March/April 2003 · Vol. 5 · No. 2

Family history: Where to go from here

Family history is an important indicator of genetic risk for a number of conditions of public health importance. This includes adult-onset conditions that are routinely encountered by internists, such as coronary artery disease (CAD), diabetes, common cancers, and thrombosis. Thus internists are well positioned to capture important familial risk information that could result in risk-appropriate recommendations for disease prevention, early detection, and referrals for genetic services.

Unfortunately, the collection and interpretation of family history information as a means to improve disease prevention efforts is lacking in clinical medicine.[1–4] In this issue, Frezzo and colleagues[5] add to this growing literature, focusing on the family history collection practices of internists in an academic practice. They determined prevalence estimates of genetic risk for common, chronic diseases and reproductive issues in 78 patient volunteers returning for a follow-up visit during a 6-month period. They randomized the subjects to two data collection methods, the "gold standard" three-generation pedigree interview by a genetics professional and a questionnaire. The collected data were compared to information documented in the chart by the physician. The authors then stratified the familial risk obtained with the pedigree interview, questionnaire, and chart review as low, moderate, or high in each disease category. Differences in referrals for genetic services and health care recommendations that could result from interpretation of each family history collection approach were also considered.

Together, the questionnaire and pedigree interview identified 79.5% of the subjects as having an increased risk for at least one of nine disease categories under study; these included mendelian conditions, CAD, diabetes, breast/ovarian cancer, colon cancer, thrombosis, and reproductive risks. A substantial number of individuals were at risk for two or more conditions. The majority of the disease-specific risk categories were common, chronic conditions, the most prevalent being CAD. Fifteen individuals had a moderate familial risk for CAD, and 15 had high risk.

Knowing the prevalence of moderate and high familial risk for common, chronic conditions is important for determining the population-attributable risks associated with family history as a screening tool. Attributable risk is a key element in assessing the clinical validity of family history or the ability of the family history to accurately predict disease risk. There is a paucity of published information regarding the prevalence of family history as a risk factor for common, chronic diseases. The article by Frezzo et al.[5] provides an important contribution in this field. However, because of the small sample size and the voluntary aspect to participation, the prevalence estimates might not be representative of the population at large. In addition, although the ethnic mix of the population was diverse, the study population was limited to a single academic internal medicine practice and females were overrepresented. Ideally, a similar study of a larger, population-based sample is needed to obtain prevalence estimates of family history of common, chronic diseases. Furthermore, a larger study population could identify personal characteristics that influence reporting of family history, such as age, gender, ethnicity, and socioeconomic status. Information from a larger study could also help determine the most appropriate age range and time interval for asking about family history that would be most optimal for informing disease prevention recommendations and genetics referrals.

Both of the family history collection methods used in the study by Frezzo et al.[5] outperformed the chart review in identifying risk for each of the common, chronic disease risk categories and the reproductive genetic concerns under study. About 20% of the patients at increased risk by questionnaire or pedigree interview were not identified by the chart review, and all of the individuals found to be at increased risk by review of the medical records were captured by one of the study tools. Furthermore, the tools were more effective in identifying high familial risk. The authors point out that this is due to lack of documentation of age of diagnosis and lack of information regarding affected second-degree relatives in the chart. Indeed, about 20% of patients with increased risk determined by one of the study methods were classified as having no increased risk on chart review, and 11 patients classified as having moderate risk by chart review were assigned a high risk using one of the study methods. Thus age of disease onset and disease status in second-degree relatives appear to improve clinical validity of family history information for common, chronic diseases, and both should be included for optimal familial risk stratification.

Most family history risk classification systems and family risk scores for common, chronic diseases use age at onset for estimating risk. Generally, the earlier the age of onset the greater the risk, although family history of most common chronic conditions at any age of onset can increase the risk.[6] Because most common, chronic diseases have onset in adulthood, limiting family history information to only first-degree relatives might underestimate the familial risk in younger individuals, as the disease might be present only in older aunts, uncles, and grandparents. For conditions limited to one gender, such as prostate cancer, most breast cancer, and ovarian cancer, information regarding second-degree relatives is often crucial for defining a familial risk. Family size is another factor that can affect risk assessment and prediction. Some of the methods used to estimate family risk consider family size by comparing the observed and expected number of relatives with

a particular disease.[7,8] Silberberg and colleagues[8] conclude in their study of methods for calculating family risk scores that if families are small and affected relatives are few, categorical definitions or simple counts, similar to that used by Frezzo et al.,[5] are likely to be adequate for estimating risk.

