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Family History Is Valuable for Prevention

People who have close relatives with certain chronic diseases, like heart disease, diabetes, and cancer, are more likely to develop those diseases themselves. Studies suggest that having a first-degree relative with one of these diseases can at least double a person's risk of developing disease; this risk generally increases with an increasing number of affected relatives, especially if their disease was diagnosed at an early age.[1] Physicians usually collect information about a patient's family history, but often do not discuss, revisit or update it over time. Thus, they may miss opportunities to offer specific prevention recommendations for diseases that run in the patient's family.[2]

What is a First-Degree Relative?

First-degree relatives include immediate blood relatives, such as parents, siblings, or children. Second-degree relatives include aunts, uncles, nieces, nephews, and grandparents. First-degree relatives have approximately half their genes in common. From a genetic standpoint, you are closer to first-degree relatives because you share more of the same genetic material.

Knowledge of increased risk for chronic diseases due to family history can influence the clinical management and prevention of a disease. Prevention strategies include:

- targeted lifestyle changes such as diet, exercise, and stopping smoking,
- screening at earlier ages, more frequently, and with more intensive methods than might be used for average risk individuals,
- use of chemoprevention such as aspirin, and
- referral to a specialist for assessment of genetic risk factors.

Screening and prevention guidelines are available for many chronic disorders,[3-6] and data are accumulating regarding the effectiveness of these strategies for high-risk individuals.[7-9]

Disease Risk Due to Gene-Environment Interactions

Most common diseases result from the complex interactions of multiple genes with multiple environmental factors. These factors can include long-term exposures to pollution or sunlight, behaviors such as smoking or inactivity, and cultural factors such as diet. Despite progress in sequencing the human genome, considerable research is needed to understand the genes that predispose to chronic diseases.

Among the genes that are being studied are genes that code for carcinogen metabolizing enzymes (e.g., *NAT2* and *GSTM1*) and genes that regulate nutrient metabolism (e.g., *MTHFR*). Much work still needs to be done in order to understand how genes interact with each other and the environment to cause disease. In the meantime, family medical history represents a "genomic tool" that can capture the interactions of genetic susceptibility, shared environment, and common behaviors in relation to disease risk.

Role of Genetic Testing

Single-Gene Variant
A trait that is determined by a single gene.

Single-gene variants handed down in families may result in rare diseases such as Huntington's disease. Some of these variants (e.g., of *BRCA1* and *APC*) also result in common diseases, like breast and colorectal cancer. For more information, see *Chapter 4, Public Health Assessment of BRCA1 and BRCA2 Testing for Breast and Ovarian Cancer*. Fortunately, these variants are rare in the population, but when a harmful genetic variant is suspected in a high risk family, genetic testing may be possible.

Confirming a suspected genetic risk can relieve anxiety related to not knowing and may suggest specific preventive interventions. Genetic testing can also reassure relatives when familial susceptibility can be ruled out. A genetic specialist can determine when genetic testing might be considered and can counsel the patient on the risks and benefits of the testing process. A family history assessment is the first step towards identifying high risk families who may benefit from a genetic work-up.

Family History and the Family Tree

Family history information that is needed to assess disease risk includes the number, gender, and closeness of affected relatives, their ages at disease onset, and any associated health conditions. Organizing this information into a detailed family tree or pedigree graphically illustrates clusters and inheritance of traits within families. Instructions for recording a family history and drawing a pedigree can be found on many Web sites, including that of the National Society of Genetic Counselors (http://www.nsgc.org/consumer/familytree/index.asp).

The CDC Family History Initiative

The CDC Office of Genomics and Disease Prevention (OGDP) is collaborating with several CDC programs and the National Institutes of Health (NIH) in a family history public health initiative. The purpose of this initiative is to evaluate the use of family history for assessing risk for common diseases, as well as its role in influencing early detection and prevention strategies.

The initiative began in early 2002 with a review of the existing literature and a paper that introduced the concept of using family history for disease prevention.[1] At a workshop in May 2002, experts reviewed family history as a risk factor for several chronic diseases including cardiovascular disease, diabetes, asthma, and several cancers. Workshop participants discussed the accuracy and reliability of family medical history and attempted to gauge how useful knowledge of family history might be for motivating people to change their behavior. A series of scientific papers based on the workshop presentations was published in February 2003 as a theme issue in the *American Journal of Preventive Medicine*.[10]

Interested workshop participants joined with others to form the Family History Workgroup in order to explore, develop and test family history tools for disease prevention. This multidisciplinary group includes representatives from CDC programs, the NIH, other federal agencies, state public health programs, academia, and the health care community.

Selecting Diseases to Include in a Family History Tool

The Family History Workgroup first established the following criteria for deciding which diseases should be included in a family history tool:

- substantial public health burden,
- clear case definition,
- high awareness of disease status among relatives,
- accurately reported by relatives,
- family history is an established risk factor,
- prevalence of family history can be estimated in the population,
- effective interventions for primary and secondary prevention, and
- different recommendations for groups at different levels of familial risk.

The workgroup next reviewed other family history tools being used or developed for primary care and compiled a list of approximately 45 diseases that were included in these tools. After applying the inclusion criteria, the workgroup narrowed the list to 15 diseases.

Prototype Family History Tool

For public health purposes, family history tools should be simple, easily applied, and adaptable to different settings. Most of the existing family history tools that the workgroup reviewed were found to be too lengthy and difficult to interpret. The workgroup decided in May 2003 to develop a prototype family history tool that would include only a few diseases, making it easier to pilot test and evaluate in population-based settings. The diseases included in the prototype include:

- heart disease,
- stroke,
- diabetes, and
- colorectal, breast and ovarian cancer.

