Visualizing Hereditary Cancer Risk

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ABSTRACT

The challenges associated with data collection, algorithmic analysis, and clinical guideline interpretation currently prevent population wide screening for hereditary cancer. We describe the collaboration between the University of Massachusetts Lowell, Massachusetts General Hospital, and the Newton Wellesley Hospital to develop and deploy an integrated clinical information system for identifying patients at risk for developing hereditary breast or ovarian cancer that directly addresses these challenges. Patient and Clinician user interfaces were developed to support the case management of high risk patients, and integrated into both a mammography screening center and a high risk cancer clinic. We describe Newton Wellesley Hospital as an example use case with user comments.

KEYWORDS: Hereditary Risk Assessment, BRCA, Genetic Testing.

1 INTRODUCTION

Family history of disease can provide important insight into the potential presence of a hereditary condition, and is therefore an important tool in preventative medicine. There are many roadblocks that clinicians face in terms of collecting data, analyzing the information, and deciding on the appropriate course of action[1]. Here we present a snapshot of a toolset that has been developed to help clinicians overcome these challenges.

The users for these tools are the genetic counselors, nurse practitioners, and oncologists making decisions about when to order genetic testing and other risk mitigating interventions. As the genomic revolution takes hold, the panoply of available genetic tests will grow. The burden of decision making will then extend into other specialties, and potentially even primary care physicians[2]. This is the primary motivation to develop data entry tools that can off load the collection of structured family history data from the clinician to the patient.

The task of algorithmic data analysis and standards of care review often requires a series of niche software applications that often demand specialized training and redundant data entry. Furthermore, understanding which risk models can be used to determine the probability of being a cancer susceptibility mutation carrier, and which make statements about the future risk of disease can be difficult. For these reasons clinical decision support is essential to the efficient processing of structured family history data.

2 METHODS AND DISCUSSION

In the mammography screening setting at Newton Wellesley Hospital, a limited set of data entry screens were used by mammography technicians to collect structured family history and patient demographics. Risk model computations were then automatically performed in an integrated workflow that included reporting and electronic health record elements. Those patients found at an elevated risk level were referred to the neighboring risk clinic for follow-up.

In the risk clinic, the patients completed a more exhaustive computerized survey administered on a tablet PC. The information from prior visits was used to help the patient complete the data entry. This augmented data was then used again for more informed analysis and reporting.

At this point the decision support screens in the clinician interface were used to determine a care plan for the patient that covers genetic testing, chemoprevention, and surgery. Two screens are shown in Figures. 1 and 2, and are intended to help answer the most important decision in hereditary risk assessment: is it appropriate to conduct genetic testing on the patient or some member(s) of his/her family?

2.1 Synthesis of Mutation Risk

The visual element marked as Synthesis of Risk, seen in Figure 1, represents the clinician's final assessment of the likelihood that the patient carries a genetic mutation. This value is based on the clinician synthesizing the output of multiple risk models and the complete family history shown in the pedigree. It drives the subsequent decision support and reporting mechanisms. The annotated slider allows the users to line up their answer with one of the models, split the difference, or choose another value.

An unexpected use of this screen is that users change the level of mutation risk to observe the effect this has on the future risk of developing cancer and the associated care recommendations, thereby exploring ranges of solutions and alternative testing options depending on the risk level.

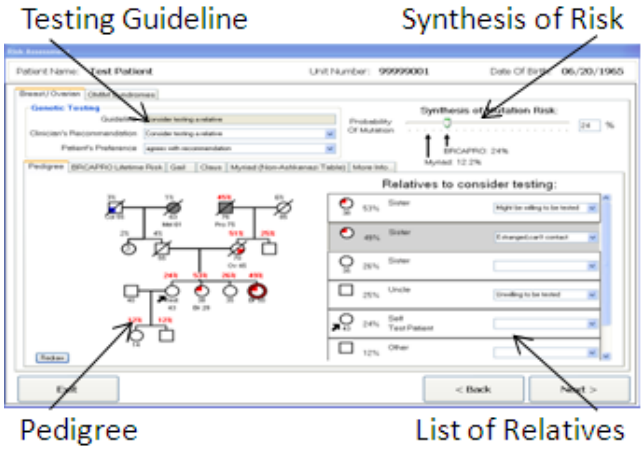

Figure 1. The display of hereditary risk showing genetic testing guideline, synthesis of mutation risk, pedigree, and a sorted list of relatives used to record individualized testing recommendations for family members.

2.2 Pedigree

The most important visual aid in hereditary risk assessment is the pedigree, or genogram [3]. Here we show the mutation probability for all family members directly on the interactive pedigree. Those

at a 10% or greater threshold are shown in red and bold, and those at low risk in black. This has had an effect on how clinicians perceive the distribution of risk in the family. This enriched pedigree is now being used by clinicians to directly compare risk among family members, highlighting previously subtle factors such as age of onset of disease.

