Health Heritage[®], a Web-Based Tool for the Collection and Assessment of Family Health History: Initial User Experience and Analytic Validity

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Key Words

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Abstract

A detailed family health history is currently the most potentially useful tool for diagnosis and risk assessment in clinical genetics. We developed and evaluated the usability and analytic validity of a patient-driven web-based family health history collection and analysis tool. Health Heritage[®] guides users through the collection of their family health history by relative, generates a pedigree, completes risk assessment, stratification, and recommendations for 89 conditions. We compared the performance of Health Heritage to that of Usual Care using a nonrandomized cohort trial of 109 volunteers. We contrasted the completeness and sensitivity of family health history collection and risk assessments derived from Health Heritage and Usual Care to those obtained by genetic counselors and genetic assessment teams. Nearly

half (42%) of the Health Heritage participants reported discovery of health risks; 63% found the information easy to understand and 56% indicated it would change their health behavior. Health Heritage consistently outperformed Usual Care in the completeness and accuracy of family health history collection, identifying 60% of the elevated risk conditions specified by the genetic team versus 24% identified by Usual Care. Health Heritage also had greater sensitivity than Usual Care when comparing the identification of risks. These results suggest a strong role for automated family health history collection and risk assessment and underscore the potential of these data to serve as the foundation for comprehensive, cost-effective personalized genomic medicine.

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Background

The completion of the Human Genome Project has provided the ability to detect the heritable component of many common diseases. By 2008, there were an estimat-

Table 1. The ideal family history tool

Elements of the ideal family health history tool
Patient-completed (e.g. paper, desktop, telephone, or web input)
Adapted to patient age, gender, ethnicity, and common conditions
Elicits specific patient concerns
Brief, understandable and easy to use
Compatible with multiple clinical applications (paper, electronic medical record, PDA)
Contains clinical decision support
Branches and prioritizes based on clinical significance

ed 1,600 clinical genetic tests available [1]. This rapidly growing capacity to detect important but relatively small incremental contributions of total disease burden [2, 3] makes family health history information collection increasingly important. Most of the results from the new genome-wide association studies, for example, require family history data for more accurate identification of at-risk individuals. This information has the potential to serve as the basis for risk stratification for disease preventive measures in public health [4–7] and to serve as the ‘cornerstone for individualized disease prevention’ [8, p 2333].

Existing methods of collecting, recording and updating family health history information, however, do not meet these projected or even contemporary clinical needs. As the Institute of Medicine recently summarized: ‘The current system for delivering genetic services is based on a model of intensive counseling for rare diseases. As the use of genomic technology becomes more prevalent, providers and patients will need new ways of communicating about genetic information and how it may change health care options’ [9].

The integration of the family health history into clinical care is likely to be placed primarily in the hands of the primary care provider [10]. Primary care providers recognize that obtaining a family health history is an important part of routine care but are challenged to systematically collect, document and interpret it [11–13]. This task is further compounded when many patients (70.2% in one Centers for Disease Control [CDC] survey) do not collect the health histories of their close relations, despite the fact that the vast majority (96.3%) believed this information to be important to their own personal health [14].

Primary care physicians are also being asked to better integrate the collection of family health history information into an already time-constrained patient visit. They need a time-saving way to collect and manage family health history information, augment their limited cur-

rent genetic health training and keep up with rapidly changing genetic knowledge [15].

It is widely acknowledged that most primary care providers do not possess the expertise to provide genetic counseling services, especially for multi-factorial diseases [16, 17], in addition to other profession-wide general barriers to resource utilization [18–21]. Current initiatives, such as the Genetics in Primary Care: A USA Faculty Development Initiative, are striving to improve the training of medical students and residents, especially in interpreting the family health history [22].

In 2002, the CDC convened an expert working group to discuss the use of family health history in public health and disease prevention. This working group called for a ‘public health oriented, family health history tool designed for use in diverse populations that is simple, easily applied, and inexpensive’ and that this tool must also ‘maintain a balance between keeping it simple and gathering enough information to make prediction possible’ [23]. The specific characteristics of the ideal family health history tool identified by this group are summarized in table 1. Since then, the American Health Information Community’s (AHIC) Personalized Health Care Workgroup has called for incentives to advance health information technology standardization and adoption and has released a report that identifies some of the challenges that surround the exchange of family health history between consumers and clinicians [24].

Family health history tools are currently being developed and used to increase awareness and public utilization [25–27]. The CDC developed Family Healthware™ (a web-based tool designed to assess risk and provide prevention recommendations in six disease areas) [28], and the U.S. Surgeon General’s Family History Initiative developed My Family Health Portrait (a web site that allows individuals to enter information about family members to create a family tree and summary of family health history). Recently, O’Neill et al. described a cluster ran-

domized controlled trial that demonstrated the Family Healthware application delineated a substantial burden of family-history-based risk for 6 diseases in an adult, primary care population [29].

