

## The Genomic Medicine Model: An Integrated Approach to Implementation of Family Health History in Primary Care

By: Lori A Orlando, [Vincent C. Henrich](#), Elizabeth R. Hauser, Charles Wilson, Geoffrey S. Ginsburg

Orlando, L.A., Henrich, V.C., Hauser, E.R., Wilson, C., Ginsburg, G.S. (2013). The genomic medicine model: An integrated approach to implementation of family health history in primary care. *Personalized Medicine*, 10(3), 295-306. doi: 10.2217/pme.13.20

Made available courtesy of Future Medicine Ltd.: <http://dx.doi.org/10.2217/pme.13.20>

\*\*\*© Future Medicine Ltd. Reprinted with permission. No further reproduction is authorized without written permission from Future Medicine Ltd. This version of the document is not the version of record. Figures and/or pictures may be missing from this format of the document. \*\*\*

### Abstract:

As an essential tool for risk stratification, family health history (FHH) is a central component of personalized medicine; yet, despite its widespread acceptance among professional societies and its established place in the medical interview, its widespread adoption is hindered by three major barriers: quality of FHH collection, risk stratification capabilities and interpretation of risk stratification for clinical care. To overcome these barriers and bring FHH to the forefront of the personalized medicine effort, we developed the genomic medicine model (GMM) for primary care. The GMM, founded upon the principles of the Health Belief Model, Adult Learning Theory and the implementation sciences, shifts responsibility for FHH onto the patient, uses information technology (MeTree<sup>®</sup>) for risk stratification and interpretation, and provides education across multiple levels for each stakeholder, freeing up the clinical encounter for discussion around personalized preventive healthcare plans. The GMM has been implemented and optimized as part of an implementation-effectiveness hybrid pilot study for breast/ovarian cancer, colon cancer and thrombosis, and risk for hereditary cancer syndromes in two primary care clinics in NC, USA. This paper describes the conceptual development of the model and key findings relevant for broader uptake and sustainability in the primary care community.

**Keywords:** community health | decision support | disease prevention | health education | risk assessment

### Article:

In 2002, the CDC launched the Family History Public Health Initiative, founded upon the principle that family history is an underutilized but effective tool for risk stratification. Among the stated goals were to develop tools to enhance family health history (FHH) collection and to evaluate whether FHH-based strategies work in practice. Since primary care providers account

for the majority of care encounters in the USA, they are the natural choice as partners to study the implementation of FHH into care delivery and medical decision-making. Yet, although FHH is a standard component of the medical interview and professional guidelines recommend screening strategies based upon FHH, its widespread adoption is hindered by three major barriers: quality of FHH collection, risk stratification capabilities and interpretation of risk stratification for clinical care.

### **FHH collection**

FHH is underutilized by practitioners and, therefore, represents a significant missed opportunity for risk stratification<sup>[1-3]</sup>. Barriers to FHH collection on the physician side include time constraints, lack of standardization of FHH elements and limited training in how to synthesize FHH data into a clinically actionable care plan<sup>[4-7]</sup>, while barriers on the patient side include being unaware of and unprepared to provide FHH, usually owing to lack of communication among family members or failure to appreciate its importance<sup>[7,8]</sup>. FHH tools can help overcome these barriers as evidenced by a systematic review that found a 46-78% improvement in cancer data recording by FHH tools as compared with the use of standard practice<sup>[9]</sup>. FHH tools show excellent concordance with structured pedigree interviews and the gold standard three-generation pedigree<sup>[10]</sup>. In a study of 1124 primary care patients, medical record documentation was insufficient in two-thirds of charts for FHH assessment of six common diseases<sup>[11]</sup>.

### **FHH for risk stratification**

FHH assessments have clearly been shown to identify persons at higher risk of common chronic disease, enabling preemptive and preventive steps, including lifestyle changes, health screenings, testing and early treatment, as appropriate<sup>[12]</sup>. More recently Qureshi *et al.* has prospectively shown the potential to identify presymptomatic individuals at elevated risk for common, chronic diseases and activate them to modify their risks<sup>[13]</sup> - an enormous opportunity to improve public health by implementing risk-based screening and prevention strategies. In this study, systematic collection of FHH for cardiovascular risk assessment demonstrated a 40% increase in the identification of individuals at high risk. However, risk-stratification algorithms applicable to primary care are multiplying and most are complex; some, such as the Gail Score, are too complex to be calculated without the aid of a calculator or computer. This leads to a limited awareness of available risk algorithms and difficulty implementing risk stratification in clinical workflow, even when awareness is high.

### **Clinical interpretation**

Clinical interpretation is the final step in the pathway that converts FHH data into concrete clinical actions (i.e., FHH's clinical utility). Without an associated clinical action, risk stratification has little to no impact on clinical care; however, for FHH there exists strong evidence linking risk to action. For example, a number of clinical guidelines, such as those for

colon cancer, breast cancer and cardiovascular disease, recommend screening and/or treatment strategies tailored to FHH-based risk level. Yet, even for common conditions such as colorectal cancer, for which primary care physicians provide the bulk of screening, interpretation of different screening strategies is poor <sup>[7,14]</sup> and for less common conditions it is even worse <sup>[5,15]</sup> . This is not surprising given that risk stratification, upon which clinical interpretation depends, is rarely performed (as described in the 'FHH for risk stratification' section) and the barriers to both are similar <sup>[7]</sup> .