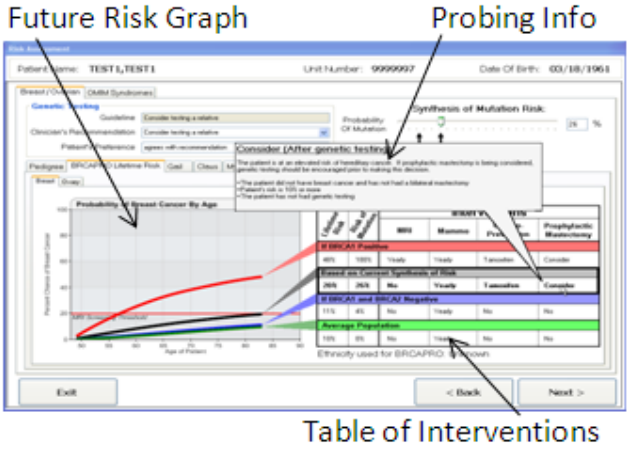

Figure 2. The display of hereditary risk showing genetic testing guideline, synthesis of mutation risk, pedigree, and a sorted list of relatives used to record individualized testing recommendations.

2.3 Sorted List of Relatives

This list is a simple way to help the clinician recognize every family member who could potentially benefit from testing. The list is linked to the pedigree and contains the same pedigree icon that describes a relative's disease state. Because genetic testing has an appreciable false negative rate, identifying the person with the highest priori odds of testing positive provides the most informative results, and it is standard of care to try to test this person first.

2.4 Line Graph of Future Risk

This line graph displays a comparison of the potential risk that a patient will develop cancer based on a variety of situations. The black line represents the future risk of disease based on the current synthesis of mutation risk. The red line represents the level of risk if the patient was tested and found to be BRCA1 positive. The green line shows the population average risk, and the blue line shows the case in which the patient was tested and found to be negative. The difference between the green and the blue is due to the false negative rate of a genetic test, which is well known to experts, but in traditional analysis is seldom appreciated. One problem that clinicians often face is the fatalistic mentality that some people feel in regards to genetic testing. They are now using this graph, where there are obvious differences between the red, black, and blue lines, to explain to people that the outcome of genetic testing can greatly affect their risk of cancer and ultimately what medical care they receive. It has become an aid in convincing patients to pursue genetic testing.

2.5 Table of Interventions

This table (Figure 2) makes the association between the potential outcomes of genetic testing (rows) and the recommendations that will be made for a set of medical interventions (columns). Probing on the displayed value in each cell displays the text that will be used in the final report, and describes the branches of a decision tree that led to this recommendation.

One interesting lesson learned was that clinicians typically don't breakup their decision making into binary trees, thereby making the description sometimes counterintuitive. For this and other reasons, a rules-based decision support mechanism is being investigated for future versions of the software.

3 Results

Between January of 2006 and October of 2008 there were 108,074 completed surveys. This represents over 40,000 unique individuals, with 1,425 identified as at high risk and referred for further specialized care. Of these referrals, 312 were seen at the risk clinic and completed the more detailed patient survey (Figure 3). There were 155 that ultimately went forward with testing. Of these, there were 16 patients who were found to have deleterious mutations and therefore require specialized care. There were 7 tests that resulted in variants of unknown significance (VUS), and 3 benign mutations found. Just as significantly, 157 people who were at an elevated risk tested negative and therefore return to a population level risk.

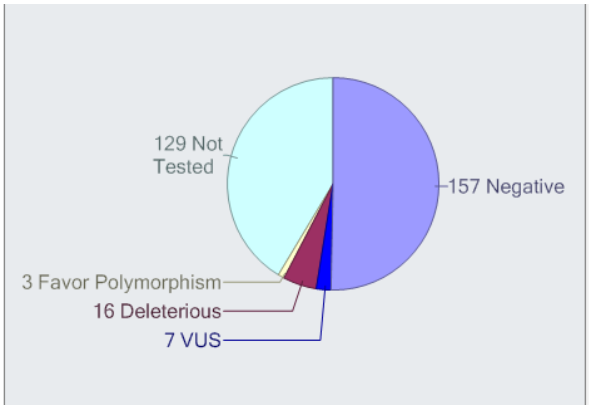

Figure 3. The distribution of testing outcomes for the 312 patients seen at the risk clinic.

4 Conclusion

By working largely within the visual landscape that is familiar to clinicians and scientists, we were able to develop an enriched display that is intuitive and support their workflow. There were an increasing number of referrals to the risk clinic, genetic testing recommendations, resulting in ultimately finding more BRCA mutation carriers, all without crippling the workflow by demanding additional resources.

It was an obvious benefit to integrate data collection and algorithmic analysis into an electronic system. These structured and quantitative data can directly be matched against standards of care for decision support. The more interesting outcome was how users responded strongly to the interactive and enriched pedigree visualization. This qualitative analysis tool was the most referred to benefit of using the software when the clinician end users were interviewed.

References

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