# National Institutes of Health State-of-the-Science Conference Statement: Family History and Improving Health

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*National Institutes of Health consensus and state-of-the-science statements are prepared by independent panels of health professionals and public representatives on the basis of 1) the results of a systematic literature review prepared under contract with the Agency for Healthcare Research and Quality (AHRQ); 2) presentations by investigators working in areas relevant to the conference questions during a 2-day public session; 3) questions and statements from conference attendees during open discussion periods that are part of the public session; and 4) closed deliberations by the panel during the remainder of the second day and morning of the third. This statement is an independent report of the panel and is not a policy statement of the National Institutes of Health or the U.S. government. The statement reflects the panel's assessment of medical knowledge available at the time the statement was written. Thus, it provides a "snapshot in time" of the state of knowledge on the conference topic. When reading the statement, keep in mind that new knowledge is inevitably accumulating through medical research.*

Many common diseases have genetic, environmental, and lifestyle antecedents that family members share, and health care professionals in the United States have long used family history information as a risk assessment tool. In addition, most hereditary diseases have been elucidated through the study of families. A person's family history has the potential to capture information about shared factors that contribute to risk for common diseases, such as diabetes, stroke, cancer, and heart disease. Family history is also used routinely in many other ways, including its well-defined use in determining who might benefit from genetic testing and its use in the interpretation of genetic test results.

The combination of these attributes makes the systematic collection of family history a potentially important step in personalizing health care. Several tools are in development to allow family history information to be effectively incorporated into health information technology systems, including electronic health records, personal health record systems, and family history risk assessment tools. Understanding the scientific foundation of family history is important if clinical decision aids (based on the information) are to be useful to clinicians and persons in typical practice settings and in improving clinical outcomes.

Although the term *family history* is commonly used, it does not have a common definition—that is, various clinicians and patients understand it differently. Available family history questionnaires include information about a wide range of genetic, social, cultural, and environmental factors. Furthermore, family history questions may be embedded in complex risk assessment tools that incorporate many other demographic and health factors. Moreover, the definition of *family* varies when viewed from the perspectives of geneticists, generalist and specialist clinicians, family therapists, and members of some ethnic and cultural groups.

The accuracy of patient-provided information is limited by a person's awareness, understanding, recollection, and willingness to disclose health issues of family members. The expected use of information from family history and the ex-

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Appendix Table
Conversion of graphics into slides

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* Panel statement from an NIH State-of-the Science Conference held on 22–24 August 2009 at the National Institutes of Health, Bethesda, Maryland. For a list of the members of the NIH State-of-the-Science Conference Panel and other participants, see the **Appendix** (available at www.annals.org).

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pected outcomes of acting on the information also vary depending on the clinical context. Important questions remain about the usefulness of family history information for disease prediction and improvement of individual health outcomes. Finally, the addition of new methods for systematically collecting family histories may alter the cost of care.

Given the unprecedented proliferation of genomic information and the possibility of health care reform, it is imperative to clarify the role of the family history, its validity in the primary care setting, and its effect on individual and population health outcomes. Accordingly, the National Human Genome Research Institute and the Office of Medical Applications of Research of the National Institutes of Health convened a State-of-the-Science Conference to review the topic of family history and improving health. The Planning Committee narrowed the scope of the review to *family history for common diseases as seen by clinicians in primary care*, specifying a review to assess the available scientific evidence about the following 6 questions:

1. What are the key elements of a family history in a primary care setting for the purposes of risk assessment for common diseases?
2. What is the accuracy of the family history, and under what conditions does the accuracy vary?
3. What is the direct evidence that getting a family history will improve health outcomes for the patient or family?
4. What is the direct evidence that getting a family history will result in adverse outcomes for the patient or family?
5. What are the factors that encourage or discourage obtaining and using a family history?
6. What are future research directions for assessing the value of family history for common diseases in the primary care setting?

The questions defined the scope of the review, which was further limited by the Technical Expert Panel in collaboration with the McMaster Evidence-based Practice Center. Inclusion criteria were common diseases, primary care population, and clinical outcomes recorded for individual patients rather than a group of patients. The evidence-based practice center further limited the review to include only studies published in English since 1995 that also reported quantitative data. For the questions reporting clinical outcomes, only controlled interventional trials were included. Consequently, it is important to emphasize that the review covers only a small portion of the evidence that might generally link family history to improved health.