### **Rationale for tools combining FHH collection & clinical decision support**

FHH collection, risk stratification and clinical interpretation can be performed efficiently and effectively using a variety of software platforms that have the potential to overcome the barriers created by a reliance on physicians to gather, record and analyze FHH. Given the patient and physician barriers previously cited, one solution is that patients, instead of physicians, could be an important locus for data input. In addition, computerized tools can link risk stratification to clinical care through the use of clinical decision support (CDS). The goal of CDS is "to provide the right information, to the right person, in the right format, through the right channel, at the right point in workflow to improve health and healthcare decisions and outcomes" and a roadmap has been developed to achieve this goal <sup>[16]</sup> . A systematic review found that adoption of CDS significantly improved clinical practice with a 94% success rate when CDS provided computer-generated recommendations at the point of decision-making and was integrated into the clinical workflow <sup>[17]</sup> . Therefore, in 2003 the Genomedical Connection, a collaboration between Duke University (NC, USA), the University of North Carolina-Greensboro (NC, USA), and Cone Health (NC, USA), developed the genomic medicine model (GMM) for primary care to determine if integration of an evidence-based tool allowing patient-entered FHH to be linked to CDS is feasible, effective and sustainable. In 2004, development and implementation of the model was initiated through funding by the US Department of Defense. This paper describes each of the model components, the implementation processes and key findings from the early implementation period.

### **The GMM**

The following section describes the development and theory underlying the GMM and its components, the implementation processes used to integrate and adapt the model to real world clinical practice, and a clinical trial to evaluate the impact/effectiveness of the model across stakeholders.

#### **\* Model components**

While the core of the GMM is an internet-based FHH collection and CDS tool (MeTree<sup>®</sup>), it is but one component of a broader education platform represented by the GMM <sup>[18]</sup> . The development of, and the later integration of the GMM into primary care, is founded upon the premise that providing the means for risk stratification and clinical interpretation is not sufficient

- it must be tightly linked to stakeholder awareness and activation, which is particularly important for overcoming patient barriers to FHH collection. Below is a description of the steps taken and the resulting elements that were incorporated into the GMM to achieve this goal.

## **Education**

The educational program's development was preceded by several front-end needs assessments carried out with the project's stakeholders: physicians, patients and community members, to better understand the barriers and needs relevant for the development and implementation of the GMM in primary care. Each of these assessments have previously been described <sup>[19-21]</sup>, but in brief:

- \* A telephone survey of knowledge, attitudes and risk perception related to genomics and FHH was administered to 1136 NC (USA) community members;
- \* A written patient survey (the same as that administered verbally to community members) was completed by 1350 individuals in four primary care practices in NC, USA;
- \* Individuals in four physician focus groups, comprised of 14 internists from NC, USA and two mid-level providers were asked open-ended questions about concerns and potential solutions related to genomics, FHH and the integration of both into clinical practice.

The educational elements of the GMM derived from these needs assessments are described for each stakeholder below. All educational interventions were based upon principles of adult learning, which depends upon identifying perceived personal needs to motivate learning <sup>[22]</sup>. Materials were written at an 8th grade reading level (aged 13-14 years) and were piloted by stakeholders. In addition, a website was developed as an educational resource and to host all of the GMM educational materials <sup>[101]</sup>. The educational deliverables resulting from the assessments were distributed prior to the widespread implementation of MeTree in participating practices.

### ***Community education***

A substantial proportion of individuals believed that a genetically or FHH-based disease risk could not be modified and many were concerned about genetic discrimination, although most supported the use of FHH to guide preventive care <sup>[19,20]</sup>. To address these concerns we developed community-oriented educational materials about FHH risk, the ability to modify that risk and who to talk to about their risk. These materials also were distributed by local health organizations, such as the congregational nurses, who agreed to assist us, and by the GMM team at local health fairs. In addition, local media, both print and television, and local businesses were contacted to promote FHH and the GMM through magazine and newsletter articles, presentations to many local service and business organizations, and television interviews.

### ***Patient education***

The patient assessment results did not differ from those identified during the community assessment. To address their concerns we developed patient-oriented educational materials based upon the principles of the Health Belief Model, that is, that a patient's willingness to act proactively depends upon their perception that there is a significant personal health risk; taking action is likely to have a positive impact, while not taking action could have a significant negative effect, and the action is doable <sup>[23]</sup>. These perceptions are typically based upon either personal experience or the experience of a close family member. Therefore, we developed educational materials for each stage in the GMM process: raising awareness to promote participation, to facilitate the use of MeTree and to understand the CDS output. To raise awareness, three educational brochures, one for each of the three diseases analyzed by MeTree (breast/ovarian cancer, colorectal cancer and thrombophilia) were developed. To encourage action, all of the brochures include the slogan: "Talk to your Family, Talk to your Doctor". To facilitate use of MeTree, instructions on how to use MeTree, a brochure describing family relationships and how to collect FHH, a booklet on the principles and value of FHH developed in collaboration with the Genetic Alliance <sup>[24]</sup>, and a worksheet for documentation of the collected FHH were also produced. To facilitate understanding the CDS output, we developed patient-oriented CDS output that includes a copy of their pedigree and a report that highlights their personal risk level, the triggers for their risk level and topics of discussion with their doctor. Additional educational materials to be given to individuals assigned to moderate- or high-risk categories were developed using images to facilitate understanding of risk concepts and these are available at the project's website <sup>[101]</sup>.

### ***Physician education***

Physicians were uncertain about how to stratify risk and clinically interpret FHH, and were supportive of an automated CDS to assist their decision-making <sup>[21]</sup>. They expressed concerns about the impact on clinical workflow, including lengthy and/or unclear CDS output, availability of resources to learn more about CDS recommendations if desired, lack of time to discuss CDS results with patients, and implications of inaccurate patient-provided pedigrees. To address these concerns the GMM included:

- \* Continuing medical education (CME) modules developed in conjunction with the Area Health Education Center on FHH, breast cancer risk, colon cancer risk and thrombosis risk <sup>[102]</sup>;
- \* Physician-oriented CDS output organized in a simple summary format with a section at the end containing the factors contributing to risk level and references;
- \* The ability to update FHH and rerun CDS if important inaccuracies in FHH are identified;
- \* A detailed manual and orientation session describing the conceptual foundation of the GMM, the evidence-based algorithms upon which CDS runs, and answers to frequently asked questions.

