Family Cancer History: Healthy Skepticism Required
Rachel A. Freedman, Judy E. Garber

In 2004, the Surgeon General declared Thanksgiving as “National Family History Day” and encouraged families to gather and document health problems as a means to ensure a “longer and healthier life together” (1). Detailed and accurate family history is particularly relevant for cancer, where provider recommendations for screening and prevention strategies often depend on the estimate of an individual’s risk for developing a specific malignancy. Although taking a family history is a straightforward concept, multiple factors may prevent providers from successfully completing this task. Barriers include truncated visits with limited time to conduct and document interviews, as well as patients’ incomplete recall of their family history. Inaccurate or incomplete family histories may have significant consequences. If a reported family history leads to overestimation of risk, patients may be exposed to inappropriate interventions as well as increased emotional stress. On the contrary, underestimation of risk could lead to underutilization of screening, genetic testing, and more direct risk-reducing interventions, including chemoprevention and prophylactic surgery.

In this issue of the Journal, Mai et al. (2) examine the accuracy of reported family history for first- and second-degree relatives in the Family Health Study, a population-based telephone survey. They used random-digit-dialing in Connecticut households in 2001 to collect cancer-related family histories on first- and second-degree relatives from adult participants. In the initial survey, 1380 respondents answered questions about personal and family demographics and cancer history. A follow-up interview in 1019 respondents sought permission to contact living relatives to gather further information on reported cancer diagnoses. Among the 20,578 relatives reported in both interviews, 2605 met inclusion criteria and were selected for the cancer confirmation portion of the study. The authors went to considerable effort to confirm reported cancer cases, utilizing tumor registry data, Medicare claims, the National Death Index, death certificates, health-care facility records, and interviews with living relatives or proxies to match relatives using available personal identifiers. Positive predictive value (PPV), negative predictive value (NPV), sensitivity, and specificity of the reported family history were then calculated for each cancer type.

The study focused on the most common cancers—lung, colorectal, breast, and prostate—and found that sensitivity and PPV of the reported family history were low, ranging from 27.3% to 61.1% and 40.0% to 61.3%, respectively, whereas specificity and NPV were high (>96%). Of note, a higher specificity and PPV were observed for first-degree relatives (vs second degree), which have been observed previously (3). In addition, cancer type affected the accuracy of results, with breast cancer reports having the highest sensitivity and colorectal cancers, the lowest sensitivity and PPV. Although the authors used robust efforts to confirm cancer cases, diagnoses in family members may also have been missed, either because of difficulty matching cases for which minimal details were available or because cancer registry data were incomplete. Confirmation of true-negative cases is always difficult. It is also unclear how authors resolved conflicts if discrepancies in confirmation were noted or how often this occurred.

Other investigators have previously observed more accurate reporting of family history (3–5), although this may be due to the population-based design of the Family Health Study, in which relatively few participants had a personal history of cancer. Cancer patients may be more motivated to understand their family cancer history in greater detail, especially if multiple family members have been affected by a particular diagnosis. In addition, factors such as age or ethnicity might influence patients’ knowledge of their family history (6), due to cultural or generational differences in how disease is discussed within families. Although demographic information on participants was not provided in the article, the authors do note that women were non-statistically significantly more likely to report accurate histories.

If Mai et al. (2) repeated their study today, 10 years after its completion, we can hope that they would observe different results because of improved public awareness of the importance of family history through education in the media (7,8), enhanced online communication with relatives, and the availability of genetic testing, access to which often depends on specifics of family cancer history. Some increased public and provider understanding of the potential impact of family history may be indirectly evident from the increased rates of genetic testing for BRCA1 and BRCA2, Lynch syndrome, and other familial syndromes over time (9,10). However, there is also evidence of persistent inequalities in health media use by race, ethnicity, and socioeconomic status, which may contribute to ongoing healthcare disparities in this arena (11).

The observations of Mai et al. (2) highlight the limitations of relying on patient reports of their family cancer histories for risk assessment. In smaller studies, others have documented limited awareness of intra-abdominal or gynecological cancers or rare malignancies such as sarcomas or brain tumors in close relatives, even among members of remarkably affected kindreds (12–14). Efforts to encourage documentation of family members’ cancer diagnoses to determine eligibility for genetics testing or to initiate early screening and other risk-reducing interventions are often left to cancer genetics/risk assessment professionals, although the initial family history is generally what prompts a genetics referral. Even for motivated patients, the effort required to collect documentation of cancer diagnoses in relatives can be time-consuming, frustrating, and often unsuccessful. Regulations under the Health Insurance Portability and Accountability Act have complicated efforts to retrieve records, which seems an unfortunate and
unintended consequence of attempts to protect privacy. The conflicting priorities should be reexamined in the current debate on electronic medical records. Investigating family history through multigenerational population registries in the United States, as they exist in Scandinavia (4,15) is not currently feasible. There may be opportunities to enhance registry data in the future, and perhaps some of the on-line family history tools available or in development will prove helpful in this regard, as long as families make efforts to ensure the accuracy of the information they record.

Our reliance on family history is unlikely to decrease in the early years of personalized medicine, the remarkable power of full genome sequencing notwithstanding. If anything, accurate family history will remain essential to the provision of the critical context for interpretation of sequencing results (16). However, we can expect that, as knowledge of germline genomes increases, family history may ultimately become less critical. In the future, genomic analyses will likely become a routine part of primary care, with predispositions to cancer and other diseases identified at young ages. The risks and benefits of genetics services models are currently under discussion (17).

For the foreseeable future, detailed family cancer histories will continue to provide the basis for identification of susceptibility genes for many cancer syndromes and are still critical for defining the component tumors and age-specific cancer risks for individuals from affected families. Mai et al. (2) have pointed out the limitations of simply asking patients for this information. Although encouraging discussions over Thanksgiving dinner is unlikely to be sufficient, it is a beginning. There is also a growing number of on-line family history tools—the Surgeon General’s pedigree tool, genealogy websites, and Facebook pages, which can be easily updated by family members with the ability to preserve histories electronically over time. However, if we want to be able to appropriately integrate family history into personalized clinical care, studying systematic ways to enhance family history ascertainment should be a research priority. The implications of having accurate histories are far-reaching. For the present, we apparently need to approach the family history information our patients provide with healthy skepticism. Although we should thoughtfully listen to our patients’ histories, we must listen even harder for what they “could” be telling us, especially when specific information could influence their care and the care of their relatives.

References

Affiliation of authors: Dana-Farber Cancer Institute, Department of Medical Oncology, Harvard Medical School, Boston, MA (RAF, JEG).