All interviews were recorded and transcribed, and interviewers also took notes. Data collection ceased when we reached thematic saturation, meaning that we determined it was unlikely that additional insights would be gleaned from participants' feedback.

2.2.4.3. Data analysis. Each interview transcript was analyzed focusing on data pertinent to the concepts of relevance, readability and acceptability. We analyzed interview transcripts sequentially, discussed findings with the steering committee each week, and shared a revised version of the decision aid with subsequent interview participants. The steering committee revised parts of the prototype if multiple participants mentioned similar concerns about relevance or acceptability or if revisions were deemed to improve readability and clarity. Suggestions by participants were not incorporated if the committee decided (1) they were not widely applicable; (2) the suggested content would limit the use of the tool outside the study context; or (3) their incorporation would make the decision aid significantly longer. For example, several participants suggested including information in the decision aid about the turnaround time for receiving the results, but this was not included as it would not be generalizable outside of the CHARM study. All data analysis was done manually, no qualitative software programs were utilized due to the small number of transcripts.

3. Results

3.1. Design

3.1.1. Pre-focus group survey

In the pre-focus group consensus survey, most of the eight values and ten knowledge constructs were rated as somewhat or very important (Table 2). However, the focus group on the values constructs revealed a more nuanced discussion of the unique importance and relevance of each construct. Participants suggested eliminating the construct "worrying about adverse impact on lifestyle." Participants felt this construct was redundant with two other constructs: "anxiety about a higher genetic risk" and "concerns for additional doctor's visits." Thus, there were seven remaining constructs from which statements were drafted for the values clarification exercise.

During the focus group on the knowledge constructs, members identified four constructs that they felt were paramount to a participant having sufficient relevant knowledge to make an informed choice: (1) "All conditions represented by additional findings are medically actionable"; (2) "Negative results, i.e., a lack of additional findings, does not mean a 'clean bill of health'"; (3) "A positive result, i.e. the presence of an additional finding, indicates an increased genetic risk, not a clinical diagnosis;" and (4) "These additional findings are typically incidental and patients have no symptoms." Three of these had scored the highest in the pre-focus group survey. The focus group members ranked down two knowledge constructs, residual risk and cascade testing (rated as highly important on the pre-focus group survey) to lower priorities. The construct of residual risk of other genetic conditions (i.e., absence of additional findings does not rule out another, undetected genetic condition) was thought to be redundant with the construct that negative results (i.e., absence of additional findings) do not mean a "clean bill of health." The concept of cascade testing (i.e., "Relatives can be tested if there is an additional finding") was deemed not highly relevant for a participant at the point of deciding about receiving additional findings given it could be addressed in post-test counseling in the event of a positive additional result. Twelve true/false questions (three for each of the four prioritized constructs) were drafted to make up the comprehension assessment.

3.1.2. Post-focus group survey

Table 3 lists the final seven statements for the values clarification exercise and twelve questions with their relevance

Box 1. Patient Quotes

"If there's something else going on with my health, I'd like to know now. If there's treatment or things that I'm doing that I need to stop doing, I'd definitely like to know that."
"I'd rather be surprised than know a health problem is coming, even if it would have changed my doctor's recommendations. I don't think I want to live the rest of my life knowing that I have a higher chance of something than most people."

Box 2. Summative Guidance

Your answers suggest that you strongly/somewhat agree with getting these results, but you can still choose not to get the results if you do not want them.
Your answers suggest that you strongly/somewhat disagree with getting these results but you can still choose to get the results if you want them.

Table 3
Construct validation.

