NIH State-of-the-Science Conference

Family History and Improving Health

Program and Abstracts

August 24–26, 2009

William H. Natcher Conference Center
National Institutes of Health
Bethesda, Maryland

Presented by

National Human Genome Research Institute, NIH
Office of Medical Applications of Research, NIH
The Johns Hopkins University School of Medicine, Educational Provider

Cosponsors

Eunice Kennedy Shriver National Institute of Child Health and Human Development, NIH
National Cancer Institute, NIH
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Partners

Centers for Disease Control and Prevention
Maternal and Child Health Bureau, Health Resources and Services Administration
Office of the Surgeon General

The Agency for Healthcare Research and Quality provided additional conference development support.

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health

About the Program

The National Institutes of Health (NIH) Consensus Development Program has been organizing major conferences since 1977. The Program generates evidence-based consensus statements addressing controversial issues important to healthcare providers, policymakers, patients, researchers, and the general public. The NIH Consensus Development Program holds an average of three conferences a year. The Program is administered by the Office of Medical Applications of Research within the NIH Office of the Director. Typically, the conferences have one major NIH Institute or Center sponsor, with multiple cosponsoring agencies.

Topic Selection

NIH Consensus Development and State-of-the-Science Conference topics must satisfy the following criteria:

- Broad public health importance. The severity of the problem and the feasibility of interventions are key considerations.
- Controversy or unresolved issues that can be clarified, or a gap between current knowledge and practice that can be narrowed.
- An adequately defined base of scientific information from which to answer conference questions such that the outcome does not depend primarily on subjective judgments of panelists.

Conference Type

Two types of conferences fall under the purview of the NIH Consensus Development Program: State-of-the-Science Conferences and Consensus Development Conferences. Both conference types utilize the same structure and methodology; they differ only in the strength of the evidence surrounding the topic under consideration. When it appears that there is very strong evidence about a particular medical topic, but that the information is not in widespread clinical practice, a Consensus Development Conference is typically chosen to consolidate, solidify, and broadly disseminate strong evidence-based recommendations for general practice. Conversely, when the available evidence is weak or contradictory, or when a common practice is not supported by high-quality evidence, the State-of-the-Science label is chosen. This highlights what evidence about a topic is available, the directions future research should take, and alerts physicians that certain practices are not supported by good data.

Conference Process

Before the conference, a systematic evidence review on the chosen topic is performed by one of the Agency for Healthcare Research and Quality's Evidence-Based Practice Centers. This report is provided to the panel members approximately 6 weeks prior to the conference, and posted to the Consensus Development Program Web site once the conference begins, to serve as a foundation of high-quality evidence upon which the conference will build.

The conferences are held over 2 1/2 days. The first day and a half of the conference consist of plenary sessions in which invited expert speakers present information, followed by "town hall forums," in which open discussion occurs among the speakers, panelists, and the general public in attendance. The panel then develops its draft statement on the afternoon and evening of the second day, and presents it on the morning of the third day for audience commentary. The panel considers these comments in executive session and may revise their draft accordingly. The conference ends with a press briefing, during which reporters are invited to question the panelists about their findings.

Panelists

Each conference panel comprises 12–16 members who can give balanced, objective, and informed attention to the topic. Panel members:

- Must not be employees of the Department of Health and Human Services.
- Must not hold financial or career (research) interests in the conference topic.
- May be knowledgeable in the general topic under consideration, but must not have published about or have a publicly stated opinion on the topic.
- Represent a variety of perspectives, to include:
  - Practicing and academic health professionals
  - Biostatisticians and epidemiologists
  - Clinical trialists and researchers
  - Public representatives (ethicists, economists, attorneys, etc.)

In addition, the panel as a whole should appropriately reflect racial and ethnic diversity. Panel members are not paid a fee or honorarium for their efforts. They are, however, reimbursed for travel expenses related to their participation in the conference.

Speakers

The conferences typically feature approximately 21 speakers; 3 present the information found in the Evidence-Based Practice Center's systematic review of the literature. The other 18 are experts in the topic at hand, have likely published on the topic, and may have strong opinions or beliefs. Where multiple viewpoints on a topic exist, every effort is made to include speakers who address all sides of the issue.

Conference Statements

The panel's draft report is released online late in the conference's third and final day. The final report is released approximately 6 weeks later. During the intervening period, the panel may edit their statement for clarity and correct any factual errors that might be discovered. No substantive changes to the panel's findings are made during this period.

Each Consensus Development or State-of-the-Science Conference Statement reflects an independent panel's assessment of the medical knowledge available at the time the statement was written; as such, it provides a "snapshot in time" of the state of knowledge on the conference topic. It is not a policy statement of the NIH or the Federal Government.

Dissemination

Consensus Development and State-of-the-Science Conference Statements have robust dissemination:

- Continuing Medical Education credits are available during and after the conference.
- A press conference is held the last day of the conference to assist journalists in preparing news stories on the conference findings.
- The statement is published online at http://consensus.nih.gov.
- Print copies are mailed to a wide variety of targeted audiences and are available at no charge through a clearinghouse.

The conference statement is published in a major peer-reviewed journal.

Contact Us

For conference schedules, past statements and evidence reports, please contact us:

NIH Consensus Development Program
Information Center
P.O. Box 2577
Kensington, MD 20891

1-888-NIH-CONSENSUS (888-644-2667)
http://consensus.nih.gov

Upcoming Conferences

NIH State-of-the-Science Conference:	**Diagnosis and Management of Ductal Carcinoma In Situ** *September 22–24, 2009*
NIH State-of-the-Science Conference:	**Enhancing Use and Quality of Colorectal Cancer Screening** *February 2–4, 2010*
NIH Consensus Development Conference:	**Lactose Intolerance and Health** *February 22–24, 2010*
NIH Consensus Development Conference:	**Vaginal Birth After Cesarean: New Insights** *March 8–10, 2010*
NIH State-of-the-Science Conference:	**Preventing Alzheimer's Disease and Cognitive Decline** *April 26–28, 2010*
NIH Consensus Development Conference:	**Inhaled Nitric Oxide Therapy for Premature Infants** *October 27–29, 2010*

To receive registration notifications and updates about conferences and other program activities, please join the NIH Consensus Development Program Information Network at **http://consensus.nih.gov/alerts.htm**.

Recent Conferences

NIH Consensus Development Conference:	**Management of Hepatitis B** October 20–22, 2008
NIH Consensus Development Conference:	**Hydroxyurea Treatment for Sickle Cell Disease** *February 25–27, 2008*
NIH State-of-the-Science Conference:	**Prevention of Fecal and Urinary Incontinence in Adults** *December 10–12, 2007*
NIH State-of-the-Science Conference:	**Tobacco Use: Prevention, Cessation and Control** *June 12–14, 2006*
NIH State-of-the-Science Conference:	**Multivitamin/Mineral Supplements and Chronic Disease Prevention** *May 15–17, 2006*
NIH State-of-the-Science Conference:	**Cesarean Delivery on Maternal Request** *March 27–29, 2006*
NIH State-of-the-Science Conference:	**Manifestations and Management of Chronic Insomnia in Adults** *June 13–15, 2005*
NIH State-of-the-Science Conference:	**Management of Menopause-Related Symptoms** *March 21–23, 2005*
NIH State-of-the-Science Conference:	**Improving End-of-Life Care** *December 6–8, 2004*
NIH State-of-the-Science Conference:	**Preventing Violence and Related Health-Risking Social Behaviors in Adolescents** *October 13–15, 2004*
NIH Consensus Development Conference:	**Celiac Disease** *June 28–30, 2004*
NIH Consensus Development Conference:	**Total Knee Replacement** *December 8–10, 2003*

To access previous conference statements, videocasts, evidence reports, and other conference materials, please visit **http://consensus.nih.gov**.

General Information

CME Information

Description

The NIH Consensus Development Program is convening a state-of-the-science conference to assess the available evidence on family history and improving health. The conference statement will be prepared by an independent panel on the basis of a systematic literature review, expert presentations, and audience commentary. Widely distributed to the biomedical community and covered by the news media, the statement will help inform both healthcare providers and the general public, and shape the research agenda for this complex topic.

Who Should Attend

It is important that all key stakeholders be represented, as attendees will have the opportunity to participate in engaging discussions that will influence the panel's statement. This conference is intended for physicians and other health practitioners, healthcare system professionals, health policy specialists, public health experts, researchers, and interested members of the public.

Objectives

At the end of this activity, participants will demonstrate the ability to:

- Identify the key elements of a family history in a primary care setting for the purpose of risk assessment for common diseases.
- Describe the accuracy of the family history, and under what conditions accuracy varies.
- Outline what direct evidence is available to indicate that getting a family history will improve health outcomes for the patient and/or family.
- Outline what direct evidence is available to indicate that getting a family history will result in adverse outcomes for the patient and/or family.
- Identify the factors that encourage or discourage obtaining and using a family history.
- Describe future research directions for assessing the value of family history for common diseases in the primary care setting.

Accreditation Statement

This activity has been planned and implemented in accordance with the Essential Areas and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of The Johns Hopkins University School of Medicine and the National Institutes of Health. The Johns Hopkins University School of Medicine is accredited by the ACCME to provide continuing medical education for physicians.

