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Family history: Still relevant in the genomics era

■ ABSTRACT

Even at the dawn of the genomics era, the family history is still very relevant, being a proxy for genetic, environmental, and behavioral risks to health. The family history can be used to inform risk stratification, allowing for judicious use of screening and opening the door to early and even prophylactic treatment. This review aims to re-energize our use of the family history in primary care practice.

■ KEY POINTS

The family history is an underused tool for predicting the risk of disease and for personalizing preventive care.

Barriers to the appropriate collection and use of the family history include concerns over the reliability of patient reporting, a lack of time and reimbursement, and provider knowledge gaps.

Use of family history to inform genetic testing for hereditary cancer syndromes has been shown to improve outcomes and may reduce overall health care costs.

Future solutions need to focus on creating time-effective ways to collect and analyze the family history, and on developing innovative methods of educating medical providers at all levels of training as to how to apply the family history in clinical practice.

AT THE DAWN of the genomics era, is the family history still relevant? The answer is a resounding yes.^{1,2}

The family history is clinically useful because it is a proxy for genetic, environmental, and behavioral risks to health. It can be used to inform risk stratification, allowing for judicious use of screening and opening the door to early and even prophylactic treatment.^{3–8} As people live longer, we will need to detect common chronic conditions early in their course so that we can continue to improve health outcomes. Family history can help physicians personalize preventive care for conditions such as diabetes, osteoporosis, and cancers of the breast, colon, and prostate.^{2,9–15}

However, there is ample evidence that the family history is underused. Most practitioners ask about it infrequently and inconsistently.^{16,17} Why is this, and how can we encourage the use of this powerful tool to enhance our daily clinical practice and improve care?

We will discuss here some of the challenges that make it difficult for physicians to collect and use the family history in clinical practice, and review strategies for collecting and using the family history in a more consistent manner. We anticipate that this discussion will be helpful to clinicians, as the family history is an essential input to personalized, preventive care plans.

■ CHALLENGE 1: ARE PATIENTS' REPORTS RELIABLE?

A question that often arises when discussing the utility of the family history is the reliability of patients' reports. Can we trust that patients can accurately report their family history? For many conditions, the answer is yes.^{18,19}

Ziogas and Anton-Culver²⁰ asked 1,111 cancer patients whether their relatives had ever had cancer and verified their answers. In more than 95% of cases, if the patient said that a first-degree or second-degree relative did not have cancer of any type, that relative truly did not have cancer. Overall, over-reporting of cancer was rare, occurring in 2.4% of cases.

If the patient said that a relative did have cancer, that statement was usually true as well. The reliability of a report of cancer in first-degree relatives was greater than 75% for most types of cancer (female breast, ovarian, esophageal, colorectal, pancreas, lung, melanoma, brain, thyroid, lymphoma, leukemia). For several of these types of cancer (female breast, colorectal, and brain), the reliability was 90% or higher. For second-degree relatives, the reliability of a reported positive history was moderate (50% to 80%) for the same types of cancer, and for third-degree relatives, the reliability dropped further for all types of cancer except female breast, brain, pancreas, and leukemia, for which the reliability of a positive report remained at 70%.

Wideroff et al²¹ had similar findings in a study of more than 1,000 patients and more than 20,000 of their relatives.

Yoon et al,¹⁸ at the US Centers for Disease Control and Prevention, developed a Web-based risk-assessment tool called Family Healthware, currently undergoing validation trials. They found that patients' reports were highly reliable for coronary heart disease, stroke, diabetes, and breast, ovarian, and colorectal cancers. They also calculated the degree of risk associated with a positive family history and the prevalence of a family history of each of these diseases.

For the primary care physician, these studies support the reliability of patients' reports and provide guidance for targeting specific conditions when obtaining a family history.

■ CHALLENGE 2: NO TIME OR REIMBURSEMENT

Perhaps the most obvious barriers to collecting a family history are lack of time and reimbursement.

Acheson et al,¹⁷ in an observational study of 138 primary care physicians and 4,454 pa-

tient visits, found that family history was discussed during 51% of new patient visits and 22% of established patient visits. The rate at which the family history was taken varied from 0% (some physicians never asked) to 81% of all patient visits. On average, physicians spent less than 2.5 minutes collecting the family history.

Not surprisingly, the family history was discussed more often at well-care visits than at illness visits, as the former type of visit tends to be longer and, by definition, to be spent partly on preventive care. A difficulty with this strategy is that, given the shortage of primary care physicians, limited access, and patient preference, most preventive-care visits are combined with problem-focused visits, further decreasing the time available to collect and discuss a family history. While some argue that the family history should routinely be obtained and discussed during preventive-care visits regardless of reimbursement and time, the reality is that it may simply drop on the list of priorities for each visit.

Rich et al³ estimated that taking a family history would increase reimbursement for only one new patient evaluation and management code (99202) and one return-visit code (99213) in *Current Procedural Terminology*. This action would increase reimbursement enough to support about 10 minutes of physician effort for collecting, documenting, and analyzing the family history. While this is certainly better than the average of less than 2.5 minutes observed by Acheson et al,¹⁷ doctors would probably do it more if they were paid more for it.