Values Statement	Relevance score	Clarity score
I want to know as much as possible about my health	1	1
I would worry if I knew I had a higher chance of a health problem	1	1
I am comfortable working with my doctors to take care of my health	0.9	0.9
I want to let family members know if my test result is not normal so that they can think about being tested too.	0.8	0.7
I am worried that these results might affect my ability to get life or disability insurance	1	1
I want to take steps to prevent, find or treat future health problems	1	1
It would be difficult for me to take more medication of to have more medical appointments right now.	1	1
Knowledge T/F Question	**Relevance score**	**Clarity score**
If the results for these other health problems is normal, I could still get other health problems	1	0.6
If the test results are normal, I can stop going to my doctor for check ups.	0.9	0.9
If the results are normal, I will definitely be healthy for years to come.	0.8	0.9
If the test finds that I have a higher chance of having a health problem, I will definitely get that health problem in the future.	0.8	0.9
Even if the test shows I have a higher chance for a heart problem, I know I won't get the heart problem because everyone in my family is healthy.	0.9	0.9
If the test results show a higher chance for a health problem, I might get that health problem.	0.8	0.9
If the test shows that I have a higher chance of high cholesterol, there is nothing that can be done to protest me from heart problems from high cholesterol.	0.9	0.9
If the test finds a higher chance for a heart problem, my doctor may recommend more check ups or certain medications.	0.9	1
If the results show a higher chance for a health problem, a chance in my medical care could help me.	0.8	0.7
Some people choose to get these additional findings because it could lead to finding a health problem early.	0.8	0.7
I do not feel sick so my test results will definitely be normal.	0.6	0.8
I could have a result that is not normal even though I see my doctor every year for a check up and have always been healthy.	0.8	0.9

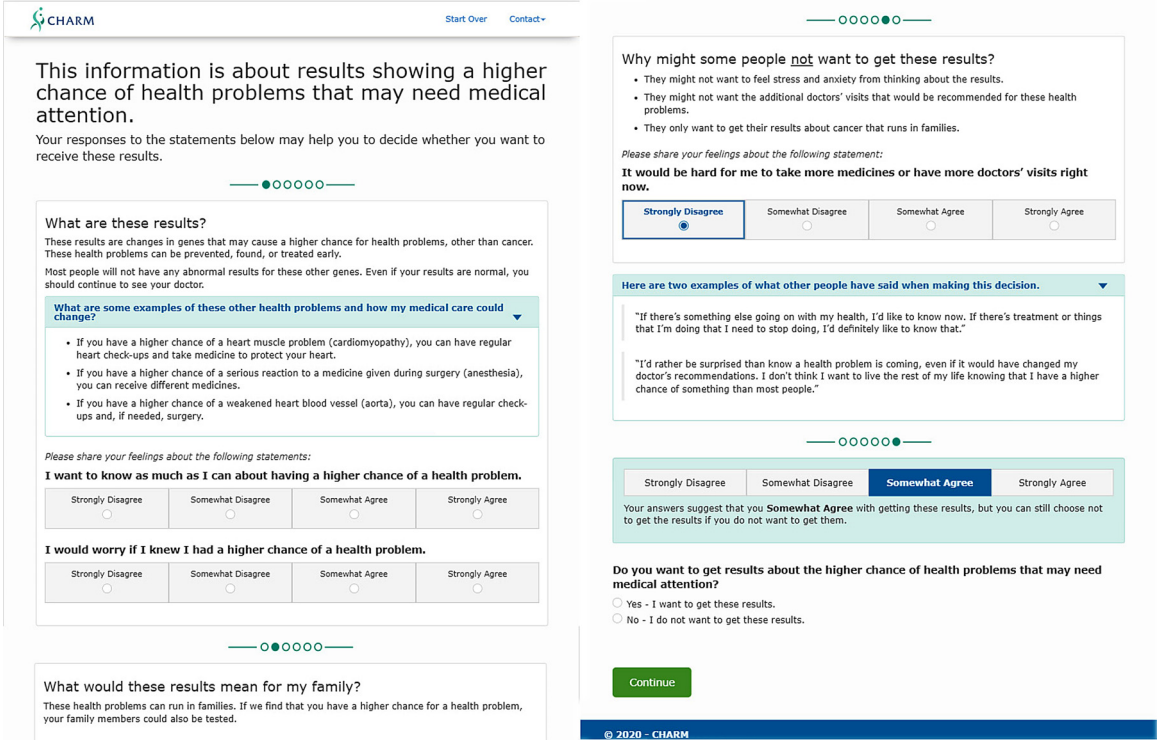

Fig. 2. Sample screen shots. These screen shots show part of the values clarification exercise as well as the patient quotes and summative guidance.

and clarity scores from the post-focus group survey (Table 3). Most were rated as highly relevant and clear. Statements with a score less than or equal to 0.7 were revised by the steering committee prior to incorporation in the prototype.