Credit Designation Statement

The Johns Hopkins University School of Medicine designates this educational activity for a maximum of 12.50 *AMA PRA Category 1 Credits*™. Physicians should only claim credit commensurate with the extent of their participation in the activity.

This activity has been reviewed and is acceptable for up to 11.75 prescribed credits by the American Academy of Family Physicians.

Policy on Speaker and Provider Disclosure

It is the policy of The Johns Hopkins University School of Medicine that the speaker and provider disclose real or apparent conflicts of interest relating to the topics of this educational activity, and also disclose discussions of unlabeled/unapproved uses of drugs or devices during their presentation(s). The Johns Hopkins University School of Medicine Office of Continuing Medical Education has established policies in place that will identify and resolve all conflicts of interest prior to this educational activity. Detailed disclosure will be made in the activity handout materials.

The Johns Hopkins University School of Medicine takes responsibility for the content, quality, and scientific integrity of this CME activity.

Policy on Panel Disclosure

Panel members signed a confirmation that they have no financial or other conflicts of interest pertaining to the topic under consideration.

Videocast

Live and archived videocasts may be accessed at http://videocast.nih.gov. Archived videocast will be available approximately 1 week after the conference.

Dining

The dining center in the Natcher Conference Center is located on the main level, one floor above the auditorium. It is open from 6:30 a.m. to 2:30 p.m., serving hot breakfast and lunch, sandwiches and salads, and snack items. An additional cafeteria is available from 7:00 a.m. to 3:30 p.m., in Building 38A, level B1, across the street from the main entrance to the Natcher Conference Center.

Message Service

The telephone number for the message center at the Natcher Conference Center is 301–594–7302.

Online Content

All materials emanating from the NIH Consensus Development Program are available at http://consensus.nih.gov.

Contents

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

Background

Many common diseases have genetic, environmental, and lifestyle causes that family members may share. An individual's family health history captures information about shared factors that contribute to that individual's risk for developing diseases such as diabetes, stroke, cancer, and heart disease. Family health history information collected from patients has long been used as a risk assessment tool by healthcare providers in the United States. Family history is also critical to determining who will benefit from genetic testing for both common and rare conditions, and can facilitate interpretation of genetic test results. The combination of these attributes makes the collection of family history an important first step in personalized medicine.

Recently there have been a number of national efforts to ensure that family history information is effectively incorporated into health information technology systems including electronic health records and personal health record systems. An ultimate goal of these efforts will be to provide clinicians with automated clinical decision tools based on family history information; this will require a sound scientific foundation on which to develop such tools.

Although most individuals are accustomed to providing some form of family history information when they visit health professionals, there is wide variation in the way family history is collected and used by healthcare providers. Moreover, the accuracy of a patient-gathered history may be limited by an individual's awareness, understanding, and recollection of their family members' health issues. Important questions remain regarding the effectiveness of family history information for disease prediction and improvement of patient health outcomes.

There may also be adverse effects for both individuals and society, thus far not fully understood, of depending too heavily on a family history to assess disease risk. It is possible that emphasizing family history may have economic costs as well, as limited resources are allocated across a wide variety of health promotion activities in the primary care setting.

In order to take a closer look at this important topic, the National Human Genome Research Institute and the Office of Medical Applications of Research of the National Institutes of Health will convene a State-of-the-Science conference from August 24 to 26, 2009, to assess the available scientific evidence related to the following questions:

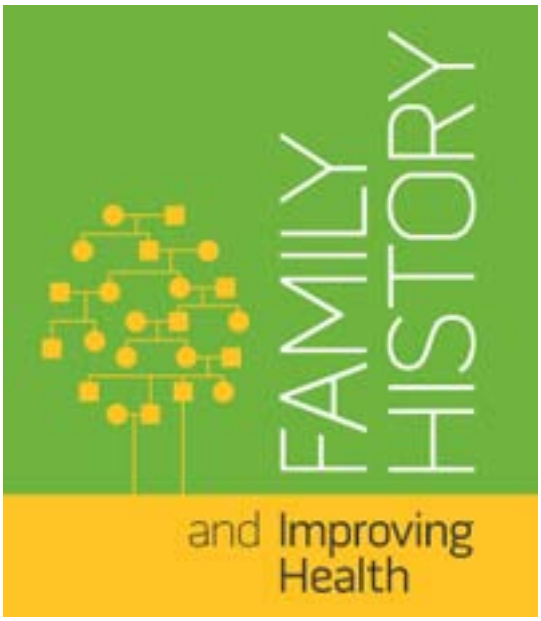
- What are the key elements of a family history in a primary care setting for the purposes of risk assessment for common diseases?
- What is the accuracy of the family history, and under what conditions does the accuracy vary?
- What is the direct evidence that getting a family history will improve health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

At the conference, invited experts will present information pertinent to these questions, and a systematic literature review prepared under contract with the Agency for Healthcare Research and Quality will be summarized. Conference attendees will have ample time to ask questions and provide statements during open discussion periods. After weighing the scientific evidence, an unbiased, independent panel will prepare and present a consensus statement addressing the key conference questions.

Artwork

The artwork on this volume's cover and used on a variety of materials associated with this conference boldly presents the conference title alongside a stylized tree. This interpretation of a "family tree" features elements of a pedigree chart used by healthcare providers and in research to graphically illustrate an individual's family health history.

The image was conceived and created by Bryan Ewsichek of the National Institutes of Health's Division of Medical Arts and is in the public domain. No permission is required to use the image. Please credit "NIH Medical Arts."



Agenda

Monday, August 24, 2009

8:30 a.m. Introduction
Alan E. Guttmacher, M.D.
Deputy Director
National Human Genome Research Institute
National Institutes of Health

8:35 a.m. Opening Remarks
W. Gregory Feero, M.D., Ph.D.
Senior Advisor for Genomic Medicine
National Human Genome Research Institute
National Institutes of Health

8:40 a.m. Charge to the Panel
Jennifer Miller Croswell, M.D.
Acting Director
Office of Medical Applications of Research
Office of the Director
National Institutes of Health

8:50 a.m. Conference Overview and Panel Activities
Alfred O. Berg, M.D., M.P.H.
Panel and Conference Chairperson
Professor
Department of Family Medicine
University of Washington

9:00 a.m. Family History, Personalized Medicine, Primary Care, and Improved Health
Muin J. Khoury, M.D., Ph.D.
Senior Consultant in Public Health Genomics
National Cancer Institute
Director, Office of Public Health Genomics
Centers for Disease Control and Prevention

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

9:20 a.m. Evidence-Based Practice Center Presentation I: A Summary of the Evidence for Key Elements of Family History for Risk Assessment of Common Disorders Affecting Pediatric and Adult Populations
Brenda Wilson, M.B.Ch.B, M.Sc., M.R.C.P. (UK), F.F.P.H.
Associate Professor
Department of Epidemiology and Community Medicine
University of Ottawa

9:40 a.m. Discussion

Monday, August 24, 2009 (continued)

I. What Are the Key Elements of a Family History in a Primary Care Setting for the Purposes of Risk Assessment for Common Diseases? (continued)

10:00 a.m. Family History as a Determinant of Risk for Chronic Disorders: Common Conditions and Beyond: I
Maren T. Scheuner, M.D., M.P.H., FACMG
Natural Scientist, RAND Corporation
Research Health Scientist
Veterans Administration Greater Los Angeles Healthcare System
Adjunct Associate Professor, Department of Health Services
University of California, Los Angeles School of Public Health

10:20 a.m. Family History as a Determinant of Risk for Chronic Disorders: Common Conditions and Beyond: II
Paula W. Yoon, Sc.D., M.P.H.
Epidemiologist
Division for Heart Disease and Stroke Prevention
Centers for Disease Control and Prevention

10:40 a.m. Research Challenges in Assessing Risk With Family History
Louise S. Acheson, M.D., M.S.
Professor
Department of Family Medicine
Case Western Reserve University
University Hospitals Case Medical Center

11:00 a.m. Discussion

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

11:30 a.m. Evidence-Based Practice Center Presentation II: A Summary of the Evidence for the Accuracy of Self-Reporting Family History Across Different Diseases
P. Lina Santaguida, Ph.D.
Assistant Professor
Department of Clinical Epidemiology and Biostatistics
Associate Director
McMaster University Evidence-Based Practice Centre

11:50 a.m. Accuracy of Family History Information for Risk Assessment in Clinical Care
Harvey J. Murff, M.D., M.P.H.
Assistant Professor of Medicine
Institute for Medicine and Public Health
Vanderbilt University

12:10 p.m. Discussion

12:30 p.m. Lunch

Monday, August 24, 2009 (continued)

III. What Is the Direct Evidence That Getting a Family History Will Improve Health Outcomes for the Patient and/or Family?