As the existing Evaluation of Genomic Applications in Practice and Prevention process and others have emphasized, the ultimate value of a genetic test or family health history tool depends on the following: its analytic validity (including sensitivity and specificity), clinical validity, clinical utility and ethical, legal and social issues. A family health history tool's analytic validity needs to address how accurately the tool identifies disease in family members compared to a well-defined gold standard [30, 31].

Health Heritage

We developed Health Heritage[®] to address the difficulties of collecting and interpreting family health history described above and to initially assess its analytic validity. The development of Health Heritage took approximately 18 months and required an interdisciplinary development team including experts in the areas of medicine, genetics, genetic counseling, family practice, computer programming, user interface design, and others. The user interface of Health Heritage has been previously described [32]. Health Heritage consists of 3 primary components: (1) collection of family health history information, (2) risk assessment for 89 conditions, and (3) provision of risk-stratified recommendations. In the first component, users are guided by a series of family health history questions to generate their own detailed pedigree. The second component, risk assessment, utilizes evidence-based algorithms created by the disease specialists of our genetic and clinical teams to assess the risk of developing assessed conditions based on family health history of first- and second-degree relatives. The third component, recommendations by 3 risk levels (high, moderate and average population), provides screening, treatment and prevention for each assessed condition. Health Heritage includes over 200 algorithms for assessing individual risk based on family health history in 5 disease specialty areas: oncology (e.g. breast, ovarian, colon, skin, prostate), cardiology (e.g. arrhythmia, cardiomyopathy), vascular disease (e.g. stroke, atherosclerosis, hypertension, metabolic lipid disorders), neurology (e.g. neuromuscular diseases, movement disorders, epilepsy), and endocrinology (e.g. diabetes, osteoporosis). Our team primarily selected conditions that were clinically important and prevalent and for which there was the ability to

screen and provide treatment. Disease specialists in each of the clinical areas developed a set of rules to assess individual risk based on the heritability patterns of the disease and the individuals' family health history. Our framework utilized known disease subtypes, identified heritable components of diseases, incorporated heritable risk factors for the diseases, and assessed overlap of syndromes, including those that cross medical specialties. A risk algorithm template was used to specify the precise logic that classified this risk into 3 categories with appropriate recommendations for prevention, treatment and referral. With the appropriate permissions, both users (patients) and their primary care provider can access the system to view risk stratification and health care recommendations for the diseases and conditions identified.

This report details our progress in the evaluation of the initial user's experience with Health Heritage and its analytic validity by assessing the accuracy of Health Heritage in assisting patients to complete their family health histories when compared to Usual Care and a genetic assessment team including a genetic counselor. We also evaluate Health Heritage's ability to provide risk assessments compared to those produced by an expert genetic assessment team.

Methods

Design

This study was reviewed and approved by the Human Investigation Committee at the University of Virginia. Informed consent was obtained from all participants. This evaluation employed a nonrandomized cohort study design that consisted of 2 arms, the intervention group (Health Heritage) and the Usual Care group (patients treated at local primary care clinics) (fig. 1). These 2 arms were compared to a generally accepted criterion or gold standard, defined as the family health history gathered by a certified genetic counselor and then assessed by genetic disease specialists. Key measures related to (a) the initial experience and satisfaction of the Health Heritage users, (b) completeness and accuracy of family health history information and (c) subsequent appropriateness of risk assessments were measured for this study.

Sample

Participants for the Health Heritage user group were recruited through local print and radio advertisements, as well as in print-based recruitment materials at 6 local primary care practices in Central Virginia. Individuals who responded were screened for inclusion and sent an introduction packet that included an informed consent and registration information. Inclusion criteria were: (1) over 18 years, (2) previous Internet use or desire to use the Internet, (3) English-speaking, (4) limited experience with genetic assessments in the past, and (5) identifiable biological parents (thus excluding those who were adopted as children and do

Fig. 1. Generation of the Health Heritage pedigree.

not know the identity of their parents). No incentives for participation were offered.

Participants who registered to use Health Heritage were given a confidential code to access the system. Once in the system, they were guided through the creation of their pedigree (fig. 1) and reporting of diseases among family members by answering a series of branching logic questions. The assessment of user risk for disease was completed and participants received stratified risk information and recommendations (fig. 2). Participants had 3 months to complete Health Heritage. Technical support was available by telephone consultation with project staff. The overall flow of the intervention is depicted in figure 3.

The Usual Care group was recruited during a 6-month period through primary care physician practices in Central and Southwest Virginia via letters and print materials available at the office. A total of 6 local primary care practices volunteered to participate using one or both of the recruitment methods above. The Health Heritage intervention group was recruited by radio and print advertisements. Eligibility criteria for both groups were: age 18 years old or older, ability to be called on the telephone, no prior evaluation by a genetic counselor and not adopted. In addition, the in-

tervention group had to be able to use the Internet or be willing to learn.