## 1. What Are the Key Elements of a Family History in a Primary Care Setting for the Purposes of Risk Assessment for Common Diseases?

Critical to consideration of the value of family history in the assessment of the risk for common diseases is clarifying the key elements to establish in a primary care setting. An important limitation of a detailed ascertainment of family history is the brief length of a typical primary care visit. The standard against which this assessment can be made is the comprehensive, 3-generation pedigree used in medical genetics, counseling, and research settings.

Key elements considered by the evidence report were 1) the number of affected relatives, 2) sex, 3) the degree of relationship (first- or second-degree relative), 4) age at onset, 5) ancestry (ethnicity or region of origin), and 6) lineage (maternal vs. paternal relatives). Other elements of family history were not considered in this review, such as consanguinity (blood relatives) and adoption status, as well as broader patterns of inheritance that are derived from a detailed and more time-consuming family history taken by a genetic counselor or medical geneticist. In addition, other elements not considered were the effect of environmental, social, and cultural factors that may influence the incidence and outcomes of common diseases and the role that family histories may have in establishing trust and good communication between the individual and clinician.

### What We Know

The evidence report focused on several common medical conditions—asthma and allergies (atopic disease), diabetes, major depression and mood disorders, stroke, and cardiovascular or heart disease—and 5 common types of cancer (breast, ovarian, colorectal, prostate, and lung). It expressed its findings in terms of the sensitivity and specificity of selected family history elements for identifying persons with these conditions. The 59 studies included in the review were either 1) longitudinal in design and focused on the development (incidence) of disease, sometimes reporting more than 20 years of follow-up, or 2) cross-sectional in design and, hence, focused on the association with existing (prevalent) disease.

The term *sensitivity*, as used in this context, refers to the probability that an affected person (someone with disease) will have a positive family history for the factor in question, whereas *specificity* refers to the probability that an unaffected person will have a negative family history. Although we would like both sensitivity and specificity to be as large as possible (that is, equal 1), in practice, the 2 measures tend to move in opposite directions. Thus, an increase in sensitivity is accompanied by a decrease in specificity and vice versa. The choice of emphasizing sensitivity or specificity depends on the cost or value of each option.

The evidence report examined additional measures, such as the predictive value, relative risk, and odds ratio of a positive family history. For a particular aspect of family history (for example, having an affected first-degree relative), a high positive predictive value would exist if persons with such a history have a high probability of also having (or developing) disease, and a high odds ratio or relative risk would exist if those with a family history had or developed the disease with greater frequency than those without a family history. Relative risk, odds ratio, and predictive value all vary, not only with the sensitivity and specificity of the reported family history, but also with the

prevalence of a disease in the population. For a given sensitivity and specificity, positive predictive value increases as the prevalence of disease increases. By contrast, the ability of a positive family history to predict disease can be very low, despite high sensitivity and specificity, if the disease reported occurs with very low frequency in the population.

The most common family history methods covered in the evidence report were simple assessments of either any family history of a condition or history in a first-degree relative. Other aspects of family history for which information was available include family history in more distant relatives, lineage (maternal or paternal), age of onset in affected relatives, and sex of the affected relative. The evidence report provided little support to differentiate among these various measures. For almost all of the conditions for which data are available, sensitivities and positive predictive values were low (typically <25% for sensitivity and <10% for predictive value). Exceptions were for atopic diseases, mood disorders, and major depression, in which sensitivities were closer to 50% or more and predictive values ranged from 25% to 50%. Specificities, by contrast, tended to be very high (typical range, 90% to 98%). Atopic conditions and mental illnesses were again exceptions, with specificities ranging from 50% to 75%. Cross-sectional data generated somewhat higher sensitivities than longitudinal data. However, as stated in the evidence report, the literature supported the conclusion that family history, as currently measured in isolation, is neither a sensitive nor a highly predictive measure of common disease. Because most of the reported evidence was for recall of disease in a first-degree relative (and rarely for a second-degree relative, age of onset, and lineage) and many data were derived from research studies in a non–primary care setting, little evidence exists to help differentiate the key elements of a family history in a primary care setting.