1:30 p.m. Evidence-Based Practice Center Presentation III: Systematic Family History Collection in Primary Care Populations: Impact on Health Outcomes and Factors Affecting Collection
Nadeem Qureshi, M.B.B.S., D.M., M.Sc.
Clinical Associate Professor in Primary Care
Division of Primary Care
School of Graduate Entry Medicine and Health
University of Nottingham
Derby City General Hospital

1:50 p.m. Perspectives on the Utility of Family History as a Screening Tool: The CDC Family Healthware™ Experience
Wendy S. Rubinstein, M.D., Ph.D., F.A.C.P., FACMG
Medical Director
Center for Medical Genetics
NorthShore University HealthSystem

2:10 p.m. Perspectives on the Utility of Family History as a Screening Tool: The Utah State Experience
Ted D. Adams, Ph.D., M.P.H.
Adjunct Assistant Professor
Cardiovascular Genetics Division
University of Utah School of Medicine
Program Director
Health and Fitness Institute, LDS Hospital, Intermountain Healthcare

2:30 p.m. Discussion

3:00 p.m. Perspectives on the Utility of Family History as a Screening Tool in Pediatric Populations
Ridgely Fisk Green, Ph.D., M.M.Sc.
TKC Integration Services Contractor
National Center on Birth Defects and Developmental Disabilities
Centers for Disease Control and Prevention

3:20 p.m. Research Challenges in Demonstrating the Utility of Family History in Obstetrical and Pediatric Settings
Siobhan M. Dolan, M.D., M.P.H.
Associate Professor of Obstetrics and Gynecology and Women's Health
Albert Einstein College of Medicine
Montefiore Medical Center
Consultant to March of Dimes

Monday, August 24, 2009 (continued)

III. What Is the Direct Evidence That Getting a Family History Will Improve Health Outcomes for the Patient and/or Family? (continued)

3:40 p.m. Family History and Those Providing Care for Patients With Genetic Disorders: The Customer's Perspective
Sharon F. Terry, M.A.
President and CEO
Genetic Alliance

4:00 p.m. Research Challenges in Affecting Behavioral Change With Family History Information: Patients and Providers
Colleen M. McBride, Ph.D.
Chief, Social and Behavioral Research Branch
National Human Genome Research Institute
National Institutes of Health

4:20 p.m. Discussion

5:00 p.m. Adjournment

Tuesday, August 25, 2009

IV. What Is the Direct Evidence That Getting a Family History Will Result in Adverse Outcomes for the Patient and/or Family?

8:30 a.m. The Potential Costs of Screening for Risk With Family History
James E. Haddow, M.D.
Co-Director
Division of Medical Screening and Special Testing
Womens and Infants Hospital of Rhode Island
Professor (Research)
Department of Pathology and Laboratory Medicine
Warren Alpert Medical School of Brown University

8:50 a.m. Perspectives on the Clinical Applications of Family History as a Screening Tool Across Multiple Populations
Chanita Hughes Halbert, Ph.D.
Associate Professor
Department of Psychiatry
Director
Community-Based Research and Cancer Disparities Program
Abramson Cancer Center
University of Pennsylvania

Tuesday, August 25, 2009 (continued)

IV. What Is the Direct Evidence That Getting a Family History Will Result in Adverse Outcomes for the Patient and/or Family? (continued)

9:10 a.m. Research Challenges in Assessing the Economic Costs of Using Family History as a Screening Tool in Primary Care
Scott D. Ramsey, M.D., Ph.D.
Professor, Department of Medicine
University of Washington School of Medicine
Director, Cancer Prevention Clinic
Seattle Cancer Care Alliance
Member, Public Health Sciences
Fred Hutchinson Cancer Research Center

9:30 a.m. Discussion

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

10:00 a.m. A Summary of the Use of Family History in Primary Care From Across the Pond(s)
Jon Emery, M.B.B.Ch., D.Phil., M.A., FRACGP
Head, School of Primary, Aboriginal and Rural Health Care
Professor, Department of General Practice
University of Western Australia

10:20 a.m. Family History and Healthcare: The Experience of the National Council of La Raza
Liany E. Arroyo, M.P.H., C.P.H.
Director, Institute for Hispanic Health
National Council of La Raza

10:40 a.m. Health IT-Based Strategies for Studying the Use of Family History in Primary Care
Kevin S. Hughes, M.D., F.A.C.S.
Surgical Director, Breast Screening
Co-Director, Avon Comprehensive Breast Evaluation Center
Massachusetts General Hospital
Associate Professor of Surgery
Harvard Medical School

Tuesday, August 25, 2009 (continued)

V. What Are the Factors That Encourage or Discourage Obtaining and Using a Family History? (continued)

11:00 a.m. Reconsidering the Use of Family History in Primary Care Revisited
Eugene C. Rich, M.D., F.A.C.P.
Professor of Medicine
Creighton University School of Medicine
Scholar in Residence
Association of American Medical Colleges

11:20 a.m. Discussion

12:00 p.m. Adjournment

Wednesday, August 26, 2009

9:00 a.m. Presentation of the Draft State-of-the-Science Statement

9:30 a.m. Public Discussion

11:00 a.m. Adjournment

2:00 p.m. Press Telebriefing

Panel

Panel Chair: **Alfred O. Berg, M.D., M.P.H.**
Panel and Conference Chairperson
Professor
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Seattle, Washington

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Salt Lake City, Utah

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Scientific Investigator/Health Economist
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Deputy Director, Helen Diller Family Comprehensive Cancer Center
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The Group Room Cancer Talk Radio Show
Studio City, California

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Behavioral Research
Director
Behaviorial Research Center
American Cancer Society
Atlanta, Georgia

William M. Vollmer, Ph.D.
Senior Investigator
Center for Health Research
Kaiser Permanente Northwest
Portland, Oregon

Janet K. Williams, Ph.D., R.N., P.N.P., F.A.A.N.
Kelting Professor of Nursing
Director, Clinical Genetics Research Postdoctoral Fellowship
University of Iowa
Iowa City, Iowa

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Salt Lake City, Utah

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Washington, DC

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Evanston, Illinois

P. Lina Santaguida, Ph.D.
Assistant Professor
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Associate Director
McMaster University Evidence-Based Practice Centre
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Abstracts

The abstracts are designed to inform the panel and conference participants, as well as to serve as a reference document for any other interested parties. We would like to thank the speakers for preparing and presenting their findings on this important topic.

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Finally, we would like to express our sincere appreciation to the staff of the NIH Library for their invaluable assistance in providing additional resources for the conference panel.

Please note that where multiple authors are listed on an abstract, the underline denotes the presenting author.

Family History, Personalized Medicine, Primary Care, and Improved Health

Muin J. Khoury, M.D., Ph.D.

In the age of rapid advances in genomic technology and interest in personalized medicine, family history still provides a readily available tool for personalized risk assessment, disease prevention, and health promotion for many common diseases. Since 2004, the U.S. Surgeon General and several federal agencies have launched a public health campaign to raise the level of awareness of family history in the population and have provided an online tool to facilitate data gathering.[1] Family health history has always been part of good medical history, is embedded in medical records, and provides a gateway for diagnosis and management of numerous genetic disorders.[2] In addition, family history is a risk factor for most diseases and represents joint effects of many genetic and environmental risk factors shared among relatives, and its use can impact health practice beyond traditional genetic disorders.[3] Nevertheless, until recently, the use of family history as a tool for risk assessment in primary care and public health practice has not been systematically evaluated. For each intended use, a multidisciplinary scientific evaluation of family history is needed to assess analytic validity, clinical validity, clinical utility, and ethical, legal, and social implications.[4] In this talk, I will summarize the promise and challenges of using family history in 21st-century primary care and public health. I will use examples from common diseases such as cancer, heart disease, and diabetes to illustrate the validity and utility of family history. I will also compare the scientific foundation of family history and personal genomics as risk assessment tools for disease prevention and health promotion.[5]

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Evidence-Based Practice Center Presentation I: A Summary of the Evidence for Key Elements of Family History for Risk Assessment of Common Disorders Affecting Pediatric and Adult Populations

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Family history (FH) represents the integration of shared genomic and environmental risk factors[1] and might be a practical and useful way to identify those to whom disease prevention efforts could be targeted. In order to develop evidence-based tools for FH taking in primary care settings, it is important to define the extent of FH enquiry that is necessary for risk prediction of complex disorders.

A systematic review was undertaken to address the following research question (#1): "What are the key elements of a family history in a primary care setting for the purposes of risk assessment for common diseases?" A review of 59 cross-sectional and cohort studies examined different definitions of 'positive FH' across a range of complex disorders in general populations. Sensitivity, specificity, and other metrics of discriminatory accuracy were calculated and scrutinized. The longitudinal analyses provided an indication of the performance of different FH definitions in predicting future risk of disease in unaffected individuals.[2–26] The sensitivities ranged from zero to 0.82, with many less than 0.5. The specificities ranged from 0.4 to 1.00.

In contrast, the cross-sectional analyses provided an indication of the performance of the specific FH definition in discriminating between individuals who do or do not have the disorder in question at the time of the study; i.e., an insight into the potential of FH for case finding of undetected disease.[27–59] The sensitivities ranged from zero to 0.83 (again with many less than 0.5) and the specificities from 0.44 to 1.00.

Generally speaking, no particular definition of "positive FH" had more than modest ability to correctly classify future risk of complex disorders in individuals. However, the cross-sectional analyses indicated that, for some conditions (e.g., diabetes), definitions of FH based on disease history in first-degree relatives might be useful for triaging individuals for definitive screening by other tests. The generally limited discriminatory accuracy of FH (any definition) for complex disorders is logical, because, by definition, they are not high-penetrance, single-gene disorders.