3.2. Decision aid prototype

Sample screen shots of the decision aid are presented in Fig. 2 and the full tool is available in Supplement 3. The steering committee organized the information into sections, each followed by 1–2 values statements that the user rates on a 4-point Likert scale from "strongly agree" to "strongly disagree." As such, the values clarification exercises are interspersed with the information rather than clustered at the end. Following the information and values statements are two patient quotes, illustrating each perspective (Box 1). The user then receives summative guidance about which decision aligns most with their responses in the values clarification exercise (Box 2). Finally, participants must make the decision to complete enrollment in the CHARM study: "Do you want to get results about the higher chance of health problems that may need medical attention?"

3.3. Alpha testing and steering committee review

3.3.1. CHARM study participant characteristics

Table 4 provides demographic information about the eleven CHARM participants interviewed in the 'alpha testing' step of development, as well as their responses to questions about participation in the CHARM study. Seventy-three percent of interviewees identified as female and all had education beyond high school. These demographics differ from the CHARM study as a whole, which has enrolled a more diverse cohort that is 79 % female, only 57 % of participants have a post-secondary degree/training, and only 46 % of participants are non-Hispanic white. Interviewees cited wanting to know their cancer risk and other genetic information as major reasons for joining the CHARM study and did not have significant concerns about joining a research study.

3.3.2. Cognitive interview results: relevance, acceptability and readability

3.3.2.1. Informational content and values clarification exercise. A representative sample of feedback from the cognitive interviews with CHARM study participants is shown in Box 3. All interview participants found the content of ORCA to be relevant for their decision-making process. They described the information and value statements as important and helpful. No interview participant reported feeling uncomfortable with responding to any individual value statement nor feeling overburdened by completing the values clarification exercise. No revisions were made to the decision aid based on considerations of relevance or acceptability.

Participants made numerous suggestions to improve the readability of the decision aid, including suggestions for transitions between paragraphs and word choice. They also suggested replacing words to facilitate comprehension. In some cases, our initial attempts to lower the reading level and eliminate medical jargon actually led to text that was more difficult to understand. For example, when describing medically actionable conditions, we used the term "weakened and dilated blood vessel" to describe aortic aneurysms. One member of the steering committee thought this could be confused for varicose veins, and an alpha testing participant asked if this referred to an aortic aneurysm. To clarify,

Table 4
Cognitive Interview Participant Characteristics.

Participant Demographics		n (%)
Age		Range 25−49 yrs, mean 40yrs
Gender identity	Female	8 (73 %)
	Male	2 (18 %)
	Non-binary	1 (9%)
Education level	Some post-high school training	1 (9%)
	Associates (2-year) college degree	1 (9%)
	Bachelor's degree	5 (46 %)
	Graduate or professional degree	4 (36 %)
Race	White or European American	6 (55 %)
	Black or African American	1 (9%)
	American Indian, Native American or Alaska Native	1 (9%)
	Mixed race and ethnicity	3 (27 %)
Household income	< $40,000	2 (18 %)
	$40,000–79,999	5 (46 %)
	≥ $80,000	4 (36 %)
Insurance type	Private, employment based	10 (91 %)
	Medicaid	1 (9%)

Participant Decision and Attitudes	n
Decision for Medically Actionable Additional Findings	
Yes	10
No	1
Reasons for joining CHARM (participants were able to make multiple selections)	
I want to know my future cancer risk	8
Knowing my risk for genetic conditions may change how I take care of myself	7
I want information that may help my family	6
Knowing my risk for genetic conditions may change my healthcare	4
I want to advance research	3
I like to use the most up-to-date technology	2
Concerns about joining CHARM (participants were able to make multiple selections)	
I do not have any concerns	5
I am worried that my genetic test result may be used against me	4
I am worried about how I will cope with the genetic information I will receive	3
I have concerns about my privacy	1