In addition, to address concerns regarding workflow impact, the implementation process elicited frequent feedback from stakeholders and was modified to optimize its acceptance and efficacy (see the 'Implementation' section for more details).

### **Patient-facing FHH collection tool with integrated CDS (MeTree)**

The goal of MeTree is to assist primary care providers in identifying high-risk individuals who may need additional screening or referrals to maximize their preventive healthcare. To this end, a standalone internet-based software program, MeTree, was developed and piloted by genetic counselors, patients and community members for content, usability and understanding<sup>[25]</sup>. To maximize usability it uses large fonts and radial buttons with text at an 8th grade reading level (aged 13-14 years), and supports a touch screen interface. It collects a three-generation FHH on 48 conditions from patients prior to their appointment and currently provides CDS output for five test conditions: breast cancer, ovarian cancer, colon cancer, thrombosis and hereditary cancer syndromes. Diseases collected by the tool are shown in Box 1.

CDS is based upon evidence-based algorithms drawn from guidelines using FHH and risk stratification<sup>[26-29]</sup>. For breast cancer the Gail model<sup>[30]</sup> and BRCAPro<sup>[31]</sup> are used for risk stratification. A dedicated multidisciplinary team maintains and updates algorithms as needed. Decision support is provided in the form of printed reports. A patient report outlines important points for patients to discuss with their providers, while a provider report contains guideline recommendations for prevention and screening based upon estimated disease risk. Both receive a copy of the pedigree and the provider is also given a tabular report of the family history as well.

### **\* Implementation**

Since it is now well established that even effective interventions are not widely incorporated into clinical practice if implementation is burdensome or complicated, we aimed to seamlessly integrate the GMM into normal primary care clinical workflow. This was a challenge, given that this standalone system does not integrate directly into electronic medical records. To do this we employed the following principles: stakeholder input (through interviews and surveys) would be elicited both prior to implementation and during regular cycles after implementation to guide adaptation; each component of the model (raising awareness, accessing and using MeTree, receiving CDS output, understanding CDS output, discussing results with provider, and changes in the clinical care strategy) would be independently evaluated and optimized; and identifying keys to sustainability would be a priority. Initial feedback, resulting model adaptations and follow-up feedback were to be recorded and categorized for development of an implementation guidebook (to guide future implementations). In addition, clinical champions would serve as liaisons between the practices and GMM personnel.

Two Cone Health primary care clinics in NC, USA consisting of 11 board-certified internal medicine providers, one board-certified family medicine physician and one nurse practitioner with 31,000 unique patient visits annually served as implementation sites. In order to minimize

the burden on patients, providers and the clinical staff, MeTree was provided on a dedicated clinic kiosk to permit access in the clinic for patients who did not have internet access at home. Just prior to the patient's appointment, CDS output could be printed by clinic staff to give the appropriate patient documents to the patient and provider documents scanned into the medical record. GMM staff were available on-site for questions by patients or staff and would enter FHH data into MeTree for those patients uncomfortable with the computer. Results of the stakeholder evaluations and optimization period are provided in the 'Results and discussion' section.

#### **\* Clinical trial**

Although implementation evaluations are extremely helpful during integration, we initiated a hybrid implementation-effectiveness controlled trial at the two implementation sites and at a third control clinic to fully understand the acceptance, clinical impact and sustainability of the GMM in primary care. A protocol paper describing the study design in detail has been previously published <sup>[25]</sup> and is shown graphically in Figure 1. For a complete description of the trial refer to <sup>[25]</sup> .

#### **FIGURE 1 IS OMITTED FROM THIS FORMATTED DOCUMENT**

In brief, all adult English-speaking primary care patients with upcoming appointments who were not adopted were invited to participate. All participants used the clinic kiosk to enter FHH data on the day of their appointment so that study coordinators could assist if needed. This limited the number of individuals who could be recruited to eight per clinic per day. Those interested in participating in the study received the GMM education and educational materials, as described above, from the study coordinator either by email or in person 2 weeks prior to their appointment. All questions were logged by the study coordinators in order to develop a patient frequently asked question list, as well as reasons for wanting to participate in the study. Patients were surveyed at baseline, just prior to completing data entry into MeTree, after their appointment with their physician, at 3 and 12 months. The baseline, 3- and 12-month surveys focused upon knowledge, attitudes, risk perception and impact of FHH, while the other two focused upon the 'user experience' for the GMM and how it impacted their visit with their primary care physician. The physicians were surveyed at 3 and 12 months on their experience with, perceived benefits of and potential barriers to using the GMM on a daily basis.

#### **Results & discussion**

##### **\* Community education results**

The extent of the educational outreach has been broad and generated a great deal of insight into sustainability of the GMM and other models like it. The following is a list of activities related to community education; those related to patient and physician education are described in the 'Implementation' and 'Clinical trial' sections:

\* The Genomedical Connection participated in 98 health fairs and 74 community events, and published 30 articles in community publications. The health fairs and community events alone reached over 21,000 individuals. Topical articles concerning genetic susceptibilities to a variety of common chronic diseases have appeared in Cone Health's quarterly magazine, *Health and You*, which has a circulation of 50,000 households. A list of these is available upon request;

\* Local media discussed the Genomedical Connection seven times and local news stations carried three interviews: one in 2006 and two in 2011. The 2011 interviews will be made available on our website <sup>[101]</sup> as they are no longer available online;

\* The website generated 496,195 hits (averaging 4400/month) from 95 countries, the highest three being the USA, China and Germany. In addition, it has 189 email subscribers, 37 US mail subscribers, 316 Facebook friends and 105 Twitter followers (data taken on 1 October 2012).