While definitive conclusions about the utility of FH could not be drawn, it is possible that FH, used in conjunction with non-FH information, might add useful incremental information in individual patient risk stratification for complex diseases. For such analyses, the "necessary" level of predictive accuracy needs to be clarified, and will depend on the decisions that follow from the risk assessment and the benefits, risks, and costs of different clinical and preventive actions. The thresholds for "good enough" accuracy will vary with the condition of interest, the nature of the patient population, and the resources available to capture the FH information.

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Family History as a Determinant of Risk for Chronic Disorders: Common Conditions and Beyond: I

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Family history risk assessment is important in guiding screening and prevention strategies for many common chronic conditions, including referral for genetic consultation and testing. A positive family history can increase an individual's risk of disease from 2 to 10 times, and this risk generally increases with an increasing number of affected relatives and earlier ages of disease onset.[1] Additional characteristics of high-risk family histories include occurrence of multifocal or bilateral disease, disease in the less-often-affected sex (e.g., breast cancer in males or coronary heart disease in women), and related diagnoses in a pattern suggestive of a single gene disorder. By recognizing the magnitude of risk associated with these family history characteristics, stratification of familial risk into different groups is possible.[1,2] Moreover, family history is often crucial for identifying individuals at risk for hereditary syndromes for whom genetic testing should be considered to further refine disease risk and guide prevention strategies.[3–5] For people with increased familial risk, appropriate preventive interventions include recommendations for lifestyle changes; screening for early cancer detection beginning at younger ages, occurring at more frequent intervals, and with more intensive methods than used for average-risk individuals; use of chemoprevention; and for those at highest risk, prophylactic procedures and surgeries.[3,6]

Thus, to most accurately characterize family history as a risk factor and make risk-specific recommendations, it is necessary to inquire about disease in specific relatives and, when affected, the age at onset and co-occurrence of other conditions must be obtained. However, how this information is gathered and documented will depend on the setting and stakeholder. Comprehensive family history collection and documentation that allows for pedigree construction and analysis takes considerable time and therefore might be best accomplished by consumers outside of the patient-clinician encounter, whereas such comprehensive family history collection and documentation is generally not possible in a busy clinical practice given the time constraints and other competing activities of the typical patient visit.[7] For the busy clinician, collection of data sufficient for recognition of increased familial risk may be preferable. Electronic health records (EHRs) offer a potential solution to improve family history documentation and risk assessment by clinicians;[8] however, most EHRs lack standards for such documentation.[9]

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Family History as a Determinant of Risk for Chronic Disorders: Common Conditions and Beyond: II

Paula W. Yoon, Sc.D., M.P.H.

What Is the Added Value of Family History in Risk Assessment Tools?

Even without reaching consensus on the specific family history elements that contribute to familial risk assessment, self-reported family histories are being incorporated into a number of risk assessment tools for common chronic diseases such as heart disease, diabetes, and cancers. While many paper-based and electronic tools are available to assist individuals with collecting and organizing family history information, new tools are being developed or modified that include risk assessment and reporting. Already, online risk assessment tools are available directly to consumers, and with increasing use of integrated medical record systems, including personal health records, it seems likely that patients will be encouraged to complete self-administered risk assessment tools prior to healthcare visits.

The use of family history information for risk assessment ranges from tools that use only family medical history to assess risk, tools that include family history plus nonclinical risk factors (e.g.,, gender, race, weight, height, yes/no answers about diet or physical activity), and tools that include clinical information and lab values (e.g., cholesterol level, blood pressure, glucose). Examples of risk assessment tools that rely on family history alone include Family Healthware™,[1] which is being evaluated in primary care practices; Be Ready Quiz (http://www.bracnow.com/) and Hereditary Cancer Quiz (http://www.myriadtests.com/quiz.htm?s=View); online tools used by Myriad Genetic Laboratories, Inc., to determine eligibility for possible genetic testing; and genetic risk in the clinical environment (GRACE), a tool that is being developed and evaluated for self-assessment of familial breast cancer risk.[2] An example of a tool that includes family history and nonclinical factors is the American Diabetes Association diabetes risk calculator (http://www.diabetes.org/food-nutrition-lifestyle/lifestyle-prevention/risk-test.jsp), an online tool that includes a question about family history of diabetes among first-degree relatives. Many tools are now being developed, or are already available, that include clinical factors. Examples of tools available online are Family HealthLink (https://familyhealthlink.osumc.edu/), a risk assessment tool for cancer and coronary heart disease developed by Ohio State Medical Center; and Your Disease Risk (http://www.yourdiseaserisk.wustl.edu/), a risk assessment tool for five chronic diseases that was developed at Harvard University but is now available through Washington University School of Medicine. Of particular interest are two risk assessment algorithms which are not yet available for self-assessment but are based on clinical data and rules derived from long-term cohort studies. One is an algorithm that assesses risk for diabetes that is based on clinical and laboratory data from the Atherosclerosis Risk in Communities Study (ARIC);[3] and the other is a modified Framingham Risk Score called the Reynolds Risk Score, which includes the usual risk factors plus family history of myocardial infarction and C-reactive protein to predict future cardiovascular events.[4,5]

The use of patient self-assessment risk scores that include family history as well as clinical and laboratory values will become more popular as patients have increasing access to data in their medical records. The benefits of this practice could be many, including empowering patients and making them more aware of disease risk factors; reducing clinician time to collect the information, allowing more time for interpretation and discussion with patients; and promoting

early disease detection and prevention. Further study is needed, however, to determine the predictive value and utility of risk assessment tools that use family history. For example, some tools might be best used as a first step in serial diagnostic strategies, while others should be closely integrated into clinical management systems that include professional counseling to explain the risk assessment. Studies have repeatedly shown that screening tools developed in one population rarely apply to others. Sensitivities, specificities, and predictive values are usually higher for the population where the tool was developed.[6,7] Risk assessment tools may have to be adapted or recalibrated to the different populations where they are being used. In addition, most of the tools in use today have very limited family history information, and the added value of including more detailed information (number of affected relatives, degree of relationship, age of disease onset, etc.) is suggested by epidemiological studies but has not been incorporated and evaluated in the tools.

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Research Challenges in Assessing Risk With Family History

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Collecting Family History

Feasible methods of systematic family history collection are a prerequisite for research that validates risk algorithms or measures effects of family history-based risk assessment (FHRA) on health. Therefore, research on the systematic use of family history in primary care is in its early stages.[1] The advent of self-administered and automated family history collection and analysis is bringing larger-scale validation and effectiveness research within reach. Self-administered family history tools, if used routinely, are likely to improve upon usual practice.[2,3] Experience gives evidence that many laypeople understand and can reliably use tools that collect family history of cancer and other common diseases[4–9] (and Rubinstein WR, O'Neill S, Kaphingst K, personal communications).

Among research challenges related to collecting family history are (1) elucidating effects of individual (e.g., gender) and social network characteristics (generation; number and social relationships of relatives),[10] on the reliability and completeness of family history; (2) obtaining family history of more stigmatized conditions (e.g., substance abuse, mental illness), which may be more challenging than those common conditions that researchers have tackled so far, and might pose additional ethical issues; (3) as family history diminishes when prevention is effective, preserving a record of disease from earlier generations and including family history of biomarkers or disease precursors in future risk assessments; (4) determining the added value of assessing family history of behavioral and environmental exposures, for revealing gene-environment interactions.

As informatics provides various means for **collecting** and sharing family history, so its development urgently poses a set of research questions regarding the practical, ethical, legal, and social concomitants of new technologies for FHRA. Evidence exists that current Internet FHRA tools are not for everyone because of (1) technical challenges,[11] (2) disparities in computer and Internet access,[12] (3) patient preferences for in-person FHRA,[13] and (4) public concerns about Internet security.[13,14] At the same time, the spread of Web-based communication and electronic health records[15] provides a fertile ground for investigating social networking modalities for families to contribute to a joint family history record[16] [e.g., http://www.geneticalliance.org/ws_display.asp?filter=fhh, accessed May 10, 2009], as well as novel, automated means to record family medical history that do not depend on self-reporting but could function by linking data generated from medical care of multiple family members.

Risk Assessment

In general, familial risk algorithms and cutoffs for stratifying risk require validation.[17,18] Many epidemiologic studies in the past collected only rudimentary family history. Therefore, studies are limited regarding additional benefit from adding age at onset, second-degree or more remote relatives, or patterns of related diseases. Furthermore, the value of each piece of family history is expected to vary according to the particular disease and its pattern of expression and inheritance. The desired sensitivity and specificity also depend on the purpose for which familial risk is used. Because the sensitivity of family history may be lower for younger individuals,

research could address the value of risk algorithms that adjust for family size and for the age of the person giving family history.

Output of the Risk Assessment: Communication of Familial Risk

Evidence is needed to decide upon the key elements of output from a FHRA, and how to provide the information effectively—to lay users, clinicians, and family members (e.g., What FHRA information do clinicians want or need at the point of care? Is the risk level alone sufficient? Are family tree diagrams valuable?). As perceptions about the personal significance of family history[19] are found to be important to health behavior, research would elucidate how to personalize risk messages in congruence with perceptions, in order to change perceptions[20] or to motivate actions to reduce risk. An important set of research questions revolves around decision support once a familial risk becomes evident. What risk-reducing actions are available—and for which family members? For example, with hereditary cancer susceptibility it is not necessarily the person seeking to predict cancer risk who should receive genetic testing initially. In the context of primary care, it is unknown how best to communicate with those who have the option of acting on the information—not only with the person who provided family history.