### What We Need to Learn

Although tools are being developed, we need evidence about where and how to collect family history systematically and how best to use this information in primary care. Furthermore, it is not clear that sensitivity, specificity, and predictive values are the best or are even appropriate measures to judge the relative value of key elements. Rather, approaches using relative risk and excess attributable risk for individual key elements compared with other elements (for example, presence of disease in a first-degree relative) and multivariable models should be explored. Beyond the key elements examined in the current evidence report, understanding the value of nongenetic elements included in a family history, such as environmental, social, and cultural aspects, is needed. These elements may vary in importance and influence in different racial, ethnic, cultural, and socioeconomic groups. Little is known about the ways in which electronic health records, modular software added to electronic health records, and other information technologies may affect the standardized collection of family history.

## 2. What Is the Accuracy of the Family History, and Under What Conditions Does the Accuracy Vary?

The accuracy of reported family history information can be viewed from the perspective of decision theory. We wish to know the true disease history of a person, but what we observe is a proxy's report of the person's disease history, and we do not know the accuracy of the information. As with the review for question 1, the evidence report presented data in terms of sensitivity and specificity. The only difference is that, for this question, *sensitivity* refers to the probability that an affected family member will be correctly identified as such, whereas *specificity* refers to the probability that an unaffected family member is correctly identified as disease-free.

### What We Know

Unlike the traditional decision-theory framework in which the "test criterion" is a well-defined measure with stable characteristics, the properties of reported family history are likely to vary from informant to informant and be related to personal factors, such as age, sex, cultural background, education, level of cognitive functioning, and whether the person who provided the information is adopted. Additional determinants of accuracy include the condition being reported (for example, breast cancer vs. depression) and how closely related the informant is to the person whose information is being provided (for example, a brother, sister, or other first-degree relative vs. a third cousin). If a person is cognitively impaired, a spouse or other surrogate, who may be less knowledgeable about the person's family history, may need to provide such information. Finally, the context in which family history is obtained may be important. For instance, parents may not wish to discuss certain issues in front of their children.

The evidence report identified 35 studies that met the eligibility criteria for the review. Of these, 16 reported on the accuracy of family history of cancer, 11 on family history of mental health conditions, and 8 on other conditions. Many important conditions were not represented. In addition, an expert speaker report included 2 studies on the accuracy of cardiovascular disease history that the evidence report did not include.

For those diseases included in the evidence report, specificity was generally high (90% to 95%), whereas sensitivity was lower and generally much more variable. The evidence report shows that the sensitivity for reports of various types of cancer ranged from 33% to 95%, whereas the sensitivity of mental health conditions ranged from 6% to 82%. In other words, persons more accurately report the absence of disease than the presence of disease in family members. Much less evidence exists for other conditions, such as autoimmune disease and substance abuse, and for relatives other than first-degree relatives.

The lower accuracy for family histories of mental health disorders may be due in part to the unique chal-

lenges and issues posed by gathering such information, as described in the evidence report. Affected persons may be a less reliable source of information about family history, and it may be necessary to use knowledgeable informants (typically relatives) to obtain such information.

Lack of access to facts on the true disease state of the relatives in question and the various methods for collecting and verifying family history may hamper the ability to assess for accuracy. Furthermore, when a response of "I don't know" is given, the accuracy of family history cannot be measured.

For informant characteristics, family history reports for first-degree relatives (children, siblings, and parents) seem to be more accurate than family history reports for higher-degree relatives. The other frequently studied characteristic is informant age. In studies of family histories of cancer, results have been mixed, with no consistent trend favoring reporting by younger or older persons. However, a meta-analysis of factors associated with family psychiatric history suggests that older informants report family history more accurately than younger informants. No consistent differences in accuracy of reporting have been noted between men and women or between informants with different educational levels, although women and those with higher educational levels tend to supply more information. The available literature also shows no consistent pattern of differences in reporting family history between informants who have disease and those who do not.

### What We Need to Learn

Based on the limited number of studies in the evidence report, much remains unknown about the accuracy of family history. Because differences were seen across disease types and even within disease type, our knowledge of the accuracy of reported family history for specific diseases is particularly limited. In addition, most information on this topic comes from studies conducted in patients from specialty clinics as opposed to primary care settings. Nonetheless, in case–control studies, the accuracy of family history provided by control participants (who often are drawn from primary care settings) has generally been similar to that from case patients. Little is known about how the accuracy of family history is affected by where and how family history is taken. The method of collection could be an important factor (for example, a paper checklist done before a clinic visit, an interactive computer tool, or in-person with a clinician).