Electronic solutions

Given that a lack of time is a barrier, what are some ways to minimize the time it takes to collect a family history?

With more physicians using electronic health records and with increasing use of Internet-based tools in the population at large, information-technology systems have been developed to help obtain the family history. One of the most widely used is the US surgeon general's *My Family Health Portrait*, available free at <https://familyhistory.hhs.gov>. It is one of the broadest electronic family-history collection tools and has been validated for use in risk assessment for diabetes and cancer of the colon, breast, and ovaries.²²

However, electronic solutions have their own challenges. Not all patients have access to the Internet, many need help using these programs, and these tools may not work well with existing electronic medical records systems.²³ Ideally, these programs would also provide built-in decision support for the provider, thereby maximizing data use for final patient risk assessment.²³ Furthermore, electronic solutions are not a one-time-only risk assessment—periodic re-review of family history and reassessment of familial risk are required.²⁴

Does taking a family history improve outcomes? Lessons from breast cancer

One of the reasons physicians don't get reimbursed for collecting a family history is that it has been difficult to measure any improvement in outcomes associated with risk prediction through family history.

The best examples of improvement in outcomes associated with family history-based risk prediction come from studies of breast cancer. From 5% to 10% of cases of breast cancer are part of hereditary cancer syndromes, many of which have a known genetic cause. The most prevalent of these genetic syndromes is the hereditary breast and ovarian cancer (HBOC) syndrome, caused by mutations in the breast cancer 1 (*BRCA1*) and breast cancer 2 (*BRCA2*) genes. Clinical testing for *BRCA* mutations has been available since 1998.²⁵ Women with a *BRCA* mutation have up to a 65% lifetime risk of developing breast cancer and up to a 40% lifetime risk of developing ovarian cancer.²⁶ Men with a *BRCA* mutation are at 10 to 100 times the risk of the general population (1% to 10% vs 0.1%) for developing breast cancer, and are also at higher risk of prostate and other cancers.²⁷

People who have a relative who developed breast cancer at a young age are more likely to harbor one of these mutations. For example, based on genetic testing in more than 185,000 people, the prevalence of *BRCA* mutations among people without cancer, not of Ashkenazi Jewish ancestry (a risk factor for breast cancer), and with no family history of early breast cancer or of ovarian cancer in any relative is 1.5%.²⁸ In contrast, people with no personal history of cancer who have a family history of breast cancer before age 50 have a

5.6% prevalence of *BRCA* mutation, and if they are of Ashkenazi Jewish ancestry, this number is 16.4%.²⁸

Medical and surgical interventions are available to reduce the risk of cancer in people with hereditary cancer syndromes such as HBOC. Options include screening more often, using advanced screening tests,²⁹ giving preventive drugs such as tamoxifen (Nolvadex), and prophylactic surgery.^{30–32} What is the evidence that early screening and intervention in these people improve outcomes?

Domcheck et al³³ prospectively followed more than 2,400 women who had *BRCA* mutations to assess the effect of prophylactic mastectomy or salpingo-oophorectomy on cancer outcomes. Mastectomy was indeed associated with a lower risk of breast cancer: 0 cases of breast cancer were diagnosed in 3 years of prospective follow-up in the 247 women who elected to undergo mastectomy, compared with 98 cases diagnosed in the 1,372 women who did not elect it over a similar period.

Women who elected to undergo salpingo-oophorectomy had a similarly lower rate of ovarian cancer compared with those who did not elect surgery (1% vs 6%). Additionally, fewer women who elected prophylactic salpingo-oophorectomy died of any cause (3% vs 10%), died of breast cancer (2% vs 6%), or died of ovarian cancer (0.4% vs 3%) compared with women who did not elect surgery.

Taking a family history reduces costs

What is the evidence that appropriate use of the family history decreases health care costs? Let us continue with the example of HBOC syndrome due to *BRCA* mutations.

Given that germline mutations account for 5% to 10% of cases of breast cancer in the United States and that the women who develop cancer associated with such mutations do so at a relatively young age, these mutations account for a disproportionate share of life-years lost due to cancer.³⁴ Through taking a family history, these women at high risk can be identified and referred for genetic testing. Genetic testing, though costly, is more cost-effective than diagnosing and treating cancer.

Patients' reports were highly reliable for coronary heart disease, stroke, and diabetes, and for breast, ovarian, and colorectal cancers

Anderson et al,³⁴ in 2006, estimated that cost-effective policies on testing and preventive treatment for persons at high risk of breast cancer could save up to \$800 million of the more than \$8 billion spent each year on breast cancer diagnosis, prevention, and treatment.

Kwon et al,³⁵ in a simulation model (not a study in real patients), compared four different criteria for *BRCA* testing in women with ovarian cancer to see which strategy would be most cost-effective in preventing breast and ovarian cancers in their first-degree relatives. The best strategy, according to this analysis, is to test women with ovarian cancer for *BRCA* mutations if they also have a personal history of breast cancer, have a family history of breast or ovarian cancer, or are of Ashkenazi Jewish ancestry. The estimated cost per life-year gained with this strategy was \$32,018, much lower than the widely accepted threshold for cost-effectiveness of \$50,000 per life-year gained.