The prototype family history tool consists of a three-step process of data collection, risk classification, and recommendations for intervention, as shown in Figure 1.

Data Collection

The family history tool prototype is called Family Healthware. It is computer-based and self-administered and can be completed in a provider's office or at home before a medical consultation. The work group decided to create an electronic version of the tool that can process complex familial risk algorithms and provide feedback to patients and physicians. When completed, the tool will be made available as a CD-ROM and as a download from the Internet. Other formats, such as paper-based or touch-screen versions, are also being considered.

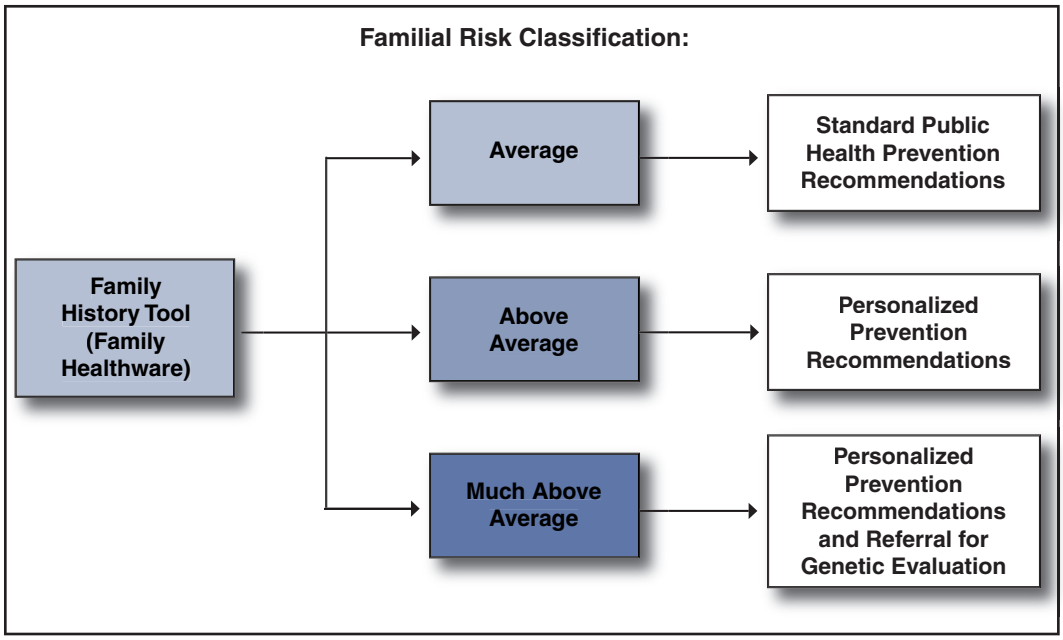
Family Healthware will collect:

- personal information, including age, gender, and race/ethnicity,
- numbers of relatives in each category (mother, father, children, siblings, grandparents, aunts, and uncles),
- personal history of heart disease, diabetes, stroke, colorectal cancer, breast cancer, and ovarian cancer, indicating whether age at diagnosis was below or above a disease-specific age threshold (e.g., age 60 for heart disease),
- history of the same six diseases for relatives and age at diagnosis in each category, and
- personal risk factors, such as body mass index (determined by height and weight), diet, exercise, use of tobacco products and alcohol, and screening behaviors such as mammogram and cholesterol screening.

Classification

Family Healthware will include software algorithms that interpret the data and provide a brief synopsis of disease risk and suggestions for follow-up. The goal is to keep data collection simple while gathering enough information to classify people into risk levels. The underlying scheme being considered includes three risk levels—average, above average, and much above average—that are determined mainly by the number and closeness of affected relatives and their ages at disease onset.[11] The risk classification would be used to guide and inform prevention activities.

Figure 1, Example: Proposed scheme for using family history to guide and inform prevention



Intervention

Family Healthware is being developed for use in primary care settings and for public health purposes. Primary care providers can play a major role in prevention by reviewing their patients' family histories and making recommendations for early detection or intervention strategies and counseling on lifestyle. Patients will be able to maintain and update their family history records at home and can discuss the implications with their providers during annual visits. The general public will also be able to retrieve the tool from the Internet and complete the assessment at home.

Family Healthware will produce an individualized assessment page that indicates the level of familial risk for each disease, and may include prevention messages about recommended behavior changes and screening.

An electronic resource manual that complements the tool is being developed for health care providers. The resource manual is organized into disease-specific chapters and includes an explanation of risk levels, including possible genetic conditions underlying "much above average" risk, and suggestions for assessment of additional risk factors. The resource manual will also include recommended preventive interventions for each level of risk (if available), and additional resources for health care providers and patients. These recommendations will be evidence-based, appropriately referenced, and supported by links to other Web sites, such the National Cancer Institute, the American Cancer Society, the National Heart, Lung and Blood Institute, the American Heart Association, Online Mendelian Inheritance in Man, and GeneClinics/GeneTests.

Evaluation Studies

Extensive pilot testing and evaluation studies are being planned to examine the validity and utility of the Family Healthware prototype. At the end of FY 2003, CDC awarded funding to three research centers—the University of Michigan School of Medicine, Evanston Northwestern Healthcare Research Institute, and Case Western Reserve University School of Medicine—for a collaborative study set in primary care clinics. The study will assess whether family history risk assessment, classification, and personalized prevention messages influence health behaviors and the use of preventive medical services. Additional studies will be developed to evaluate the tool in other public health and preventive medicine settings.

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