The resources needed to significantly improve evidence on the accuracy of family history will probably be substantial, and the findings may add only marginal improvements. It may be difficult to conduct feasible and economical studies in the United States, given the lack of record-linkage capacity. Consensus should be sought on the acceptable level of error when assessing family history, at least as an aid to prioritizing research. High accuracy may be especially critical when the action taken based on family history is a risky screening procedure or surgical intervention or when the procedure has significant cost for society. In these cases, additional research may be justified.

## 3. What Is the Direct Evidence that Getting a Family History Will Improve Health Outcomes for the Patient or Family?
## 4. What is the Direct Evidence that Getting a Family History Will Result in Adverse Outcomes for the Patient or Family?

Because it is difficult to consider the effect of the benefits of family history in the absence of potential adverse outcomes, we presented our report of these 2 questions in a single section.

Evidence exists of clinical utility for identifying persons with genetic syndromes, such as hereditary breast and ovarian cancers. Family history is also used for the assessment of risk for some common diseases in which genetics plays a smaller or less clear role, such as most cases of diabetes, cardiovascular disease, and mental health disorders. However, the clinical utility of the family history in the primary care setting in these cases is less clear than in cases in which the genetics are known and highly influential.

The evidence report process focused exclusively on direct evidence that, for the purposes of this review, included randomized, controlled trials or uncontrolled studies of behavior before and after intervention. Also, in this context, the term *getting a family history* meant a systematic process of obtaining a family history, interpretation, and communication. The evidence report did not identify any studies directly assessing morbidity and mortality. Rather, the outcomes of interest in the report were indirect assessments of health outcomes, such as individual screening intention, uptake of and adherence to screening tests and procedures, and preventive health behaviors. Prophylactic preventive treatment and surgery were also potential outcomes, but no randomized studies in this category were identified.

### What We Know

The evidence report identified 2 studies that addressed whether benefits of systematic family history collection through increased adherence to American Cancer Society breast cancer screening guidelines during a 6- to 8-month follow-up exist. These studies demonstrated an increase in breast self-examination and clinical breast examination but did not show significant improvements in adherence to mammography.

An assessment of the clinical utility of any intervention must also include potential adverse outcomes. The evidence report focused on adverse psychological effects—primarily anxiety—from the systematic collection and interpretation of family history. However, some degree of anxiety in this context may be considered a benefit if the anxiety is a motivating factor for persons to productively address their health risks. Inappropriate anxiety (anxiety in the absence of increased health risk) or excessive anxiety (anxiety out of proportion to the health risk) should be considered adverse outcomes. Studies that report group means for anxiety measures may not

differentiate between persons with modest increases in anxiety that may be beneficial and those with larger increases who may experience harm.

The evidence report identified 3 studies that addressed adverse outcomes in relation to systematic family history assessment and interpretation. These results are consistent with the literature on the psychological effects of genetic testing that generally shows modest short-term increases in anxiety in people whom the test indicates are at increased risk, with anxiety levels returning to baseline or below over time.

### What We Need to Learn

The evidence report included no studies on the value of iterative family history taken over the lifespan and, in particular, its effect on morbidity and mortality. In addition, little is known about other potential benefits, including the effect on other family members, patient choice and locus of control, and the benefits of the family history as an indivisible component within the context of comprehensive primary care.

Furthermore, the evidence report did not address the potential harm that could result from the misinterpretation or misapplication of information from a family history that may lead to invasive or unnecessary tests and procedures or whether a clinician might inappropriately reassure and neglect to foster potentially beneficial measures, despite a high risk for preventable disease.

The evidence report suggests that a family history intervention can motivate healthy behaviors, but the data are not sufficiently robust to conclude that a routine family history in primary care populations will lead to improved health outcomes. On the other hand, the psychological risks for a family history intervention seem low or nonexistent.

A relatively unique aspect of genetics is the implications of genetic information for family members of the person. Family becomes most relevant in the consideration of potential benefits and adverse outcomes when dealing specifically with diseases associated with single gene mutations, such as hereditary breast and ovarian cancers (due to *BRCA1* or *BRCA2* mutations) and hereditary nonpolyposis colorectal cancer. A family member who receives a positive test result is faced with complex issues associated with communicating information to other family members who could benefit from testing and possible interventions, which often results in a host of psychosocial and clinical consequences. The resulting benefits and potential harms to family members from a family history intervention should also be considered.