Data Collection

Prior to using Health Heritage, this group completed a baseline questionnaire that assessed basic demographics, experience with computers and genetic information and attitudes towards security. Once this questionnaire was completed, participants were given an access code and 3 months to complete Health Heritage. Following completion of Health Heritage, users participated in a phone interview with a genetic counselor to record family health history that was then independently analyzed for risk by a genetic specialist team. This team consisted of a board-certified geneticist, disease specialists and a genetic counselor. The Usual Care group also completed the baseline participant questionnaire prior to a chart review that abstracted their family health history from their primary care practice. Following the completion of the chart review, the Usual Care group also participated in a phone interview with a certified genetic counselor who recorded their family health histories for subsequent analysis by the genetic assessment team. This process was the same for both groups; the

Fig. 2. Sample risk and recommendations report for a Health Heritage participant.

genetics assessment team was blinded to whether the family health history information was collected by Health Heritage or the genetic counselor. After participants in the Health Heritage group had completed recording their family health history, they were contacted by the University of Virginia Center for Survey Research in order to complete a satisfaction questionnaire administered by telephone. The survey contained questions that assessed the features of Health Heritage that participants used and their satisfaction with those features. It also assessed the extent to which participants found the collection of family health history difficult and if they thought it was a valuable thing to do. Because of our interest in understanding the experience of the Health Heritage user from the beginning of the system (sign up, definition of family, etc.) through to the end (provision of recommendations tailored by risk), we included only those participants in this analysis who were at least 90% complete in their first and second generation family health history collection. Although not a usual requirement, we set a high level of completion so that we would be able to assess satisfaction with all the major components of Health Heritage.

Analytic Methods

The Health Heritage and Usual Care data sets were each compared to the information collected by the genetic counselor and risk assessed by the genetic assessment team, because participants did not use both the Health Heritage and Usual Care methods. Comparisons were made to assess the completeness (e.g. number of family members and potential hereditary conditions identified) and the accuracy (e.g. total number of hereditary conditions for each family health history which matched those found by the genetic counselor) based on the following parameters: (a) number

of first- and second-degree relatives recorded; (b) nature of relationship to the proband (e.g. maternal grandmother); (c) age of relatives; (d) number of potential hereditary conditions identified in family by relative (conditions counted were limited to those required to address the risks being assessed); (e) risk assessment (general population or elevated) for hereditary conditions for individual participants.

Linear regression models were used to examine relationships between each outcome criterion for either Health Heritage or Usual Care and the identical outcome identified by the genetic counselor. All ratios were examined after log transformation. Confidence intervals (95%) were created for predicted values. Multivariate comparisons between Health Heritage and the Usual Care genetic assessment teams were made for each of the above measures, controlling for family size, number of conditions, number of relatives, and number of relatives with conditions.

Risk Assessment

Three risk levels were used: 'same as the general population', 'moderately increased risk' and 'significantly increased risk'. Within the increased risk categories, we provided participants with 2 types of recommendations: (1) a health-related intervention (such as screening) and (2) referral to a genetic counselor for further evaluation (fig. 2).

Sensitivity of the Health Heritage or Usual Care method for risks ascertained based on the genetic assessment team was estimated for each of the risk-assessed conditions, if prevalence in the study population was sufficient to do so. In addition, our review of the risk assessment results included a summary of elevated risk identified by the Health Heritage or Usual Care method that was not identified by the genetic assessment team method.

Fig. 3. Health Heritage study design.

Results

Description of Participants

Approximately 700 information packets were mailed, or delivered by hand, to potential primary care patient participants for the Usual Care group. A total of 67 patients (9.5%) returned the consent forms; 55 were able to complete the interview with the genetic counselor. A total of 643 information packets were mailed to interested individuals in the Health Heritage group. 114 (17.7%) returned the consent forms and requested log-in information. Of these, 85 individuals registered for Health Heritage and 54 completed the family health history collection to the 90% level.

The self-reported personal characteristics of 108 of the 109 participants are described in table 2. The majority of participants in both groups were Caucasian, mid-

dle-aged employed members of families with moderate incomes and educational levels. Based on a pre-study questionnaire assessing hereditary disease experience, hereditary disease belief and concerns regarding computer and Internet security, the 2 groups were comparable on many of the attributes (table 3).

Health Heritage Usage

The time it took to complete Health Heritage ranged from 1 to 120 hours. About 25% ($n = 12$) of participants took 1–2 hours, 27% ($n = 13$) 3–6 hours, 27% ($n = 12$) 7–12 hours, 15% ($n = 7$) 15–20 hours, and 8% ($n = 4$) >20 hours. Participants were asked to estimate the extent to which they completed different aspects of Health Heritage including ‘entering all your relatives in your family tree’, ‘answering questions about health conditions of all your relatives’ and ‘reviewing the risk report and recommen-