Community response to the program has now extended beyond awareness and participation. Cone Health has recently initiated the development of a genetic counseling service program to serve primary care providers throughout the system, and local economic and business planners have undertaken efforts to develop services and products that could support the implementation of personalized approaches in the healthcare system.

### \* **Implementation results**

Since the implementation of the GMM consisted of several cycles of interviews for feedback and optimization of the model, several key areas important for uptake and sustainability were identified. These are further explained below and divided into two relevant stakeholder groups: physicians and patients.

#### **Physicians**

In preimplementation interviews physicians in the intervention sites were initially skeptical of both the impact of the GMM on their clinical practice and the ability of the model to integrate seamlessly. At the conclusion of the implementation period, physicians endorsed exceptionally strong support for both the ability of the model to integrate into the workflow and its ability to improve the care that they offered. In fact, through word of mouth, physicians at other local clinics started to request access to the GMM for their patients. The following adaptations were critical to this high level of support.

#### ***Physician education***

A total of 352 physicians signed up for the CME course: 131 for breast cancer; 80 for colon cancer; 100 for family history; and 41 for inherited hypercoagulable states. Completion rates averaged 33.9% with post-CME test scores averaging 86%. Course evaluations on raising awareness, knowledge acquired and quality of the presentation ranged from 3.96 out of five for the breast cancer module to 4.27 out of five for the inherited hypercoagulable states module.



Despite very positive feedback from those who took the CME course, it is clear that it has had a limited reach. In fact, all the physicians in the study clinics indicated CME as a preferred source of education, yet none took the offered CME course. Using the same Health Belief Model <sup>[23,32]</sup> and Adult Learning Theory <sup>[22]</sup> concepts that served as the foundation for developing the patient education materials, we integrated just-in-time education into the CDS physician report (described in the 'CDS physician report format' section), which leveraged the relevance of the content to clinical care by associating it with an individual patient. This approach was extremely successful and raised awareness among the participating physicians.

### ***CDS physician report format***

The initial approach to physician reports was to summarize findings and suggest actions to consider; however, physicians wanted a cleaner and more action-oriented format, while we wanted to build in just-in-time educational content. The resulting optimized report included bolded and highlighted text bullets at the top indicating the recommended action, a second section with bulleted text indicating the important elements in the history leading to the recommendation, and a third section with detailed text providing education about the triggers, guidelines and references.

### ***Report recommendations for tamoxifen & breast MRI***

Physicians felt less comfortable discussing both tamoxifen chemoprophylaxis and breast MRI screening with patients than they did discussing colon cancer screening options. In order to facilitate those discussions, they requested that the number needed to treat, a measure of efficacy that reflects the likelihood of not benefiting from the intervention, be incorporated into the reports.

### ***FHH format***

Physicians were provided with a copy of both a pedigree and a tabular FHH. The majority preferred to view the tabular format and use it in their decision-making, although they wanted to have the pedigree available in the chart for referrals and documentation.

### **Patients**

During implementation the two key areas for adaptation focused on patient educational elements. Although they found the education to be generally helpful, there were two areas that did not fulfill all their needs. The first relates to collecting FHH and the second to risk stratification. These are discussed below.

### ***FHH education & worksheets***

Patients found the educational material describing who to talk to, the list of diseases to collect, the types of information needed and the FHH worksheet for recording collected FHH to be

exceptionally helpful; however, they still felt that they lacked all of the necessary FHH information. This is evident from the fact that all patients entered a full three-generation family structure with an average of 88% of deceased relatives having an age of death, but only 21% of deceased relatives having a cause of death listed. This indicates that while the worksheets are a step in the right direction, further focus groups will be needed to identify what elements are missing to make them more effective.

### ***Target educational materials to CDS output***

After risk stratification, patients at moderate or high disease risk are eligible for more intense or alternative screening strategies as compared with routine screening. These patients have many questions about the pros and cons of each strategy, what it means for their overall health and what the cost implications are. While these issues are typically discussed during their appointment with their physician, they frequently requested additional written material to aid their decision-making, prompt them to act and remind them of points discussed by their physician. The existing targeted materials focus on understanding the concepts of risk, which is helpful, but do not address the above questions. Additional materials will be developed to highlight the pros and cons of each strategy, as well as how personal preferences and values can affect which strategy is preferred.

### **\* Clinical trial results**

The clinical trial has just completed enrollment and analyses are underway. Figure 2 shows the study flow diagram. Percentages reflect the percent of those initially meeting the recruitment criteria (8010 patients). While recruitment was limited by the number of time slots available to use the clinic kiosk, 33% of those contacted were interested in participating.

Table 1 shows participant characteristics and compares them to the baseline clinic population. There were no statistically significant differences, between the two groups.

Despite the fact that statistical analyses have just begun, several key findings from the clinical trial have become clear.

### **Recruitment**

During recruitment, the study coordinator elicited responses as to why participants were interested in collecting and entering FHH into MeTree. The most commonly cited reason was the benefit of FHH to inform their personalized healthcare prevention plan. In addition, older individuals (>60 years of age) were enthusiastic when they learned that the benefits extended to the potential to identify care strategies for their family members, particularly the younger generations. From this it is clear that continuing to develop and maintain materials that focus upon the personal impact of the intervention increases motivation and activation and is thus essential long term for sustainability.