## 5. What Are the Factors That Encourage or Discourage Obtaining and Using a Family History?

The evidence report yielded 5 studies that address individual patient, provider, or organizational factors that encourage or inhibit the process of obtaining and using the family history. One study focused on factors that promote or inhibit use of family history as a tool for clinical decision making. Our understanding of these factors is based on the evidence report and evidence presented by experts familiar with specific factors not represented in the comprehensive review or in the peer-reviewed literature.

### What We Know

Individual, family, clinician, and organizational factors may encourage or discourage the collection and use of family history in primary care settings. With the exception of a single study, the extant literature examined this issue as an adjunct to a clinical research question and not as the central feature of the analysis. Studies included in the evidence report explored individual, provider, and organizational factors influencing family history reporting and the documentation of family history by the health care provider. The studies were done using designs that involved observation of patient visits, mailed surveys and questionnaires, telephone interviews, and medical record review. All studies addressed the collection and use of family history among adult patients.

Individual characteristics identified through the evidence report that increased the likelihood that family history would be reported are being female, having health insurance, and having moderate to high socioeconomic status. Clinician characteristics identified through the evidence report were residency training and length in practice, both of which were associated with a greater likelihood of clinicians taking a family history. The time spent by clinicians and the lack of tools and technology to analyze and interpret the data obtained inhibit clinicians from routinely taking a family history. Clinicians may not be adequately compensated for the time required to obtain and interpret family history. Despite these barriers, experts noted that almost half of clinicians report collecting and using a family history in their practice. Experts reported relevance of collection of family history data outside the primary care encounter, but this setting was not included in studies reviewed in the evidence report.

### What We Need to Learn

The evidence report suggested significant gaps in the science relative to individual, family, clinical, and organizational factors that affect the collection and use of family history. The design and methods used in the studies in the evidence report limit the prospects for meaningful conclusions about these factors. Specific concerns about design and methods include the lack of a consistent and clear definition of family; the effect of response bias among persons and clinicians; and whether studies were adequately representative of the racial, social, economic, and cultural diversity and varied religious beliefs of the United States.

None of the studies in the evidence report examined how a person's knowledge about his or her family history, other than first-degree relatives, affected a person's ability to report a family history to his or her health care provider. No evidence suggested whether a person's race and ethnic-

ity, cultural background, religious beliefs, life stage, or personal health history affect his or her willingness and ability to report on family history. The panel heard discussion that the presence of certain medical conditions might affect a person's willingness to provide family history, but they found no evidence about how these factors influenced the collection and use of a family history.

Several factors concerning clinicians' behavior remain unexplored in the evidence report, including the effect of clinicians' attitudes, beliefs, and training on the collection and use of family history. The manner in which clinicians are reimbursed for services also has not been addressed.

The review provided no evidence of the effect that the organization and delivery of health care services have on the collection and use of family history. Integrated health care delivery systems, particularly those with electronic health records, may have greater opportunities to collect and use family history. The rapid changes in medical informatics may expand this opportunity.

## 6. What Are Future Research Directions for Assessing the Value of Family History for Common Diseases in the Primary Care Setting?

The ultimate goal of collecting a family history in primary care is improvement in individual clinical outcomes and population health. Many of the questions raised by these recommendations may be addressed simultaneously in the context of single studies, but because the topic requires the expertise of many disciplines, the panel did not rank these research priorities.

The evidence report did not focus on the effectiveness of family history in primary care for the identification of persons at risk for rare genetic causes of common disorders for which early diagnosis and treatment have proven benefits. Future systematic reviews and research efforts should evaluate family history, alone or in combination with genetic and environmental variables, for its predictive value and potential role in improving patient outcomes.

Research recommendations for short-term and intermediate goals can be grouped into 3 categories: 1) structure or characteristics of a family history; 2) the process of acquiring a family history; and 3) outcomes of family history acquisition, interpretation, and application (**Appendix Table**, available at www.annals.org).

## Conclusion

The panel recognized that family history has an important role in the practice of medicine and may motivate positive lifestyle changes, enhance individual empowerment, and influence clinical interventions. The panel found that it is unclear how this information can be effectively gathered and used in the primary care setting for common diseases.