Opportunities for early disease detection and prevention were also identified with the pedigree interview and questionnaire methods used by Frezzo et al.[5] The authors state they recorded whether or not the data available from the participant's chart would produce similar health care recommendations as the data gathered by the research tools, yet no specific results are provided that address this point. Because of the lack of documentation of family history information by the internists in this study, one would expect a lack of referrals for early detection and prevention strategies or genetic services. However, there is no evidence that this was the case. The authors did contact the physicians caring for most of the study subjects. With the patients' permission, a letter was sent describing the risk assessment derived from the family history information, as well as risk-appropriate recommendations. Follow-up regarding management changes recommended by these physicians as a result of the study assessment, as well as patient compliance with those recommendations, would be valuable. Currently, there is little evidence in the literature regarding the efficacy of the intervention of genetic risk assessment for common, chronic diseases in changing clinical practice and patient behaviors.

The authors could not directly compare the family history information obtained with the questionnaire to the pedigree interview, the "gold standard." It appears that the questionnaire was comparable to the interview in identifying individuals at moderate and high risk for the specific disease categories. Unlike the pedigree interview, however, there was no statistically significant difference in the number of individuals identified at increased familial risk for the common, chronic diseases by the questionnaire compared with the chart review. This might be due to the small number of study subjects and lack of power to detect a difference. Thus the added value of the questionnaire method for identifying individuals with familial risk for common, chronic disease has not yet been proven. However, important information regarding the feasibility of the questionnaire approach was provided. Substantially less time was needed to complete the questionnaire for family history collection compared with the pedigree interview (an average 8.1 minutes vs. 17.1 minutes), the interpretation of the questionnaire was easier than that of the pedigree, and the patients found the questionnaire acceptable.

It seems impractical to expect primary care providers to collect and interpret a three-generation pedigree for each of their patients year after year. In a recent survey of 339 primary care providers in the United Kingdom, the majority felt a need to provide genetic services; however, only 29% felt sufficiently prepared to take family histories and draw pedigrees, and only 15% felt prepared to counsel patients about genetic test results.[9] Acheson et al.[2] found that family practice physicians discuss family history in only about half of new-patient visits and only 22% of established-patient visits. The quality of information collected was likely limited inasmuch as the average duration of family history discussions was less than 2.5 minutes. Only 11% of patients' records included a pedigree. This was probably due in large part to the limited time available for a patient visit—10 minutes. Alternatively, there are not enough genetics professionals available to perform comprehensive pedigree interviews for all primary care patients. For these reasons, as Frezzo and colleagues concluded, a valid, self-administered family history risk assessment tool that is simple yet obtains enough information for accurate risk stratification would be indispensable. In addition, a resource for interpretation of the family history data that facilitates risk stratification and provides information about risk-appropriate management and prevention strategies and guidelines for referrals to geneticists and other specialists is also necessary.

Several national organizations have recognized the potential of using the family history as a means to identify genetic susceptibility to common, chronic diseases. Family history working groups have been created to address the needs of health professionals in the evolving field of genetics, including the National Coalition for Health Professional Education in Genetics and the Genetics in Primary Care Faculty Teaching Initiative. The Centers for Disease Control and Prevention (CDC) Office of Genomics and Disease Prevention has also responded by embarking on a family history public health initiative. In collaboration with CDC programs and the National Institutes of Health, they will evaluate the use of family history for identifying and stratifying risk for common, chronic diseases and influencing early detection and prevention strategies. More information regarding this effort can be found at the CDC Web site (http://www.cdc.gov/genomics/).

The article by Frezzo and colleagues[5] provides meaningful contributions to the field of common, disease genetics. They have confirmed a lack of family history documentation by internists, which has clearly identified a need for improvement in this area by these important primary care specialists. They have also demonstrated the ability of a self-administered questionnaire to identify and stratify disease-specific risk for several common, chronic disorders and reproductive issues. Furthermore, their use of a questionnaire for family history collection and interpretation appears to be feasible and acceptable.

Future research should focus on the development of family history risk assessment instruments, as well as algorithms for interpretation of risk and guidelines for risk-appropriate management and prevention strategies for different settings in clinical medicine and public health practice. Once developed, the validity of these instruments in identifying and stratifying disease risks, as well as the clinical utility of these tools for improving disease management, early detection, and prevention efforts, should be investigated. Ethical, legal, and social issues pertaining to familial disease risk stratification should also be addressed. If the research shows that this is a valid, feasible, and acceptable approach, this could change the practice of preventive medicine and lead to the development of a public health

campaign around the theme: "Know your family history: It could save your life."

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