## **Use of MeTree**

Assistance from study coordinators was requested by 26% of patients. These questions fell into two categories: terminology used in MeTree and concern about use of the CDS output for discrimination by insurance companies. In regards to terminology, a frequently asked question section is posted on the website <sup>[101]</sup>. The top three were 'what is the difference between inflammatory bowel disease and irritable bowel disease?', 'what is a hereditary cancer syndrome?' and 'if a family member has breast cancer does that mean you have a hereditary breast and ovarian cancer syndrome?' MeTree was modified to address these concerns by changing terminology and employing skip screens to guide people without hereditary cancer syndromes away from questions related to that group of disorders. In order to access those questions now, a patient must answer 'yes' to the following question: have you or anyone in your family had a genetic test? These changes have considerably lessened the frequency of confusion around terminology. In regards to concerns about discrimination, an additional brochure was developed describing the Genomic Information Act and the protection it provides. More detailed language was also added to the consent process.

## **Genetic counseling**

Most of the providers in the study had rarely, if ever, referred a patient for genetic counseling. During the study period, genetic counseling referrals increased, leading to a better understanding among providers of how and when to refer and what the potential benefits are. A chart review of 408 enrolled patients identified no genetic counseling referrals in the year prior to MeTree integration, while to date there have been 138 referrals from the 1184 patients enrolled in the study. Patients expressed concerns about the additional time it would take to return for a genetic counseling session and what benefits it would provide beyond what their provider was already doing. Developing focused material to aid patients in understanding the pros and cons of genetic counseling and what to expect at the visit will be an important area to optimize.

## **Conclusion**

Our model lays the groundwork for successfully engaging stakeholders in personalized medicine at the level of the community, patient and physician by raising awareness, promoting activation and realigning patient visits with discussions of prevention strategies, values and preferences, rather than data collection. The success of this model lies in its foundation on the Health Belief Model <sup>[23,32]</sup>, Adult Learning Theory <sup>[22]</sup> and an implementation science framework. Bringing these three principles together creates a learning experiential environment that is responsive to stakeholder needs, optimizes learning and minimizes burden.

Our model is not alone in this area. Since 2004, when this model was first being developed, concurrent work by others has also shown benefits of FHH use for risk stratification in the areas of disease risk perception <sup>[33,34]</sup>, acceptance by patients of patient-entered FHH tools <sup>[35-37]</sup>, and the benefit of using such tools in identification of high-risk individuals in primary care <sup>[37,38]</sup>.

This work and others like it continues to break new ground in the ability to implement personalized medicine strategies into real-world clinical environments.

The unique aspects of each clinical setting, institutional principles and work culture prevent generalizing the current findings to a broader dissemination and implementation plan; however, for systems interested in exploring implementation of FHH collection and risk assessment, the following findings could be helpful. First, demonstration of the impact of a tool either through hands-on cases or through discussion with early adopters can demonstrate the benefit of such a system far more convincingly than describing its function. Generating this early buy-in is exceedingly helpful in overcoming biases and prevents multiple small barriers to implementation from being viewed as insurmountable. Second, each practice/setting should anticipate that barriers will arise; however, with frequent monitoring and feedback, simple solutions arise that can lead to optimal performance. Third, establishing a patient educational component and obtaining feedback from all stakeholders is essential for both successful implementation and performance.

In its current form the GMM serves as a stepping stone towards the integration of other personalized medicine data, as the evidence becomes available, into primary care clinical practice. The foundation established with FHH can be expanded upon to incorporate other types of information such as genetic, genomic, patient values and quality of life, as well as to guide targeted whole-genome sequencing to genes and gene regions implicated by genome-wide association studies and other gene discovery methods. However, for the immediate future, garnering further stakeholder support will involve continued development and optimization of the educational components related to raising awareness and connecting CDS recommendations to individual preferences and values.

### **Future perspective**

Genomic medicine is a 'knowledge-based' approach that compares features of a patient's FHH with evidence gathered from previous database studies to assess the patient's disease risk and reduce it through personalized medical interventions. The obvious potential value of FHH for assessing patient disease risk will bring with it a greater emphasis on clinical research that focuses on the exacerbating environmental conditions, including health-related behaviors and genomic predispositions associated with and preceding disease onset. Already, molecular tools are rapidly evolving that will allow for a more refined genomic analysis of individual patients and their family members, and eventually will identify genetic predispositions and physiological changes that precede disease symptoms. Recent analyses suggest that FHH and molecular genetic information are complementary tools that together can improve disease risk assessment<sup>[39]</sup>. It is also evident that the full potential of a personalized medical approach using FHH will hasten changes in patient and physician roles. Patients will need to acquire a better understanding of their family relationships and their personal risk, hone their decision-making skills, improve their health literacy, and be more aware of their cultural and personal preferences

when developing a healthcare plan. Together, these suggest that health education in the future will need to be modernized to foster relevant skills and knowledge. Clinical performance will increasingly depend upon the well-developed dialog skills of its health professionals, the seamless use of information technology, the integration of FHH information with genetic/genomic tests to refine and improve medical recommendations, and a greater use of experiential learning as part of medical education. At the system level, genomic medicine will also require a revision of medical reimbursement plans to incentivize the widespread use of preventive diagnosis and management. In summary, genomic medicine will optimize medical care focused on expanding the patient's productive lifespan, but it will require that patients be continuously engaged in overseeing their own health and that their physicians will be ready to engage in an informed dialog about it.

**Table 1.** Study population characteristics.

<b>Characteristics</b>	<b>Study participants</b>	<b>Baseline clinic population</b>
Mean age (SD)	58.8 (11.81)	59.3 (13.5)
<b><i>Gender</i></b>		
Male, n (%)	490 (41.4%)	56.1%
Female, n (%)	694 (58.6%)	42.7%
<b><i>Ethnicity</i></b>		
White, n (%)	984 (83.1%)	75.2%
Black, n (%)	159 (13.4%)	15.5%
Other, n (%)	41 (3.5%)	9.3%

SD: Standard deviation.