The emerging international paradigm on using evidence-based methods to evaluate tests and interventions works best when one can trace a linear pathway from test development through randomized, controlled trials that anchor usefulness in clinical practice with quantitative evidence of benefits and harms—principles best exemplified in the field of genetics by the ACCE Model Process for Evaluating Genetic Tests (www.cdc.gov/genomics/gtesting/ACCE/index.htm) and Evaluation of Genomic Applications in Practice and Prevention (www.egappreviews.org) methods. Family history was a core element of clinical care long before the evidence-based medicine paradigm was even proposed. Therefore, it comes as no surprise that the evidence base supporting family history for common diseases in primary care, as assessed in this state-of-the-science review, is weak in defining the key elements, assessing test performance, linking results to clinical conditions, acting on results in specific clinical scenarios, evaluating potential benefits and harms, and assessing factors encouraging and discouraging use of family history. For a systematically collected family history for common diseases to become an evidence-based tool in primary care clinical settings, substantial additional research is needed. Challenges include the number, complexity, and cost of rigorous studies that can adequately address the scientific questions outlined in this panel's research recommendations. The relative priority of specific research questions on family history in the context of other health information and genetic technologies and interventions that might address the same clinical problems in different ways requires debate to ensure the best outcomes for improving health.

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## Appendix

### State-of-the-Science Conference Panel

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## *Appendix Table.* Research Recommendations

**Structure or characteristics of a family history**

- What is a parsimonious series of questions (key elements) for use as a family history screening tool in primary care practice?
- What are the environmental and lifestyle elements of a family history that are most useful in helping patients make positive changes in health-related behaviors?
- What are the best methods and key elements to collect family history across several common disease entities (e.g., several diseases vs. 1)?
- How does the accuracy and completeness of family history information vary according to the setting in which it is collected (e.g., specialty care, primary care, community outreach, or the Internet)?
- What is the optimal frequency for ascertaining and updating family history?
- What are the best tools and methods for family history collection and interpretation?
- What personnel and information technology resources and settings facilitate the collection of family histories that meet individual, community, and clinical goals?
- What are the best statistical approaches to ascertain the benefit of 1 key element of family history relative to another element?
- How does the definition of family in diverse racial, ethnic, religious, social, cultural, and economic population groups influence the collection and use of family history?
- Do key elements of family history vary by race, ethnicity, religious belief, life stage, socioeconomic status, and culture?
- How do family dynamics and health disorders affect an individual's awareness and ability to report on family health history?

**Process of acquiring a family history**

- Who is the best family informant to convey a family history (i.e., the "family history expert")?
- To what extent do demographic factors modify an informant's ability to provide an accurate family history?
- How might individuals, their families, and communities be best engaged in the collection of family history over time?
- What are methods to minimize the time for collecting family history? Are there approaches to the assessment of family history across several office visits, self-administered questionnaires, ancillary personnel, or record linkage that are effective?
- How do the clinician's knowledge, attitudes, beliefs, training, and skills influence the ability to collect, interpret, and use family history?
- How might family history, including environmental and behavioral risk factors, be improved by a systematic, technology-supported approach (e.g., electronic health records, record linkage, enhancing communication between family members)?
- What are optimal ways to use family history in a primary care setting to identify persons who can benefit from enhanced surveillance or referral to genetics services?
- What are the key facilitators, incentives, and barriers for clinicians, individuals, families, and organizations for the collection of family history in primary care practice?

**Expected outcomes of family history interpretation**

- Besides disease risk assessment, what are the additional potential benefits to the individual, family, and clinician in taking a thorough family history (e.g., building trust and partnering through a personal interview in a primary care setting)?
- How and why does family history information change the behavior of the clinician?
- How are family history interpretations and findings best communicated to the individual and family to change health and disease prevention and detection behaviors over time? What strategies will minimize potential harms?
- What are the short- and long-term effects on individuals, families, and clinicians of inaccurate, misinterpreted, or unavailable family history information?
- Can family history information be linked to genomic information or to important intermediate markers of common chronic diseases (e.g., body mass index, drug adherence, tobacco cessation) to predict change in outcome?
- What are the short- and long-term effects on family dynamics of systematic family history taking in diverse populations and cultural settings?

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