Box 3. Representative comments from interview participants

Participant 4011769: "I really appreciate it [the decision-aid document]. It was very valuable, giving reasons why I wouldn't want to find out or why I would and giving a summary of pretty much along the lines of things I was thinking about."
Participant 1001181: "I felt about other health problems, that could be reworded. It seemed a little bit vague to me. I didn't have any suggestions for how to change it, but the writing didn't sound professional."
Participant 1001168: "Right now, when you say a bad reaction that could mean a lot of different things to different people. I think making it a little bit clearer that this is a severe, life-threatening thing."
Participant 2001114: "This is actually good [the value statements]. I actually really like how it incorporates the person filling out this thing, their anxiety or interpretation emotionally of what this would mean. So I thought that this was really good."
Participant 4011653: "No, there weren't any statement I would have preferred to skip or that made me feel uncomfortable."

this was rephrased as "a weakened heart blood vessel (aorta)" for the next iteration of the prototype; subsequent interviewees did not find this wording confusing.

3.3.2.2. Comprehension assessment. The comprehension assessment consisted of 12 true/false questions, three for each of the four constructs most highly prioritized in the expert focus group. Interviewees had minimal suggestions for these questions; as well, all interviewees achieved scores of 11 or 12 on the 12 questions. We thought this may have been because interviewees could refer back to the decision aid while answering the true/false questions (they had received both by e-mail beforehand). However, we did three more interviews with CHARM participants who received only the true/false questions, and these participants scored similarly. Given these results, the steering committee decided to minimize burden by shortening the comprehension assessment to eight questions (two for each of the four constructs), selecting the questions participants had indicated were most clear and readable. Eliminating one question per construct also reduced redundancy in the questions. We also added "unsure" as an option to better evaluate whether participants believed they understood the concepts and were not simply guessing the answer.

4. Discussion and conclusion

4.1. Discussion

We developed ORCA, a web-based, patient-facing decision aid to support adults choosing whether to receive medically actionable additional findings, based on relevant knowledge and consideration of one's values (Supplement 3). The tool delivers information at a fourth-grade reading level, with content based on perceived relevance, readability, and acceptability among a sample of adults at increased risk for hereditary cancer syndromes. Patients provided input into the development process at the initial step of defining the scope and during alpha testing but not during the design step. We sought to minimize complexity, and we found that pilot scores on the comprehension assessment were high.

Informed consent documents for genomic sequencing have a mean readability score of 40, corresponding to between high-school and "some college" reading levels. Half of Americans read at or below an eighth grade level [27]. Given the current limited availability of genetics providers and the need for genetic services, a web-based decision aid that reaches patients of various literacy levels is a promising way to reach a broad population, including patients in underserved areas [11,28]. Although access to the internet is not universal even in developed countries, IPDAS recommends delivering decision aids on the internet. In the context of the CHARM study, participants can access the online content tool and the decision aid on a device provided by the study at their clinic [29]. The web-based format, accessible on a smartphone, also takes advantage of increasing use of the Internet for seeking health information [30].

Previous studies have suggested that patients and research participants may prefer a staged process, with the choice regarding additional findings made after the return of primary results. Although ORCA is being used in the CHARM study as the last step of an online education and consent tool, it was designed such that it could be used separately from the CHARM study. It was designed to be completed independently by the user or prior to meeting with a genetic counselor for pre-test counseling. It could also be used after the return of primary results to facilitate a staged consent process [31].

Both the ACMG and the Institute of Medicine suggest implementing shared decision making approaches regarding disclosure of additional findings [32,33]. Decision aids for other genetic tests have been shown to improve patients' knowledge when used alone or with genetic counseling [34]. Our values-based decision aid is a supportive tool for patients who are not familiar with genomic sequencing and may feel unprepared to decide. An emphasis on values-based decision-making is important when describing a broad list of potential genetic findings that could that have differing prevalence, inheritance pattern, disease penetrance, and disease severity. Guiding participants through consideration of the values relevant to the broader ideas of medical actionability and incomplete penetrance allows them to focus on how they approach their own health management, rather than on detailed explanations of genetics and disease concepts.