Table 2. Demographic and personal characteristics of participants

Variable	Usual Care n (%)	Health Heritage n (%)	Total n (%)
Gender	55	54	109
Male	22 (40.7)	10 (18.5)	32 (29.6)
Female	32 (59.3)	44 (81.5)	76 (70.4)
Ethnicity (n = 107)			
Non-Hispanic White	47 (88.7)	51 (94.4)	98 (91.6)
Other	4 (7.6)	2 (3.7)	6 (5.6)
Native American	2 (3.8)	0	0
Asian or Pacific Islander	0	1 (1.9)	1 (0.9)
Age in years (n = 108)			
18–25	0	3 (5.6)	3 (2.8)
26–35	6 (11.1)	6 (11.1)	12 (11.1)
36–45	13 (24.1)	12 (22.2)	25 (23.1)
46–55	14 (26.0)	18 (33.3)	32 (29.6)
56–65	7 (13.0)	9 (16.7)	16 (14.8)
66–75	8 (14.8)	5 (9.3)	13 (12.0)
Older than 75	6 (11.1)	1 (1.9)	7 (6.5)
Marital status now (n = 108)			
Married	39 (72.2)	44 (81.5)	83 (76.8)
Never married	7 (13.0)	5 (4.6)	12 (11.1)
Separated or divorced	5 (9.3)	3 (5.6)	8 (7.4)
Widowed	3 (5.6)	2 (3.7)	5 (4.6)
Employment status now (n = 108)			
Working full-time	24 (44.4)	32 (59.3)	56 (51.9)
Retired	16 (30.0)	8 (14.8)	24 (22.2)
Homemaker	8 (14.9)	6 (11.1)	14 (13.0)
Working part-time	2 (3.7)	4 (7.4)	6 (5.5)
Other	4 (7.4)	4 (7.4)	8 (7.4)
Highest of level education completed (n = 108)			
Less than high school	4 (7.4)	0	4 (3.7)
High school or GED	7 (13.0)	0	7 (6.5)
Some college but did not complete	11 (20.4)	6 (11.1)	17 (15.7)
2-year college (associate degree)	6 (11.1)	5 (9.3)	11 (10.2)
4-year college (bachelor degree)	5 (9.3)	9 (16.7)	14 (13.0)
Some graduate work	6 (11.1)	4 (7.4)	10 (9.3)
Completed graduate work	15 (27.8)	30 (55.6)	45 (41.7)
Annual household income from all sources (n = 107)			
Under \$15,000	3 (5.6)	1 (1.9)	4 (3.7)
\$15,000–\$35,000	11 (20)	4 (7.4)	15 (14.0)
\$35,001–\$50,000	5 (9.3)	8 (15.1)	13 (12.1)
\$50,001–\$75,000	8 (14.8)	15 (28.3)	23 (21.5)
\$75,001–\$100,000	8 (14.8)	4 (7.6)	12 (11.2)
>\$100,000	11 (20.4)	12 (22.6)	23 (21.5)
Prefer not to answer	8 (14.8)	9 (17.0)	17 (15.9)
Health status (n = 108)			
Excellent	10 (18.5)	13 (24.1)	23 (21.3)
Very good	18 (33.3)	27 (50.0)	45 (41.7)
Good	14 (26.0)	9 (16.7)	23 (21.3)
Fair	10 (18.5)	4 (7.4)	14 (13.0)
Poor	2 (3.7)	1 (1.9)	3 (2.8)

Fig. 4. Completeness and accuracy of Health Heritage compared to Usual Care. Completeness and accuracy is defined as compared to a genetic counselor. Percentages exceed 100% when Health Heritage captures more conditions or relations than the genetic counselor.

Table 3. Hereditary disease experience, knowledge and beliefs

Questionnaire item	Usual Care n (%)	Health Heritage n (%)	Total n (%)
Immediate family member had an inherited disease	16 (29.6)	17 (31.5)	33 (30.6)
You have an inherited disease	10 (18.5)	6 (11.1)	16 (14.8)
You received genetic counseling	1 (1.9)	2 (3.7)	3 (2.8)
You had genetic testing	1 (1.9)	2 (3.7)	3 (2.8)
Someone else in your immediate family had genetic testing	2 (3.7)	3 (5.6)	5 (4.6)
Had a health care provider talk with you about 'diseases that run in families'	36 (66.7)	43 (81.1)	79 (73.2)
If you had inherited a gene that made you more likely to develop inherited disease, you would want to be told	52 (96.3)	49 (92.5)	101 (93.5)
If you had inherited a gene that made you more likely to develop inherited disease, you would want to tell your relatives	41 (76.0)	40 (75.5)	81 (75.0)

dations'. Nearly half (41.7%, $n = 20$) of the participants indicated that the site reported health risks; 35.4% ($n = 17$) said this risk information was easy to understand. Only 19% ($n = 9$) reported that the site gave recommendations about their health. An additional 33% ($n = 16$) 'were not sure'. Of those who reported receiving a recommendation, 56% ($n = 5$) indicated that the information would change their health behavior.

Satisfaction

When asked, 'How difficult was it to actually use the Health Heritage web site to complete your family health history?', 54.2% ($n = 26$) responded 'Not at all difficult'

and 29.2% ($n = 14$) responded 'A little difficult'. Health Heritage participants were also asked, 'How difficult was it to find the information you needed to complete your family history?', to which 22.9% ($n = 11$) responded 'Not at all difficult', 27.1% ($n = 13$) 'A little difficult', 39.6% ($n = 19$) 'Somewhat difficult', and 10.4% ($n = 5$) responded 'Very difficult'.