**Box 1.** Diseases collected by MeTree<sup>®</sup>.

<b><i>Cancers</i></b>	
* Brain	
* Breast	
* Cervical	
* Colon	
* Kidney	
* Leukemia	
* Liver	

<ul style="list-style-type: none"> <li>* Lung</li> <li>* Lymphoma</li> <li>* Melanoma</li> <li>* Ovarian</li> </ul>	
<ul style="list-style-type: none"> <li>* Pancreatic</li> <li>* Prostate</li> <li>* Skin (not melanoma)</li> <li>* Small bowel</li> <li>* Stomach</li> <li>* Testicular</li> <li>* Thyroid</li> <li>* Unknown</li> <li>* Uterine</li> <li>* Other, specify</li> </ul>	
<b><i>Other conditions</i></b>	
<ul style="list-style-type: none"> <li>* Alzheimer's disease/dementia</li> <li>* Anemia</li> <li>* Asthma</li> <li>* Blood clots in veins</li> <li>* Colon polyps</li> <li>* Diabetes</li> <li>* Glaucoma</li> <li>* Heart attack</li> <li>* High blood pressure</li> <li>* High cholesterol</li> <li>* Inflammatory bowel disease</li> </ul>	
<ul style="list-style-type: none"> <li>* Lupus</li> <li>* Macular degeneration</li> <li>* Multiple miscarriages</li> <li>* Multiple sclerosis</li> <li>* Osteoporosis</li> <li>* Parkinson's disease</li> <li>* Rheumatoid arthritis</li> <li>* Seizures</li> <li>* Stroke</li> <li>* Thyroid disease</li> </ul>	
<b><i>Hereditary cancer syndromes</i></b>	
<ul style="list-style-type: none"> <li>* Cowden syndrome (<i>PTEN</i> gene)</li> <li>* Familial adenomatous polyposis (<i>APC</i> gene)</li> </ul>	

* Hereditary breast and ovarian cancer ( <i>BRCA1/BRCA2</i> genes)	
* Hereditary nonpolyposis colon cancer ( <i>MLH1/MSH2/MSH6</i> genes)	
* Li-Fraumeni syndrome ( <i>TP53</i> gene)	
* Other cancer syndromes	

Reproduced from <sup>[25]</sup> .

Executive summary

### ***Background***

- \* Risk stratification is endorsed by numerous guidelines and medical societies to target risk-based prevention strategies, such as breast MRI.
- \* Consistent use of risk stratification is limited by both barriers to family health history (FHH) collection and synthesizing data into actionable care plans.
- \* The genomic medicine model (GMM) for primary care was developed to overcome many of these obstacles and encourage uptake of evidence-based prevention strategies tailored to patients' risk level.

### ***The GMM***

- \* The GMM is comprised of two integrated components: a internet-based program that collects and analyzes FHH providing medical recommendations, MeTree<sup>®</sup> , and educational programs for physicians, patients and community members.
- \* Education was designed using the principles of the Health Belief Model and Adult Learning Theory and is provided before, during and after using MeTree.

### ***Implementation & clinical trial***

- \* An implementation sciences approach to incorporating the GMM into two primary care practices focused upon frequent stakeholder feedback cycles regarding overall experience, perceived barriers and adaptations to resolve them.
- \* A clinical trial is assessing the GMM's impact by assessing users' experiences, identifying patients at higher than population level risk, changes in clinical care and changes in health-related behaviors.
- \* All adult English-speaking patients at the two clinics were invited to participate and followed for 1 year.

### ***Implementation & trial results***

- \* Community education outreach response has been broad.

\* Adaptations to the model based upon stakeholder feedback during implementation included modifying physician reports and patient educational materials.

\* Physician sentiments regarding the benefits of the GMM and FHH evolved from skepticism to broad acceptance.

\* To date, the clinical trial has shown that the model appeals to general clinic populations, MeTree is acceptable and easy to use, and more description of health-related terms is important.

\* Genetic counseling referrals have increased compared with baseline and will need to be a major consideration in any broad uptake initiatives.

### ***Conclusion***

\* GMM integration into clinical practice is not only feasible but can activate patients and physicians, and achieve broad support by demonstrating that it fills a gap in clinical care, providing directed clinical decision support and just-in-time education for both patients and physicians, and gathering feedback and making adaptations to address local needs.

\* Continued development is needed to fulfill its potential.

\* An ongoing clinical trial will identify the impact of the GMM on clinical diagnostics, patient-physician relationships and the economies of the healthcare system, and inform broader implementation.

### ***Future perspective***

\* Future evaluation of FHH will combine it with genomic, environmental (including health behaviors), clinical and psychosocial measures to further refine risk stratification and prevention strategies.

\* Broader incorporation of the above measures into clinical practice will further activate patients to collect and share important health information, improve health literacy, motivate positive behavior changes and enhance communication with physicians, all of which will encourage a shared decision-making healthcare model.

### **CAPTION(S):**

Figure 1. The genomic medicine model overview and clinical trial flow.

FHH: Family health history; recs: Recommendations; SES: Socioeconomic status.