Studying Effects of Family History Risk Assessment on Health

Finally, research to measure the health effects of FHRA has at least two crucial conceptual challenges not characteristic of most clinical research: (1) Since family history may already be familiar to participants, it is likely to have lifelong influences on the outcomes of interest, before and after any intervention; therefore, conceptualizing discrete effects of the intervention to be studied is important and difficult. (2) A decision must be made regarding for whom the health effects should be measured. Interventions involving FHRA could be conceptualized as prompting the discovery of previously unknown family medical history; recording family history for clinicians or family; influencing personal risk perceptions; providing individuals or clinicians with new information about disease risk or prevention; increasing the salience of familial risk (e.g., by linking it to clinical reminders for preventive care); stimulating or facilitating communication with family members; and/or streamlining referral. Empirical data are needed on the likely time course for such effects. It is a challenge to extend the measurement of effects of FHRA to the health of multiple individuals in the family and social network, and perhaps to study the health of a family as a whole, over time.[21,22]

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Evidence-Based Practice Center Presentation II: A Summary of the Evidence for the Accuracy of Self-Reporting Family History Across Different Diseases

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Background

Family history (FH) is an important risk factor for many common diseases. A number of factors may influence the accuracy of FH obtained in practice, including informant factors (e.g., whether or not they are themselves affected by the disease), disease factors (e.g., whether it is common or rare), family factors (e.g., size of family), relative factors (e.g., degree of relatedness), and clinical context factors (e.g., availability and use of tools).

The formal assessment of the accuracy of reporting requires a reference standard for both what patients "should" know and what clinicians "should" be able to obtain. In its simplest conception, an "accurate" FH is one which is sensitive (actual disease in relatives is correctly identified) and specific (actual lack of disease in relatives is correctly identified).

Purpose

The aim of this systematic review was to address the following research question (#2): "What is the accuracy of the family history, and under what conditions does the accuracy vary?" across a variety of diseases.

Methods

Standard systematic review methodology was employed and the specification of eligibility criteria was guided by input from the Technical Expert Panel and partners. Bibliographic databases searched for this review included MEDLINE®, EMBASE®, CINAHL®, Cochrane Controlled Trial Register (CCTR)®, and PsycINFO. Years searched were 1995 to March 2, 2009, inclusive. Eligibility criteria included studies published in English evaluating the collection of FH for any disease. Populations or settings were not restricted. All quantitative study designs were eligible, but qualitative design studies were excluded. The outcomes included metrics of accuracy (e.g., sensitivity, specificity, percent agreement, etc.). The intervention was defined as a structured/systematic collection of FH (index test). A number of reference standards for FH taking were included (1) comprehensive data obtained directly from relatives, (2) data obtained from hospital or physician records or disease registers, and (3) comprehensive data from all available death certificates and medical records. Note that the concept of accuracy, which incorporates both sensitivity and specificity, requires verification not only of the existence of disease within relatives (where this is reported), but also of the absence of disease in relatives who were reported to be unaffected.

Results

A total of 35 publications evaluated the accuracy of reporting FH and were eligible for data extraction. There were 16 studies that evaluated accuracy of reporting cancer FH. These studies recruited probands with breast cancer,[1–4] colorectal cancer,[5–7] prostate cancer,[8,9]

ovarian cancer,[10] mixed cancers (breast, ovarian, colorectal),[11,12] Ewing's sarcoma,[13] lymphoma,[14] melanoma,[15] and unspecified cancer.[16] Subjects were recruited predominately from specialized settings or cancer registries and the majority had cancer; this would suggest both a high risk of spectrum and selection biases. A total of 10 studies evaluated accuracy in persons with mental health disorders, and these included persons with schizophrenia,[17–19] dementia or depression,[20–23] and mixed disorders.[24–27] Seven studies evaluated other diseases that included Parkinson's disease,[28,29] diabetes,[30,31] hypertension,[32,33] and other cardiovascular disease.[34]

The methods for FH collection varied across studies, as did the questions or tools used to collect FH. Some studies used highly standardized instruments (e.g., mental health disorders) and others used dichotomous probing (presence or absence of disease in any relative). Methods used to verify relatives' disease status were primarily multimodal (medical records, disease or death registry, or contact with relative).

Most studies probed the accuracy of reporting the same disease as that within the proband/ informant; some studies evaluated a variety of disease outcomes within the relatives (e.g., any cancer or any mental health disorder). Overall, specificity across all disease types and with varying modes of FH collection was consistently high. Sensitivities were generally lower in magnitude and more variable depending on the disease outcome (e.g., some anxiety disorders had the lowest sensitivities and breast cancer/cardiovascular disease had the highest sensitivities).

Several studies evaluated predictors of accuracy in reporting FH. Factors related to the proband/informant include age, gender, disease status, education level, race, marital status, type of disease, setting, and insurance status. Predictive factors associated with the relatives include degree of relation, type of first-degree relative (1DR), disease subgroup, age, gender, and time since diagnosis. No clear trend emerges with age, gender, and education level of the informants and their impact on accuracy. There was a consistent trend towards increased accuracy of reporting relating to 1DRs compared to 2DRs or 3DRs; however, the majority of studies evaluated only 1DRs. Overall, these studies had a high risk of spectrum bias (populations highly selected and not reflective of primary care), verification bias (different methods used inconsistently), and masking bias, which may lead to an overestimation of accuracy.

Discussion

In order for FH to be of value in clinical decision making, patients must report, and primary care practitioners be able to ascertain, accurate FH information. Assessing accuracy also requires a clear idea of an appropriate standard—what patients "should" know, and what clinicians "should" be able to obtain. Thus, an "accurate" FH could be considered to be one which is sensitive (disease in relatives is correctly identified) and specific (lack of disease in relatives is correctly identified). In order to fully explore the question of accuracy of reporting we did not restrict the population to those within a primary care setting, as we correctly anticipated that there would be few accuracy studies within this population. In this regard, the majority of studies evaluated subjects with the disease or 1DRs, who are by definition at high risk. Overall, the applicability of these findings from specialized clinical settings to primary care settings may be limited. Although the attributes of the probands/informants were described, those of the relatives (e.g., gender or even the relation to the proband) were not reported well, particularly in studies within the mental health area. Although we have some degree of insight regarding accuracy, it is possible that probands/informants affected by a disease may seek out more complete

information on their FH (after their initial diagnosis). Future evaluations should consider formally examining factors such as sex, age, and cultural background. Overall, the few rigorous studies which fully evaluated accuracy consistently suggested that informants are more accurate in identifying which relatives are free of the disease (specificity) than in identifying relatives who have been affected by cancer (sensitivity).

The accuracy of reporting by probands/informants, controls, or relatives cannot be separated from the performance of the methods used to gather FH. We observed great variation in how FH was captured, and this ranged from simple dichotomous questions to more complex standardized tools that had established psychometric properties. For mental health disorders, FH is an important component in establishing the presence of disease and as such was included in both the index test and the reference standard. The FH of the relative (not just medical history) formed part of the case definition of what was collected in order to establish the presence of the disorder in the proband (e.g., bipolar disorders); disentangling medical history and FH in these studies was challenging. Future evaluation within mental health studies would be strengthened by clarifying these differences.

Conclusions and Recommendations

The accuracy of self-reported FH has implications for the correct risk assessment and management of patients. Accurate reporting of the absence of disease (specificity) appears to be greater than accurate reporting of presence of disease (sensitivity) across most diseases. Estimates of sensitivity show greater variation and the magnitude varies with different diseases. Although there is limited evidence, the accuracy of recall and reporting may be influenced by both proband/informant or relative factors, and by the method used to collect FH (which is also related to the disease area). Recommendations for the direction of future research include the following:

- Future efforts to improve accuracy of reporting would be improved by explicit consideration of whether sensitivity or specificity is the primary goal, which is dependent on the clinical context and purpose of an FH-oriented strategy

- Future studies in accuracy should be undertaken in populations reflective of the primary care setting and representative of the spectrum of disease risk. Future studies should endeavor to better characterize the attributes of the informant/proband, and especially the relatives; the potential of these factors to influence the accuracy of reporting should be consistently evaluated. Future evaluation should be undertaken in the areas of asthma and atopy, affective mental health disorders, cardiovascular diseases, and diabetes.

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Accuracy of Family History Information for Risk Assessment in Clinical Care

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A positive family history can increase one's risk for many diseases and several clinical guidelines utilize family history information in order to "personalize" specific recommendations. Despite the general use of family history information for directing clinical care, only a limited number of studies have evaluated the accuracy of patient-reported family health histories.