In response to the item, 'Some of the questions made me worry', 18.8% ($n = 9$) of participants chose 'Somewhat disagree' and 81.3% ($n = 39$) selected 'Strongly disagree'. Half of the respondents were 'Very satisfied', and an additional 39.6% ($n = 19$) were 'Somewhat satisfied' with 'the confidentiality provided by Health Heritage', while

Table 4. Completeness of first- and second-degree relatives

	Genetic counselor									
	family size – 12		family size – 15		family size – 20		family size – 27		family size – 37	
	No. rel.	ratio	No. rel.	ratio	No. rel.	ratio	No. rel.	ratio	No. rel.	ratio
Health Heritage	14	1.1 (0.891–1.416)	15	1.0 (0.804–1.169)	16	0.8 (0.682–0.943)	18	0.7 (0.545–0.794)	20	0.5 (0.414–0.690)
Usual Care	4	0.3 (0.267–0.426)	4	0.3 (0.241–0.352)	5	0.2 (0.205–0.283)	5	0.2 (0.164–0.238)	6	0.2 (0.125–0.206)

The number of relatives (No. rel.) and estimated ratio of Health Heritage/genetic counselor or Usual Care. Genetic counselor (ratio) are predicted values for selected percentiles of the empirical distribution of the number of relatives identified; the corresponding 95% confidence limits are provided.

47.9% (n = 23) were ‘Very satisfied’ and an additional 45.8% (n = 22) were ‘Somewhat satisfied’ with ‘the security provided by the web site’.

Participants were asked to rate the overall quality of the site: 39.6% (n = 19) rated the site as ‘Excellent’ and 35.4% (n = 17) as ‘Good’; 18.8% (n = 9) thought the site was ‘Fair’ and 4.2% ‘Poor’ (n = 2); 2.1% said ‘Don’t know’ (n = 1). When asked if they had shared the Health Heritage risk information with other family members, 39.6% (n = 19) indicated that they had. A total of 90% of the participants discussed their family health history with immediate family members and 42% with extended family members. The majority (58.4%, n = 28) of the Health Heritage users also indicated that the information gained was ‘worth the time and effort’.

Family Health History Completeness

Total Number of First- and Second-Degree Relatives Identified. The Health Heritage method consistently identified more relatives than the Usual Care method for every family size, often by a substantial number. For example, for family sizes of 12 to 37 members, Health Heritage identified 54–116% of those relatives identified by the genetic counselor, compared to 16–33% for Usual Care (fig. 4). For a family of 15, Health Heritage identified all 15 (100%), while Usual Care recorded only 4 (27%). For most family sizes, and especially as the number of relatives identified by the genetic counselor increased, Health Heritage captured fewer relatives (table 4).

Total Number of Relationships and Ages of Relatives Identified. Health Heritage was substantially more com-

plete than Usual Care in identifying the relationships and ages of the relatives in the participant’s family health history (fig. 4). Health Heritage was not significantly different from the genetic counselor in identifying the relationships or ages of relatives (fig. 4). For a family in which Health Heritage identified the same number of family members as the genetic counselor, it identified 99.7% of completely specified relationships and a greater number (103.5%) of the ages or ages at death of the family members. Usual Care identified fewer relationships and ages of relatives than the genetic counselor for all proportions of relatives identified by the genetic counselor. The difference between Health Heritage and Usual Care was not significant for identifying the relationship at the lowest proportion of relatives gathered by the genetic counselor.

Total Number of Conditions Identified. Health Heritage was more complete than Usual Care in the identification of conditions in a participant’s family health history. Health Heritage also consistently identified more conditions than did the genetic counselor (fig. 4). However, this difference decreased as the number of conditions identified by the genetic counselor increased. In families with 4 conditions, Health Heritage identified 4.6 times the number identified by the genetic counselor. In families with 28 conditions, Health Heritage identified 1.6 times the number identified by the genetic counselor. In contrast, Usual Care always identified fewer conditions than the genetic counselor; this difference also increased with the number of conditions identified by the genetic counselor (table 5).

Table 5. Completeness of conditions

	Genetic counselor									
	No. of conditions		No. of conditions		No. of conditions		No. of conditions		No. of conditions	
	4		9		14		20		28	
	# cond.	ratio	# cond.	ratio	# cond.	ratio	# cond.	ratio	# cond.	ratio
Health Heritage	16	4.6 (3.394–6.168)	27	3.0 (2.463–3.560)	33	2.3 (2.004–2.723)	39	2.0 (1.646–2.261)	45	1.6 (1.336–1.942)
Usual Care	3	0.9 (0.672–1.097)	5	0.6 (0.473–0.652)	6	0.4 (0.372–0.516)	7	0.4 (0.298–0.439)	7	0.3 (0.238–0.383)

The number of conditions (# cond.) and estimated ratio of Health Heritage/genetic counselor conditions or Usual Care. Genetic counselor conditions are predicted values for selected percentiles of the empirical distribution of the number of conditions identified; the corresponding 95% confidence limits are provided.