Although decision aids have been developed for other types of genetic testing such as newborn screening and targeted gene panels [35–37], to date, there has been limited research on the use of decision aids for describing the benefits and risks of additional findings; in particular, there is an absence of decision aids on this topic designed for use in the absence of in-person pre-test genetic counseling [14–17,38–41]. The previously developed Genomics ADvISER decision aid provides guidance on five categories of additional findings (medically actionable, common disease risk, rare genetic diseases, brain diseases, carrier status) as an adjunct to pre-test clinical counseling for adults [14,17]. A randomized trial found that its use increased knowledge of additional findings and significantly reduced time spent in the subsequent pre-test genetic counseling session, but it did not reduce decisional conflict [17]. This evaluation was hypothetical: study participants did not actually receive genomic sequencing, so the decisional conflict evaluation may not be valid. Genomics ADvISER focuses on explaining each type of additional finding; this aid would be most appropriate for use in centers where all of these types of additional findings are available, and where pre-test genetic counseling can supplement the relative complexity of the information [14,17]. In contrast, ORCA focuses on the category of additional findings most offered in U.S. clinical labs—medically actionable findings [42]. It can be used by adults with a wide range of literacy levels, by

emphasizing simple language and reflection on a limited number of concepts and values before deciding. Altogether, ORCA constitutes a novel contribution to research on decision aids for additional findings from genomic sequencing.

Two other genomics related decision aids focus on parents considering genomic sequencing and additional findings for their children. DECIDE describes several categories of additional findings, describes the pros and cons of receiving them, and assesses parents' goals and values, with summative guidance at the end [15]. Similar to the alpha testing for ORCA, DECIDE was alpha tested in a small group of parents who had already made decisions about additional findings from genomic sequencing; this group found this decision aid acceptable and useful, but since it was not tested in a diverse group, it is unknown whether it would be effective in a broad population including those with low-literacy [15]. The decision aid for the Baby Beyond Hearing Study was provided in a paper-based format to be filled out and brought to a later genetics counseling appointment [16]. Beta testing in 106 parents of infants affected by congenital hearing loss found that thirty-two percent chose not to receive additional findings [16]. These results suggested that people make different choices about additional results based on their values and personal circumstances. Furthermore, although decisional regret was low, over a quarter of families changed their choice before return of results indicating the need for decisional support on this topic [16].

4.2. Conclusion

The research participants who participated in alpha testing of ORCA were more highly educated and of higher average socioeconomic status than the general study population of CHARM, and participants were predominantly women. This limited our ability to fully assess the accessibility of the tool to low-literacy patients. However, ORCA is being evaluated in a randomized trial among a subset of CHARM participants; the results of this evaluation will provide additional insight into its broader use in more diverse populations.

Analysis of responses to the tool will also help us understand how value clarification affects the choice to receive additional findings and whether decision aid users achieve informed values-choice congruence more often than those viewing web-based information only. Secondary outcomes will include decisional conflict, decisional regret, and time spent to make the choice.

4.3. Practice implications

We created a novel decision aid to give patients and research participants values-centered support in the choice of whether to receive additional results from genomic sequencing. Alpha testing demonstrated that the tool is relevant, readable and acceptable. Effectiveness of the tool to help users make informed, values-congruent choices, and to reduce decisional conflict and regret, will be evaluated in an ongoing randomized controlled trial. This web-based, patient facing tool could be used to support shared decision making for patients receiving genomic sequencing results.

CRediT authorship contribution statement

Amanda S. Freed: Conceptualization, Funding acquisition, Methodology, Investigation, Formal analysis, Writing - original draft, Writing - review & editing, Visualization. **Inga Gruß:** Methodology, Investigation, Writing - original draft. **Carmit K. McMullen:** Methodology, Writing - review & editing. **Michael C. Leo:** Methodology, Funding acquisition, Formal analysis. **Tia L. Kauffman:** Conceptualization, Project administration. **Kathryn M. Porter:** Writing - original draft, Writing - review & editing. **Kristin R. Muessig:** Project administration. **Donna Eubanks:** Software. **Katrina A.B. Goddard:** Supervision, Funding acquisition. **Benjamin S. Wilfond:** Supervision, Funding acquisition, Conceptualization, Writing - review & editing. **Elizabeth G. Liles:** Supervision, Conceptualization, Funding acquisition, Methodology, Investigation, Writing - review & editing.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.pec.2020.10.038.

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