Although many professional organizations, including the US Preventive Services Task Force, have endorsed family-history-based eligibility criteria for genetic counseling and *BRCA* testing, awareness of the value of genetic testing in people who have been prescreened by family history has been relatively slow in seeping out to insurance carriers, especially Medicaid.^{12,36} As evidence continues to accumulate showing that this approach can improve outcomes for at-risk family members, reimbursement and time allotted for obtaining and using the family history should be adjusted.

■ CHALLENGE 3: A KNOWLEDGE GAP IN CLINICIANS

Another challenge often cited as a cause of the underuse of the family history as a predictor of disease risk is that clinicians may not know enough about the topic. Several studies indicated that even when physicians had obtained some components of the family history, they did not document risk appropriately or recognize the significance of the pattern of inheritance observed.^{37–39}

In a study comparing primary care physicians and gastroenterologists in their use of

the family history to predict the risk of hereditary colon cancer, gastroenterologists were more likely to elicit a family history of colorectal cancer and implement appropriate screening strategies, but overall compliance with screening guidelines was suboptimal in both groups.⁴⁰

A 2011 report by an advisory committee to the secretary of the US Department of Health and Human Services concluded that lack of genetics education in medical school limits the integration of genetics into clinical care.⁴¹

How can we close this knowledge gap?

Recognizing a need, the National Coalition for Health Professional Education in Genetics was established in 1996 by the American Medical Association, the American Nurses Association, and the National Human Genome Research Institute (www.nchpeg.org). Its mission is to promote the education of health professionals and access to information about advances in human genetics to improve the health care of the nation. It offers educational materials, including a newly updated “Core Principles in Family History” program, which can be used to educate medical providers and their patients about various concepts related to genetics and family history.

In addition, physicians can use many risk assessment tools based on family history in patient care. Two of the best known are:

- The Gail breast cancer risk assessment model, hosted by the National Cancer Institute (www.cancer.gov/bcrisktool/)
- The FRAX osteoporosis risk assessment model, developed by the World Health Organization (www.shef.ac.uk/FRAX).

As we continue to educate the medical community about the value of the family history in predicting disease, it will be important to increase efforts in medical schools and residency programs and to find new, more interactive ways of teaching these concepts.

A possible strategy is to highlight the use of pedigree drawing to recognize patterns of inheritance.² In a study of physician attitudes toward using patient-generated pedigrees in practice, such as those produced by the US surgeon general’s *My Family Health Portrait*, 73% of physicians stated that the patient-generated pedigree would improve their ability to assess the risk

TABLE 1

Conditions in which family history changes screening

CONDITION	CHANGE IN STANDARD SCREENING TO CONSIDER	RECOMMENDED BY
Family history of breast cancer	Earlier, more frequent mammography; breast MRI	National Comprehensive Cancer Network ^a
Family history of colorectal cancer	Earlier, more frequent colonoscopy	National Comprehensive Cancer Network ^b
Family history of diabetes	Earlier initiation of blood screening for diabetes	American Diabetes Association ^c
Family history of abdominal aortic aneurysm	Targeted abdominal ultrasound in addition to physical palpation	Society for Vascular Surgery ^d

^aNational Comprehensive Cancer Network. Breast cancer screening and diagnosis, version 1.2011. Available at nccn.org

^bNational Comprehensive Cancer Network. Colorectal cancer screening, version 2.2011. Available at nccn.org.

^cStandards of medical care in diabetes—2011. Diabetes Care 2011; 34(suppl 1):S11–S61.

^dChaikof EL, Brewster DC, Dalman RL, et al. The care of patients with an abdominal aortic aneurysm: the Society for Vascular Surgery practice guidelines. J Vasc Surg 2009; 50(suppl 4):S2–S49.

of disease, and the majority also agreed that it would not extend the time of the assessment.¹⁶

Is this information clinically useful?

A question that often arises when educating the public and especially medical providers about the value of the family history is whether the information is clinically useful. What can be done about predicting the risk of disease on the basis of family history or genetics in people without symptoms? In fact, screening protocols are modified on the basis of family history for several diseases (TABLE 1).

Furthermore, knowing they are at risk might empower people and encourage them to engage with the medical system. For example, counseling people at risk of diabetes as reflected in the family history has been shown to increase their understanding of the risk and of preventive behaviors. Further study is needed to determine if such messages can engender lasting changes in

behavior across many diseases.^{42–46}

■ TOWARD PERSONALIZED CARE

Especially now that caregivers are striving to provide value-based health care with emphasis on preventive care, the family history remains an important tool for detecting risk of disease. The evidence clearly indicates that medical providers have room for improvement in taking a family history and in using it.

We hope that asking patients about family history and recognizing patterns of disease will help us create personalized preventive-care plans, providing greater opportunity to educate and motivate our patients to work with us towards better health. Future solutions need to focus on time-effective ways to collect and analyze family history and on innovative methods of teaching medical providers at all levels to apply the family history to clinical practice. ■

People with a relative who developed breast cancer at a young age are more likely to harbor a BRCA mutation

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