Total Number of Relatives with Any Condition Identified. Health Heritage consistently provided a more complete history of the relatives with conditions than did Usual Care, 182–90% compared to 53–26%. Health Heritage performed better than, or as well as, the genetic counselor in identifying relatives with at-risk conditions (fig. 4). Health Heritage's performance varied depending on the number of relatives with conditions identified by the genetic counselor. When the genetic counselor had identified few relatives (e.g. 4–9 genetic counselor relatives with conditions), Health Heritage identified more relatives with conditions than the genetic counselor (ratios from 1.8 to 1.3). As the number of relatives with conditions identified by the genetic counselor increased to 12 and above, Health Heritage and the genetic counselor method became indistinguishable (ratios 1.1–0.9) (table 7).

Family Health History Accuracy: Total Number of Conditions Matching Those Found by the Genetic Counselor

Health Heritage was more accurate than Usual Care in the identification of the conditions found by the genetic counselor. Health Heritage frequently performed well in gathering the number and type of conditions compared to the genetic counselor. However, as the number of conditions identified by the genetic counselor increased, Health Heritage found a smaller proportion of matched conditions, from a ratio of 1.0 for 4 conditions to a ratio of 0.6 for 28 conditions. Usual Care found sig-

nificantly fewer conditions than the genetic counselor throughout the range of numbers of conditions identified by the genetic counselor (table 7).

Risk Assessment

The genetic counselor and the genetic assessment team found at least one participant with an increased risk in one or both of the study arms (Usual Care or Health Heritage) for 45 of the 89 possible hereditary conditions (table 8). 25 (55%) of these 45 had sufficient prevalence to determine sensitivity among the various methods. In 17 of the 25 conditions (e.g. atherosclerosis, diabetes, hypertension), Health Heritage was more sensitive than Usual Care (in 5 cases the sensitivities were the same). There were 3 instances – breast cancer, colon cancer and type Ia diabetes mellitus – where Usual Care performed better than Health Heritage. Because of small numbers in each cohort, however, these differences were not statistically significant (table 8).

Conclusions

We successfully developed and initially evaluated the usability of a web-based family health history tool for the collection and interpretation of family health history information by individuals and their families. While development and initial evaluation was complex, we believe that the value of a tool that includes a specific assessment of many of the most common adult-onset conditions, ad-

Table 6. Completeness of relatives with conditions

	Genetic counselor									
	4 relatives with conditions		6 relatives with conditions		9 relatives with conditions		12 relatives with conditions		17 relatives with conditions	
	No. rel. w/cond.	ratio	No. rel. w/cond.	ratio	No. rel. w/cond.	ratio	No. rel. w/cond.	ratio	No. rel. w/cond.	ratio
Health Heritage	7	1.8 (1.464–2.252)	7	1.5 (1.271–1.755)	11	1.28 (1.071–1.408)	13	1.0 (0.924–1.237)	15	0.9 (0.753–1.085)
Usual Care	2	0.527 (0.437–0.634)	3	0.433 (0.374–0.501)	3	0.356 (0.308–0.412)	4	0.3 (0.261–0.368)	4	0.3 (0.211–0.326)

The number of relatives with conditions (rel. w/cond.) and estimated ratio of Health Heritage/genetic counselor conditions or Usual Care/genetic counselor relatives with conditions are predicted values for selected percentiles of the empirical distribution of the number of relatives with conditions; the corresponding 95% confidence limits are provided.

Table 7. Accuracy of conditions

	Genetic counselor									
	conditions 4		conditions 9		conditions 11		conditions 14		conditions 28	
	No. cond. matches	ratio	No. cond. matches	ratio	No. cond. matches	ratio	No. cond. matches	ratio	No. cond. matches	ratio
Health Heritage	4	1.0 (0.779–1.340)	7	0.8 (0.689–0.956)	10	0.7 (0.626–0.819)	13	0.6 (0.562–0.744)	17	0.6 (0.497–0.695)
Usual Care	2	0.4 (0.311–0.491)	3	0.3 (0.268–0.359)	4	0.3 (0.237–0.316)	5	0.2 (0.208–0.294)	6	0.2 (0.182–0.277)

The number of matches to conditions identified by the genetic counselor (No. cond. matches) and estimated ratio of Health Heritage/genetic counselor or Usual Care/genetic counselor are predicted values for selected percentiles of the empirical distribution of the number of conditions identified; the corresponding 95% confidence limits are provided.

dressed by individuals and their health care providers, was worth the development effort and will provide a sound foundation for future efforts.