Most published reports on family history accuracy have focused on information related to solid tumors and psychiatric diseases. In general, a report of a family history of breast, colorectal, or prostate cancer in first-degree relatives tends to be moderately to highly accurate;[1] however, other tumors such as uterine, lung, and melanoma suffer from much lower sensitivities and specificities. Studies on psychiatric diseases have tended to demonstrate more accurate reporting for clinically severe diseases, such as schizophrenia or mania, and less accuracy for conditions such as anxiety, personality disorders, and depression.[2] However, the sensitivities for family psychiatric history are still far below those of breast or colon cancer. For other adult-onset chronic disease, sensitivities for family histories of coronary artery disease, diabetes, and hypercholesterolemia can reach as high as 85 to 90%; however, this is limited to a very small sample of applicable studies.[3,4]

Numerous factors may influence the accuracy of family history information: factors such as communication patterns within families, knowledge of medical terminology, characteristics of the informant, and the method of family history collection. Several studies have evaluated patient characteristics that might influence the accuracy of family history reporting. However, the factors assessed have not been consistent across studies.

The most frequently investigated patient characteristic is proband age. Hastrup et al. compared the accuracy of family medical history reports in three different age groups: adolescents (ages 11–15 years), undergraduates, and middle-age informants.[5] Accuracy in reporting a family history of myocardial infarction, diabetes mellitus, stroke, and any cancer was similar in all age groups. In adolescents, correct knowledge of medical terminology did not influence the accuracy of reported family history information. This finding might explain why education level has not been related to reporting accuracy consistently. For cancer family history, no clear trends exist between informant age and reporter accuracy.[1] A meta-regression of factors associated with accuracy of family psychiatric health history suggested that older informants reported more accurately than younger informants.[2]

The most consistently reported factor associated with family history accuracy is degree of relatedness of the individual identified by the proband. In general, family history reports for second- and third-degree relatives appear less accurate compared to those for first-degree relatives, and this trend seems stable across different disease states. Another important factor that influences family history accuracy is the disease status of the proband. In most, but not all, studies, affected probands tend to report more accurately compared to disease-free informants. Rarely have studies evaluated how informant family dynamics might influence the accuracy of family history reports. In a twin study of the accuracy of paternal and maternal alcohol use, negative perceptions of paternal parenting style tended to be associated with discordant twin reports of paternal alcohol use.[6]

The method used to collect family history information may also influence overall accuracy. Family history information recorded within patient medical charts as part of routine clinical care greatly underestimates the number of affected relatives when compared to self-completed surveys or formal genetic assessement,[7] and this lack of accuracy may have important clinical effects. In a study of 213 cancer cases, 11% (23) of cases had a change in their clinical management after family history verification. For 15 of these cases, intense cancer surveillance was determined to be unnecessary.[8] Sijmons et al. verified cancer family histories in 129 families referred to a clinical genetics clinic. Verification resulted in a change in management in 5% (six) of families, with five of six cases being assigned a decreased level of genetic risk.[9] Schneider et al. found that 58% of Li-Fraumeni syndrome families underreported their family cancer history.[10]

Time constraints and competing clinical demands likely influences the poor accuracy of clinical records. Fortunately, patient-entered collection processes appear promising. A recent systematic review identified four family history questionnaires that performed reasonably well when validated against formal genetic interviews.[11] The authors noted that despite a growing number of available family history tools, very few have been formally evaluated. Potential collection methods such as paper-based, telephone-based, or computer-based questionnaires appear acceptable to patients and collect similar family data compared to direct-interview methods.[11–13] In addition, a brief follow-up survey administered as part of the Childhood Cancer Survivor Study was able to clarify over 80% of uncertain cancer histories collected previously via paper-based questionnaires.[14] Most studies that have compared family history collection methods to direct genetic interviews have focused primarily on family cancer histories. A single study comparing a family history questionnaire to formal genetic interviews for male patients with infertility found that 75% of patients failed to report relevant family history elements such as stillbirths, birth defects, or developmental delay.[15]

In conclusion, the heterogeneity of current study designs prohibits the pooling of study results and makes it challenging to discern the overall accuracy of patient-reported family history information. Additionally, few factors have been identified to assist clinicians in identifying patients who may be more likely to inaccurately report their family health history. For the clinician, the limitations of patient-reported family history need to be balanced against any potential risks associated with clinical management based on such information. While the accuracy level of a family's breast cancer history may be high enough to expose a patient to the potentially unnecessary radiation exposure through breast imaging, this level of accuracy would not be acceptable to promote prophylactic invasive interventions. Thus, conditions where family history information can influence decisions to engage in clinical interventions with known complication rates should be a priority for future investigations. Due to the logistical challenges inherent in family history validation studies, it will be important to carefully target conditions for further study and apply only the most rigorous referent standard. In addition, to better identify any determinants of accurate reporting, researchers must comprehensively collect information on informant characteristics and family dynamics. Finally, with time constraints and competing demands greatly limiting the adequate collection of family history information in clinical practice, more work is needed in assessing patient-completed family history tools and their integration into patient care.

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Evidence-Based Practice Center Presentation III: Systematic Family History Collection in Primary Care Populations: Impact on Health Outcomes and Factors Affecting Collection

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The collection of family history (FH) is an integral part of clinical practice in primary care, and its potential to identify genetic risk is recognized but still underdeveloped in this setting.[1] For most common chronic diseases, the impact of a positive FH has been recognized. There is empirical evidence to support the common observation that a positive FH confers an extra risk for many common complex diseases.[2] Even if the family history is confirmed to accurately report medical conditions in relatives and predict future disease, systematic family history collection and interpretation will not be adopted by nonspecialist primary care providers unless there is robust evidence that these processes lead to positive health outcomes, while not introducing adverse effects. Further, many factors will affect how family history is collected, and this information is relevant when collating and interpreting information on illnesses in relatives.

The focus of this presentation is on FH collection within the primary care context, where unselected populations present the full range of disease risks, and where the activity is undertaken by primary care providers. This systematic review addressed five research questions, of which three questions are presented here.

> **Question 3.** What is the direct evidence that getting a family history will improve health outcomes for the patient and/or family?
>
> **Question 4.** What is the direct evidence that getting a family history will result in adverse outcomes for the patient and/or family?
>
> **Question 5.** What are the factors that encourage or discourage obtaining and using a family history?

Methods

Standard systematic review methodology was employed. Bibliographic databases searched for this review included MEDLINE®, EMBASE®, CINAHL®, Cochrane Controlled Trial Register (CCTR)®, and PsycINFO. Years searched were 1995 to March 2, 2009, inclusive. Interventions were defined as a structured/systematic collection of FH (Q3, Q4) or as correlates or factors facilitating or hindering the collection and/or use of FH (Q5). Populations were limited to those unselected for risk and typical for primary care settings. Observational studies (Q3 and Q4) and qualitative studies (Q3, Q4, Q5) were excluded.

Results

Question 3. What is the direct evidence that getting a family history will improve health outcomes for the patient and/or family?

We selected studies that identified the impact on health-related outcomes of systematic collection of FH in a typical, nonselected primary care/general population. Of 34 studies

reviewed at full text, only 2 eligible studies were identified.[3,4] Both studies were uncontrolled before-after designs and focused on breast cancer risk assessment, including FH collection, as the target intervention. In both studies there was limited improvement in the clinically relevant process measure: mammography screening. In one study,[3] mammography screening improved from 76 to 93%; however, the matched sample was small (n=29) and the change in screening did not reach statistical significance (p=0.057). In the second study, there was also limited improvement in adherence to mammography in all women (p=0.796). Both studies also demonstrated improvements in adherence to other process measures: breast self-examination (BSE) and clinical breast examination (CBE). Both studies were at high risk of selection bias, sufficient to affect the interpretation of the results.

Question 4. What is the direct evidence that getting a family history will result in adverse outcomes for the patient and/or family?

After reviewing 38 studies at full text, 3 studies met all eligibility criteria.[5–7] These comprised a randomized controlled trial[7] and two uncontrolled before-after studies.[5,6] All three studies recruited patients from single British primary care offices. These studies suggest that structured FH collection and feedback of familial risk information had no deleterious psychological effects on patients at 6 to 12 weeks after FH intervention. One study[5] further identified the relationship between breast cancer familial risk status and psychological impact. As well as no deleterious psychological effect in any of the risk groups, for women who were at or just above average risk, the FH risk assessment may have led to appropriate reductions in perceived risk.

Question 5. What are the factors that encourage or discourage obtaining and using a family history?

Six studies were identified, four of which were undertaken in primary care offices.[8–11] The other two studies' populations were derived from patients being screened in the general population.[12,13] Factors associated with FH collection or discussion were the primary outcome of interest of three studies.[10,11,13] The identified outcomes of interest were FH documented in medical records;[8,10] FH discussed by doctor, either confirmed by direct observation[11] or patient survey;[9,12] and self-reported FH.[10,13] Women appeared to be better informants than men and younger physicians were more enthusiastic about discussing FH. There were disparities in FH collection and reporting in underserved groups, specifically nonwhite ethnic groups,[10,13] those with lower educational status,[13] and those on state health insurance.[11]

Discussion

The review identified improved screening for breast cancer risk when FH collection is incorporated in multifactorial risk assessment (Q3). But evidence for other conditions is lacking. Further, incorporating FH collection into a multifactorial risk-assessment tool does lead to difficulties in disentangling the effect of the FH intervention from other factors. When considering the adverse effects of such interventions (Q4), the three studies did actually look at the impact of FH collection. All were small studies but, reassuringly, they demonstrated that general anxiety scores did return to preintervention levels by 6 to 12 weeks.