### **References**

Papers of special note have been highlighted as: \* of interest \*\* of considerable interest



- 1 Rubenstein WS. Family history and health risk assessment tools. In: *Genomic and Personalized Medicine (2nd Edition)*. Ginsburg HF (Ed.). Academic Press, MA, USA (2012).
- 2 Berg AO, Baird MA, Botkin JR *et al*. National Institutes of Health State-of-the-Science conference statement: family history and improving health. *Ann. Intern. Med.* 151, 878-885 (2009).
- \*\* Outlines the potential utility, major challenges and information gaps that currently exist and which must be filled in order to evaluate and implement the wider use of family health history (FHH) in primary care.
- 3 Doerr M, Teng K. Family history: still relevant in the genomics era. *Cleve. Clin. J. Med.* 79(5), 331-336 (2012).
- 4 Acton RT, Burst NM, Casebeer L *et al*. Knowledge, attitudes, and behaviors of Alabama's primary care physicians regarding cancer genetics. *Acad. Med.* 75(8), 850-852 (2000).
- 5 Gramling R, Nash J, Siren K, Eaton C, Culpepper L. Family physician self-efficacy with screening for inherited cancer risk. *Ann. Fam. Med.* 2(2), 130-132 (2004).
- 6 Qureshi N, Wilson B, Santaguida P *et al*. Family history and improving health. *Evid. Rep. Technol. Assess. (Full Rep.)* 186, 1-135 (2009).
- 7 Wilson BJ, Qureshi N, Santaguida P *et al*. Systematic review: family history in risk assessment for common diseases. *Ann. Intern. Med.* 151(12), 878-885 (2009).
- 8 Audrain-McGovern J, Hughes C, Patterson F. Effecting behavior change: awareness of family history. *Am. J. Prev. Med.* 24(2), 183-189 (2003).
- 9 Qureshi N, Carroll JC, Wilson B *et al*. The current state of cancer family history collection tools in primary care: a systematic review. *Genet. Med.* 11(7), 495-506 (2009).
- 10 Reid GT, Walter FM, Brisbane JM, Emery JD. Family history questionnaires designed for clinical use: a systematic review. *Public Health Genomics* 12(2), 73-83 (2009).
- 11 O'Neill SM, Starzyk EJ, Kattezhram RA, Rubenstein WS. Comparison of family healthware and physicians' family history documentation among 1124 patients. Presented at: *the American Society of Human Genetics* . Philadelphia, PA, USA, 11-15 November 2008.
- 12 Heald B, Edelman E, Eng C. Prospective comparison of family medical history with personal genome screening for risk assessment of common cancers. *Eur. J. Hum. Genet.* 20(5), 547-551 (2012).

13 Qureshi N, Armstrong S, Dhiman P *et al.* Effect of adding systematic family history enquiry to cardiovascular disease risk assessment in primary care: a matched-pair, cluster randomized trial. *Ann. Intern. Med.* 156(4), 253-262 (2012).

14 Barrison AF, Smith C, Oviedo J, Heeren T, Schroy PC 3rd. Colorectal cancer screening and familial risk: a survey of internal medicine residents' knowledge and practice patterns. *Am. J. Gastroenterol.* 98(6), 1410-1416 (2003).

15 Murff HJ, Byrne D, Syngal S. Cancer risk assessment: quality and impact of the family history interview. *Am. J. Prev. Med.* 27(3), 239-245 (2004).

16 Downing GJ, Boyle SN, Brinner KM, Osheroff JA. Information management to enable personalized medicine: stakeholder roles in building clinical decision support. *BMC Med. Inform. Decis. Mak.* 9, 44 (2009).

17 Kawamoto K, Houlihan CA, Balas EA, Lobach DF. Improving clinical practice using clinical decision support systems: a systematic review of trials to identify features critical to success. *BMJ* 330(7494), 765 (2005).

18 Christianson CC. The Genomedical Connection: on-line education program on genomic medicine for primary care providers. In: *National Coalition for Health Professional Education in Genetics*. Bethesda, MD, USA (2008).

19 Hahn S, Letvak S, Powell K *et al.* A community's awareness and perceptions of genomic medicine. *Public Health Genomics* 13(2), 63-71 (2010).

\* Assesses a community's attitudes and knowledge about genetics and the use of family history and found that education level, age and previous medical experience with a familial disease were major drivers for community interest in genomic medicine.

20 Christianson CA, Powell KP, Hahn SE *et al.* Findings from a community education needs assessment to facilitate the integration of genomic medicine into primary care. *Genet. Med.* 12(9), 587-593 (2010).

21 Christianson CA, Powell KP, Hahn SE, Blanton SH, Bogacik J, Henrich VC. The use of a family history risk assessment tool within a community health care system: views of primary care providers. *J. Genet. Couns.* 21(5), 652-661 (2012).

22 Knowles M. *The Modern Practice of Adult Education: From Pedagogy to Andragogy* (2nd Edition). Cambridge Books, NY, USA (1980).

\*\* Outlines the basic tenets of the Health Belief Model and the importance of understanding the perceptions that must be considered when thinking about what is necessary to motivate patients to take action concerning their own health.

23 Champion V, Skinner C. The health belief model. In: *Health Behavior and Health Education: Theory, Research, and Practice*. Glanz K, Rimer BK, Viswanath K (Eds). Wiley and Sons, NJ, USA, 45-66 (2008).

24 Powell K, Edelson V, O'Leary J, Christianson C, Henrich V. Focus group evaluation of customized family health history education materials in a North Carolina community. *Am. J. Health Educ.* 42, 161-170 (2011).

\* Describes the basic protocols that were used to implement the genomic medicine model described in this article.

25 Orlando LA, Hauser ER, Christianson C *et al.* Protocol for implementation of family health history collection and decision support into primary care using a computerized family health history system. *BMC Health Serv. Res.* 11, 264 (2011).

26 US Preventive Services Task Force. Genetic risk assessment and *BRCA* mutation testing for breast and ovarian cancer susceptibility: recommendation statement. *Ann. Intern. Med.* 143(5), 355-361 (2005).