One challenge for all family health history instruments will be the input of a sufficiently complete history that can serve as a meaningful basis for individual health recommendations. Slightly less than 30% (54/184) of our originally registered participants assembled 90% of their

first- and second-generation family histories. This is an essential area for improvement. We hypothesize that the barriers to completion for our participants include: (1) organizational difficulty in gathering the requisite health information (thinking through the structure and health of the family), (2) length of time required for completion, (3) difficulty/awkwardness in requesting personal health history from relations, and (4) low incentives for volun-

Table 8. Sensitivity of Usual Care and Health Heritage of detecting conditions compared to the genetic counselor and genetic assessment team

Condition	Usual Care sensitivity, %	Health Heritage sensitivity, %
Cancer		
BRCA1	0 (0/7)	50.0 (1/2)
BRCA2	0 (0/8)	50.0 (1/2)
Colon cancer	20.0 (1/5)	16.7 (1/6)
Cowden syndrome	0 (0/1)	66.7 (2/3)
Familial adenomatous polyposis	0 (0/1)	0 (0/2)
Hereditary non-polyposis colorectal cancer	0 (0/4)	85.7 (6/7)
Li-Fraumeni syndrome	0 (0/1)	NRD
Other cancer-associated syndromes	0 (0/1)	0 (0/1)
Ovarian cancer	0 (0/1)	NRD
Skin cancer	NRD	100.0 (1/1)
Thyroid (medullary) cancer	NRD	100.0 (1/1)
Thyroid cancer	NRD	0 (0/1)
Cardiology		
Structural abnormalities of the heart	0 (0/7)	33.3 (1/3)
Vascular		
Atherosclerosis	42.9 (12/28)	69.6 (16/23)
Cerebrovascular hemorrhage	NRD	0 (0/1)
Collagen vascular	0 (0/2)	0 (0/3)
Connective tissue	0 (0/2)	40.0 (2/5)
Embolic disease	0 (0/1)	NRD
Hemoglobinopathies	0 (0/2)	0 (0/1)
Hemostatic	11.1 (1/9)	14.3 (1/7)
Hypercoagulable	0 (0/3)	0 (0/1)
Hyperfibrinogenemia	0 (0/1)	NRD
Hypertension	33.3 (7/21)	64.5 (20/31)
Intracranial aneurysm	NRD	66.7 (2/3)
Intracranial hemorrhage	NRD	0 (0/1)
Metabolic lipids	36.8 (7/19)	76.2 (16/21)
Potential secondary hypertension	NRD	100.0 (1/1)
Primary hypertension	0 (0/18)	43.5 (10/23)
Syndromes with vascular complications	NRD	50.0 (1/2)
Vascular headache	0 (0/3)	70.0 (7/10)
Endocrinology		
Gestational diabetes mellitus	0 (0/1)	100.0 (2/2)
Osteoporosis	25.0 (2/8)	83.3 (5/6)
Type Ia diabetes mellitus	100.0 (1/1)	0 (0/1)
Type II diabetes mellitus	50.0 (10/20)	84.2 (16/19)
Neurology		
Dementia	0 (0/2)	60.0 (6/10)
Epilepsy	50.0 (1/2)	NRD
Motor neuron disease	0 (0/1)	NRD
Myasthenia gravis	NRD	100.0 (1/1)
Parkinson's disease	0 (0/3)	100.0 (1/1)
Other hereditary conditions		
Bleeding problems or blood disorders	NRD	100.0 (3/3)
Kidney disease	NRD	80.0 (4/5)
Liver problems	NRD	100.0 (1/1)
Lung disease	NRD	33.0 (1/3)

Comparison of the sensitivity for determining increased risk for all conditions where the genetic counselor found at least one case of increased risk in one or both of the study arms (45 of the 89 possible hereditary conditions). Comparison is with increased risk assessment as recorded by a genetic assessment team (medical geneticist and genetic counselors) versus number of conditions identified by the Usual Care or Health Heritage method with case numbers shown in parentheses (UC or HH/GC). NRD = Represents study arms where no risk was detected by the genetic counselor and genetic assessment team. See text for further explanation.

teers to complete the online tool since it was not connected to their electronic medical record. We are gearing the second phase of our research and development to systematically address these challenges.

Health Heritage demonstrated, however, that a stand-alone web-based tool could be developed to collect and analyze family health history information for some of the most common conditions with a hereditary component (such as atherosclerosis, hypertension, and type II diabetes mellitus) as well as complex syndromes (such as metabolic lipid syndrome and hereditary nonpolyposis colorectal cancer). Our results also suggest that the Health Heritage system is superior to the current practice of primary care providers for gathering and interpreting family health history. Specifically, we found that Health Heritage consistently outperformed Usual Care for all measures of family health history completeness and accuracy when both conditions were compared to the genetic assessment team. This is an important finding because it is important to compare to a gold standard (genetic assessment team) [6, 30, 31]. In addition, our comparison showed that Health Heritage consistently performed at, or close to, the completeness of the family health history recorded by genetic counselors. There was greater than 80% agreement for risks for common conditions like osteoporosis, type II and gestational diabetes, potential secondary hypertension, and Parkinson's disease with those determined by the genetic assessment team. In cases where there was disagreement between Health Heritage and the genetic assessment team, it was often due to additional conditions and risks identified by the Health Heritage method. These differences in number and identity of conditions may arise from questions in Health Heritage that address distinct disease etiologies that impact hereditary. For example, to identify different stroke subtypes, data regarding a number of additional conditions were collected, but these may have resulted in the relatively poor agreement in related risks (e.g. cerebrovascular hemorrhage, intracranial hemorrhage, hypercoagulable and hemostatic conditions).