Both studies that evaluated improved health outcomes and one of the three studies assessing adverse outcomes used a disease-focused FH enquiry.[3–5] The other two studies used more generic FH tools.[6,7] The nature of the FH collection and the chosen health outcomes will be dependent on the purpose of the inquiry, and this needs to be considered in future research.

The outcomes selected need to be clinically relevant, either leading to improved mortality or morbidity or surrogate measures with strong evidence of links to health outcomes.

The evidence base for addressing Q5 is heterogeneous and limited to six studies exploring the association between various factors and FH reporting, documentation, and discussion. In most studies, the nature of the FH discussed or reported was not clearly identified, often just reported as dichotomous variables. Representativeness of these studies is also limited by response bias and recall bias. Collectively, these issues limit the generalizability of the study findings. Further, there is insufficient evidence on whether organizational factors, such as electronic health records, make a meaningful difference to FH capture or recording. Further research is required to clarify the most important patient and practitioner factors that may affect the collection and use of FH. Where inequities are identified, interventions should be designed to ameliorate these factors in future trials and service provision.

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Perspectives on the Utility of Family History as a Screening Tool: The CDC Family Healthware™ Experience

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Background

Recognizing that family health history is rarely used to its full potential by healthcare practitioners, the Centers for Disease Control and Prevention (CDC) developed Family Healthware™, an interactive, Web-based tool that assesses and stratifies familial risk for coronary heart disease (CHD), stroke or cerebrovascular accident (CVA), diabetes mellitus (DM), and colorectal (CRC), breast (BC), and ovarian (OC) cancers and provides risk-based recommendations for screening tests and lifestyle changes.[1] The CDC selected three academic centers to evaluate the clinical utility of Family Healthware™, which designed and conducted the Family Healthware™ Impact Trial (FHITr). Because most preventive services are delivered in primary care, the effects of Family Healthware™ on preventive care were evaluated in primary care practices.

We hypothesized that patients who record their family history and receive, along with their primary care clinician, specific information about their familial risk levels and prevention messages tailored to those levels will be more likely to make health behavior changes, adhere to risk-appropriate screening, and use preventive health services than patients who do not have their family history assessed and who receive only generic (not personalized) prevention messages. This study also provides the first estimate of the prevalence of family history risk for common, chronic diseases in a primary care population without these diseases and examines the relationship between health risk perceptions and health-related behaviors.

Methods

The FHITr is a cluster-randomized clinical trial, conducted from 2005–2007, to evaluate the clinical utility of Family Healthware™, a self-administered, Web-based tool that assesses familial risk for six common, chronic diseases: CHD, CVA, DM, CRC, BC, and OC.[2] A total of 3,786 patients aged 35 to 65 years with no known diagnosis of these 6 diseases were enrolled consecutively from 41 primary care practices involving 187 clinicians in 13 states. Subjects were prerandomized into intervention or control groups. All participants completed a 128-item baseline survey. Study outcomes were assessed in both groups through a similar follow-up survey administered after 6 months. The intervention group completed Family Healthware™ at baseline and received risk-tailored prevention messages. The control group received generic prevention messages after the baseline survey and completed Family Healthware™ after the 6-month follow-up survey to make possible risk-based stratifications in the analyses.

Results

Participants had a mean age of 50.6 years and were primarily Caucasian (91%) and female (70%). The study population had a usual source of medical care, health insurance (96%); and was highly educated (72% >4 years college) and affluent (63% >$75,000 annual household income). The recruitment rate was 18% and the retention rate was 89% from consent to baseline survey and 88% from baseline to follow-up. A total of 3,585 FHITr study participants used Family Healthware™ with an average online completion time of 17 minutes.

Analysis of familial risk prevalence data showed that 82% had a strong (S) or moderate (M) familial risk for at least one of the diseases: CHD (S=33%, M=26%), CVA (S=15%, M=34%), DM (S=11%, M=26%), CRC (S=3%, M=11%), BC (S=10%, M=12%), OC (S=4%, M=6%). In a substudy at one site comparing Family Healthware™ to chart-based risk assessment among 1,124 participants, there was insufficient information in the medical chart for adequate risk assessment for 38–64% of patients (depending on the disease), and 23% of these patients had a moderate or strong risk for at least one of the six diseases.

A total of 92% of FHITr participants reported that knowledge of family history was important for their own health. While most participants were accurate in their risk perception, many at strong or moderate risk underestimated their risk (optimistic bias). This was particularly true for CHD (41%), DM (22%), and CVA (37%) and was also sizeable for BC (12%) and CC (8%). Family Healthware™ increased risk perception among underestimators for CHD, DM, CVA, and CC, with borderline significance for BC (strong risk group).

For preventive behaviors, the familial-risk-tailored message moved significantly more participants to “at goal” for physical activity. There was no impact on smoking or aspirin use. At baseline, adherence to screening behaviors was very high for metabolic diseases (~90 for blood pressure, cholesterol, and blood glucose screening) and cancer (~75% for colon cancer screening and mammography; 94% for clinical breast exam). In addition, baseline screening adherence for breast cancer and colon cancer correlated positively with higher perceived risk. Improvements in screening behaviors were not detected in intervention versus control groups, nor was an effect seen for referral to specialists. Among patients with “room to move,” a high percentage did become current (~90% for blood pressure, 55–70% for cholesterol, ~60% for mammography, ~35% for colon cancer screening), but few differences were seen between intervention and control groups. Some paradoxical effects were seen whereby the control group improved more than the intervention group (e.g., health maintenance examinations for DM and CVA; adherence for cholesterol screening and clinical breast exam), raising questions about effectiveness of the messaging. Communication about family health history was influenced in the intervention group, in which participants were more likely to collect information from relatives and more likely to talk with a healthcare provider. We noted several statistically significant differences between men and women regarding reporting of and communication about family health history, baseline risk perception, change in risk perception, and health behavior screening at baseline.

Discussion

The FHITr study demonstrates that a segment of the primary care population is interested in family health history. The usability and acceptance of Family Healthware™ are high. Familial risk prevalence is high. Compliance with recommended lifestyle and screening behaviors among this population is quite high. Therefore, some questions remain about the clinical utility of Family Healthware™. A large-scale comparison of Family Healthware™ and chart-based

family history shows that computer-based family history risk assessment provides more information, enabling risk assessment for a larger proportion of patients.

While the saliency of family history is well-recognized, a sizeable proportion of patients at strong and moderate familial objective risk underestimate their risk. There is evidence that use of Family Healthware™ can help align perceived risk with objective familial risk among underestimators, a target group. Yet, little evidence of clinical utility was observed for the intervention of family history risk assessment and notification coupled with familial-risk-tailored messages as compared with the provision of generic prevention messages—why?

While the Family Healthware™ tool performed well in terms of identifying familial risk, the limited clinical utility in effecting screening behavior changes may reflect the study population, study design, and/or effectiveness of messaging. The FHITr study lacks ethnic and racial diversity and largely represents a well educated, affluent population with access to healthcare. This population had very high adherence to screening at baseline as compared with national screening adherence rates, limiting the ability to observe improvements between intervention and control groups. The 128-item baseline survey may have served as a prompt in both the control and intervention groups (since improved adherence was seen in both groups), obscuring an effect of Family Healthware™. The output of Family Healthware™ was lengthy as compared with the concise generic prevention messages, which may limit effectiveness of the intervention. We think that the potential to change risk perception, and the link between risk perception and screening behavior, bodes well for improving healthy outcomes among those with optimistic bias. However, the intervention seems nominal and may require adjustment of the strength and/or focus of the messages, incorporation of more active interventions, and implementation of automated prompts in the electronic medical record. It will also be important to partner more effectively with healthcare providers, understand their behavior, and target interventions to them. Development of “comprehensive” risk assessment incorporating nonfamily history risk factors may be necessary to engage providers.

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Perspectives on the Utility of Family History as a Screening Tool: The Utah State Experience

Ted D. Adams, Ph.D., M.P.H., and Steven C. Hunt, Ph.D.

Utah has historically been a family-history-friendly state. The population tends toward large families, the environment promotes the keeping of family records, and the resident migration out of the state is likely less than other areas of the United States. Capitalizing on these favorable characteristics, in 1983 the Cardiovascular Genetics Division, University of Utah School of Medicine, partnered with the Utah Department of Health in launching the Health Family Tree (HFT) program.[1,2] Material development costs were supported by the U.S. Department of Health and Human Services through the Centers for Disease Control and Prevention; the National Heart, Lung, and Blood Institute (NHLBI); and Utah State general funds. From inception, this program has had four primary aims:

- Introduce to high school health classes a population-based, three-generational family history screening tool for the purpose of enhancing student and family awareness of inherited disease risk, as well as environmental influences related to health and disease;

- Identify persons and families at high risk for cardiovascular disease (CVD) and other common chronic diseases using a validated risk score;

- Facilitate interventional activities (education, testing, and referral) within the homes of families found to be at high risk using home health personnel; and

- Provide follow-up to monitor health status and to reinforce health behavior changes.