27 Buller HR, Agnelli G, Hull RD, Hyers TM, Prins MH, Raskob GE. Antithrombotic therapy for venous thromboembolic disease: the seventh ACCP conference on antithrombotic and thrombolytic therapy. *Chest* 126(Suppl. 3), S401-S428 (2004).

28 Hampel H, Sweet K, Westman JA, Offit K, Eng C. Referral for cancer genetics consultation: a review and compilation of risk assessment criteria. *J. Med. Genet.* 41(2), 81-91 (2004).

29 Vasen HF, Watson P, Mecklin JP, Lynch HT. New clinical criteria for hereditary nonpolyposis colorectal cancer (HNPCC, Lynch syndrome) proposed by the International Collaborative group on HNPCC. *Gastroenterology* 116(6), 1453-1456 (1999).

30 Gail MH, Brinton LA, Byar DP *et al.* Projecting individualized probabilities of developing breast cancer for white females who are being examined annually. *J. Natl Cancer Inst.* 81(24), 1879-1886.

31 Parmigiani G, Berry D, Aguilar O. Determining carrier probabilities for breast cancer-susceptibility genes *BRCA1* and *BRCA2*. *Am. J. Hum. Genet.* 62(1), 145-158 (1998)

32 Janz NK, Becker MH. The Health Belief Model: a decade later. *Health Educ. Q.* 11(1), 1-47 (1984).

\* Describes the clinical criteria for recommending referral for genetic counseling and provides information concerning the broad potential impact of FHH information for making recommendations in primary care.

33 Acheson L. Family history and genetic testing for cancer risk. *Am. Fam. Physician* 81(8), 934-938; author reply 934-938 (2010).

34 Wang C, O'Neill SM, Rothrock N *et al.* Comparison of risk perceptions and beliefs across common chronic diseases. *Prev. Med.* 48(2), 197-202 (2009).

35 Cohn WF, Ropka ME, Pelletier SL *et al.* Health Heritage, a web-based tool for the collection and assessment of family health history: initial user experience and analytic validity. *Public Health Genomics* 13(7-8), 477-491 (2010).

36 Hulse NC, Ranade-Kharkar P, Post H, Wood GM, Williams MS, Haug PJ. Development and early usage patterns of a consumer-facing family health history tool. *AMIA Annu. Symp. Proc.* 2011, 578-587 (2011).

37 Sweet KM, Bradley TL, Westman JA. Identification and referral of families at high risk for cancer susceptibility. *J. Clin. Oncol.* 20(2), 528-537 (2002).

38 O'Neill SM, Rubinstein WS, Wang C *et al.* Familial risk for common diseases in primary care: the Family Healthware Impact Trial. *Am. J. Prev. Med.* 36(6), 506-514 (2009).

39 Do CB, Hinds DA, Francke U, Eriksson N. Comparison of family history and SNPs for predicting risk of complex disease. *PLoS Genet.* 8(10), e1002973 (2012).

\* Describes how FHH and genetic test results are complementary when stratifying patient risk levels for disease.

**\* Websites**

101 Genomedical Connection. [www.genomedical.com](http://www.genomedical.com)

102 Area Health Education Center (AHEC) Continuing Medical Education.  
[www.aheconnect.com](http://www.aheconnect.com)

**Author Affiliation(s):**

<sup>[1]</sup> Duke Center for Personalized Medicine & Duke Institute for Genome Sciences & Policy, 3475 Erwin Road, Wallace Clinic Ste 204, Durham, NC 27705, USA

<sup>[2]</sup> Center for Biotechnology, Genomics & Health Research, University of North Carolina-Greensboro, 3701 MHRA Building, Greensboro, NC 27402, USA

<sup>[3]</sup> Center for Human Genomics, Department of Medicine, Duke University, PO Box 3445, Durham, NC 27710, USA

<sup>[4]</sup> Epidemiological Research & Information Center, Durham VA Medical Center, Durham, NC 27705, USA

<sup>[5]</sup> Cone Health, 1200 North Elm Street, Greensboro, NC 27401, USA

<sup>[1]</sup> Duke Center for Personalized Medicine & Duke Institute for Genome Sciences & Policy, 3475 Erwin Road, Wallace Clinic Ste 204, Durham, NC 27705, USA. lorlando@duke.edu

### **Author Note(s):**

\* *Author for correspondence*

### **Acknowledgements**

*The authors thank CC Christianson for her assistance in developing the genomic medicine model flow chart, her work on the assessments and on the educational strategy; KP Powell for her work in implementing the community education program and analysis; and A Agbaje for her assistance with clinical work and oversight of data collection. The Genomedical Connection study started as a collaboration between Duke University (NC, USA), the University of North Carolina-Greensboro (NC, USA) and the Moses Cone Health System (NC, USA) with contributions from: GS Ginsburg (principle investigator), LA Orlando (co-principal investigator), ER Hauser, M Donahue, A Buchanan, B Due, B Chesnut, C Blach, (Duke Center for Personalized Medicine, Institute for Genome Sciences and Policy, Center of Human Genetics and Department of Medicine, Duke University); V Henrich, K Powell, C Christianson, D Wallace, S Letvak (The Center for Biotechnology, Genomics and Health Research, The University of North Carolina at Greensboro); M Pericak-Vance, SH Blanton, S Hahn, (Duke University); J Telfair (University of North Carolina-Greensboro); and A Agbaje, C Wilson, L Wilkerson and C Freeman, physicians at Eagle Internal Medicine at Tannenbaum and LeBauer Healthcare at Jamestown Practices (Cone Health).*

### **Financial & competing interests disclosure**

*Funding for this project was provided by the US Department of the Army (W81XWH-05-1-0383). The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.*

*No writing assistance was utilized in the production of this manuscript.*