Disagreements with the genetic counselor may also arise from Health Heritage attempting to gather very specific information. For example, determination of the severity of hypertension by eliciting blood pressure values may have caused disagreement with risk assessments for both primary hypertension and potential secondary hypertension risks. There is evidence for such a discrepancy in the relatively poor agreement between Health Heritage and the genetic specialty team for primary hypertension (43.5%). In fact, there were 11 cases of hypertension and

13 cases of primary hypertension where Health Heritage predicted a lower risk than the genetic specialty team and not perhaps coincidentally 24 cases of potential secondary hypertension where Health Heritage predicted higher risk. Again, it is possible that the cases of missed risk by Health Heritage were actually classified as related (and in fact more specific) but distinct risk conditions. Whether these potential differences represent real cases of risk is difficult to determine without further attempts to validate the data provided by the participants.

Another important consideration is in the comparison of risk assessments. When comparing agreement of risk (in the 25 algorithms where there was sufficient prevalence to assess both methods), Health Heritage achieved at least 60% agreement with the genetic assessment team in 11 cases, whereas Usual Care achieved 60% agreement in only one. Health Heritage also achieved 60% agreement in algorithms where sensitivity could be determined for Health Heritage only (table 8).

Differences in agreement between the 2 methods regarding certain risk assessments might have resulted from additional criteria related to age and other conditions that further indicate a particular hereditary syndrome. For example, when compared with the genetic counselor and genetic assessment team, Health Heritage found fewer cases of general risk for breast cancer but found many additional cases of risk not identified by the genetic assessment team for more specific hereditary cancer syndromes that can also result in breast cancer (e.g. *BRCA1*). More specifically, Health Heritage predicted lower risk in 5 of 5 cases of breast cancer but predicted higher risk in 3 cases with *BRCA1*, 3 with *BRCA2*, 6 with Cowden syndrome, and 6 with Li-Fraumeni syndrome (data not shown). Therefore, it is possible that the cases of missed risk by Health Heritage were actually classified as a related (and in fact more specific) risk condition.

Future Directions and Opportunities

An issue that needs special consideration is the burden to the individual participant in collecting and maintaining their family health history. Design enhancements to the web site since this study have partially addressed this, but additional effort is needed. Participants using Health Heritage reported being able to answer less than half of the questions concerning their relatives' health conditions. While one design strength of Health Heritage is its ability to utilize both general and more specific health history information, any system for accurately determining the risk of hereditary conditions requires, as its foundation, most complete information as possible for relatives.

Obtaining this information, whether through an interview with a genetic counselor or by self-entering it into a system like Health Heritage, is very time-intensive. It was the highest hurdle we encountered even though our study population was more educated (with presumably higher literacy) than the general United States population.

To address this challenge, we are currently working to integrate Health Heritage into widely used personal health records and electronic medical records enabling its interoperability and establishing a basis for implementing the AHIC recommendations. We are also planning for Health Heritage to receive downloads from other widely available family history gathering tools like the Surgeon General's My Family Health Portrait. Once Health Heritage is fully integrated into existing electronic record approaches, we will explore the possibility of the electronic sharing (after appropriate permission) of hereditary conditions for relatives from these personal health records, electronic medical records, and their associated clinical data repositories. This approach would not decrease the need to contact and gain permission from relatives, but it should increase the frequency of correctly recording all appropriate diagnoses in all first- and second-degree relatives.

A separate, but equally compelling, future direction for Health Heritage and other tools that assess risk based on family health history is to respond to the challenge of updating risk algorithms and recommendations to keep current with new scientific and clinical knowledge. Our team has begun to explore the use of automated literature and structured text retrieval tools to speed this process of evidence collection [33].

Also important will be additional examination of the use of Health Heritage in primary care. Although we developed Health Heritage with primary care in mind, we

did not study the impact of Health Heritage on the actual work process flow. One of our next steps will be to evaluate the use of Health Heritage by primary care physicians and understand how it impacts their ability to collect and interpret family health history.

In sum, though still in its early stages of development, Health Heritage provides a resource for individuals and health providers to document multi-generational health histories. This tool will not only benefit these stakeholders, but also provide a legacy for subsequent generations. The importance of this information is bolstered by the realization that, for the majority of the post-genomic revolution population, the collection of a comprehensive family history along with epigenetic factors (such as diet, lifestyle and environmental exposures) will frequently be more influential for the development of common diseases than are the respective genetic sequences alone [34]. Therefore, detailed family health histories may serve as a valuable and inexpensive step to identify genetic predispositions for disease manifestation [3, 8]. We believe that Health Heritage will provide a useful window into this complex cascade of personalized genomic information, providing benefits to clinical care, clinical and translational research and public health.

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