The extent of which these four aims have been addressed over the past 26 years has varied in relation to program funding. In total, 52 Utah high schools have participated in the HFT program. Disease status and lifestyle practices have been collected on approximately 76,000 families, representing 152,000 pedigrees (separate families of the mother and father of the participating student) and over 1.1 million family relatives. A validation study of the HFT risk score demonstrated positive family history increases the incidence of hypertension and coronary disease in family members who were unaffected at the time the family history was determined.[3] This study also reported an approximate sensitivity of 71%, specificity of 95%, and positive and negative predictive values (71% and 94%, respectively) for proband-reported coronary heart disease (CHD) in relative versus self-report in the relatives.[3] Recently, the family risk score has been validated for common cancers, stroke, and diabetes. In an additional effort to assess how well the HFT program risk score prospectively predicts cardiovascular events, families were selected using the family risk score as being low-, high-, or very high-risk for CHD events. Family members who were without CHD at the time the HFT was completed were contacted on average 17 years later to determine whether or not they had experienced any CHD-related events or procedures (e.g., myocardial infarction, coronary arterial bypass graft, etc.). CHD relative risks were 1.66 and 2.88 for the high- and very high-risk groups compared to the low-risk group ($\chi^2 = 6.55$, $p = 0.010$ for an increased risk across groups). In addition to the benefit of family history as an independent predictor of future disease incidence, family history also can define the relatively small subset of families that account for most cases in the general population. Using data from the HFT program and the family risk score for CHD for each family,

the overall 14% of Utah families that had a positive family history of CHD accounted for 72% of all early CHD events and 48% of CHD events at any age.[4]

Although studies demonstrating whether or not increased knowledge as a result of participation in family history activities link to positive behavioral change and subsequent improvement in health are needed,[5,6] this body of literature is limited.[7,8] To explore the effectiveness of the HFT program in assisting people identified as high risk to seek follow-up medical consultation as well as increase participation in healthy lifestyle activities, 10,488 families were divided into high and low risk for common diseases based upon their family risk score. From these two groups, 681 high-risk and 671 low-risk families were randomly selected. All families from both groups received a standard HFT program report identifying their family risk score and general health and lifestyle instructions. In addition, the high-risk families received visits from home health-care nurses to assist families in reducing their risk through appropriate intervention and referral. Both groups of families received a baseline and three follow-up mailed surveys over a 10-year period to assess health behavior practices. Results demonstrated that intervention in high-risk families can effectively motivate positive behavior change. These behavioral changes were seen in both health screening and lifestyle behaviors, with the most dramatic change in the high-risk families seen from baseline to the first follow-up period. In addition, average-risk families reported an increase in certain healthy-lifestyle-related practices.

The HFT program further unifies two important approaches used in primary prevention: population-wide health promotion and targeted intervention of high-risk groups.[9] Because almost half of all families display a positive family history of one or more common chronic diseases,[10] the family history assessment can capture important information about many diseases, as well as risk factors, simultaneously. In addition, family-based risk for disease, as well as associated risk factors, can be intervened upon in appropriately identified families.

In conclusion, the HFT program represents a community-based effort in which several players (school teachers, school administrators, students, health agencies, universities, government agencies, families, and family members) work together to assess risk for disease, recommend appropriate screening and referral, and identify opportunities to improve health behaviors. Currently, efforts are under way to move the HFT program from a paper-based format to an interactive Internet format. This approach is predicted to significantly lower material and administrative costs. Perhaps the single-greatest compliment repeatedly made is that the HFT program has been the “kitchen table activity” for families. In fact, from its inception, the HFT program was designed to encourage family participation at all levels. This program represented an activity to include the student, their parent(s) or guardian, and siblings gathering around the kitchen table to record health and lifestyle data onto the large two-by-three-foot health tree paper foldout, and, when necessary, to make calls to aunts, uncles, and grandparents. The end objective of this program was and will be to inform individuals and families about their health risks and risk-related behaviors to empower them to positively impact future health outcomes.

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Perspectives on the Utility of Family History as a Screening Tool in Pediatric Populations

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Use of family history information in pediatric settings offers unique opportunities and challenges. In the clinical setting, pediatric care has the advantage over adult care of having more frequent preventive care visits, offering more chances for clinicians to collect family history.[1] Medical genetics is typically integrated into pediatric care, so that pediatric clinicians may be more comfortable with family history collection.[1] From a public health standpoint, settings such as schools offer the opportunity to potentially assess family history at the population level, as was done in the Utah Health Family Tree Study.[2] Practices such as the preparticipation physical examination for high school athletics provide a chance to focus on family history risk for specific conditions.[3] Parents report more concern about disease risk for their children than themselves[4] and may be more motivated to make behavioral changes, such as preparing healthier meals, for the sake of their children's health rather than their own.

While family history campaigns targeting adults have focused mainly on chronic conditions, use of family history information in pediatric settings includes single-gene disorders, which represent a substantial public heath burden in children.[5] Signs and symptoms of many single-gene disorders first become evident in childhood, and children can also be diagnosed presymptomatically through family-history-based prenatal screening. While most chronic conditions do not manifest until adulthood, increasing numbers of studies show that children and adolescents with family histories of these conditions can show preclinical signs of these conditions.[6] Integrating family history collection for both single-gene disorders and chronic conditions presents numerous challenges. While collection of family history information on first- and second-degree relatives is generally considered adequate for chronic conditions, more distant relatives might need to be considered for single-gene disorders. The number of conditions for which family history is collected will be greater, which could be addressed by a life-stage approach, with information on family histories of conditions collected at a time when the information would be more likely utilized. For example, information on family history of developmental delay would be collected in infancy, while obtaining information on family history of depression might be delayed until adolescence. Another important challenge to use of family history information in pediatric settings is the lack of consensus and evidence base for appropriate treatment in childhood for adult-onset conditions. Also, younger parents will be less likely to have developed chronic conditions, so that updating of family history information will be especially important.

Current clinical uses of family history information in pediatric settings parallel those in adult care. Although family history is often collected without a specific disease in mind, the information is most often used for diagnosis in symptomatic individuals to determine necessary diagnostic tests (including genetic tests) and to guide referrals.[1] Family history information can be used for risk assessment of genetic disorders, which is helpful since populationwide screening for most genetic disorders is not recommended, and for interpretation of genetic testing results. For chronic conditions, family history information can inform decisions about screening and allow for targeted patient education and prevention efforts. For example, a 1998 American Academy of Pediatrics recommendation states that children aged 2 and older be screened for hypercholesterolemia if they have a family history of premature heart disease or a parent with hypercholesterolemia.[7] Collection of family history information also helps clinicians build rapport

with patients and their families and identify shared environments and behaviors that might put an individual at higher risk for disease. These discussions can help identify inheritance patterns and correct mistaken beliefs; for instance, that a particular condition affects only one gender or skips a generation. Furthermore, family history collection is an essential component of a complete physical exam visit for a child and is required to warrant billing for that encounter.[1] Use of family history information in the pediatric setting can benefit from a family-centered approach, with shared family responsibility and ownership of data, and can demonstrate to parents the need for medical documentation of relatives' family histories and the importance of sharing this information with other relatives. For genetic disorders in particular, parents can be educated about signs and symptoms to be aware of in relatives, and diagnosis of a genetic disorder in one relative might lead to cascade testing in other family members.

Barriers to the use of family history information in pediatric primary care include lack of clinician time or training to interpret family history, lack of reimbursement, and inaccurate or incomplete family history information. Some clinicians might not prioritize use of family history if the benefits to patient care are not immediate, as would be the case with most chronic conditions. Also, guidance is needed on specific pediatric and adult-onset conditions for which family history collection in childhood is useful, as well as what constitutes a family history for these conditions. For example, the premutation phenotypes of primary ovarian insufficiency and fragile X-associated tremor/ataxia are indicative of a family history of fragile X syndrome, but information on these phenotypes is not routinely collected when screening for a family history of developmental delay. Likewise, sentinel events in family members are not necessarily collected when assessing risk for chronic diseases. In addition, recommendations are needed on next steps once a child with familial risk factors has been identified. From the patient standpoint, busy parents might not take time to research their family's health history. Other parents might be reluctant to seek out this information if it will bring back memories of loss, illness, or broken relationships.

For single-gene disorders, the clinical validity of family history information is well established, and evidence that family history is an important risk factor for chronic conditions is accumulating. For example, children with a family history of cardiovascular disease or diabetes can show preclinical signs of these conditions, indicating that the disease process can begin in childhood.[6,8] However, whether family history-based screening is the best way to identify children at risk remains unclear.[9] A subset of chronic conditions has a single gene etiology (e.g., maturity onset diabetes of the young, familial hypercholesterolemia), making family history a stronger predictor for these disorders. Traditionally, genetic testing has been contraindicated for children when detecting adult-onset conditions, so it is unclear what the next steps would be following identification of a high-risk family history that would warrant genetic testing in an adult. Some complex conditions are more relevant to the pediatric realm, such as birth defects and asthma, and evidence on utility of family history information for these conditions is growing.[10, 11] Population-based data on family history prevalence and population-attributable risk of pediatric chronic conditions is needed, as well as development of risk stratification. For rarer single-gene disorders, better understanding of penetrance and expressivity is a priority.

Demonstrating clinical utility of family history information in pediatric settings faces many of the same challenges seen in adult settings. Among children, targeted public health programs have changed knowledge, attitudes, and behaviors that might reduce risk factors for chronic conditions such as cardiovascular disease and diabetes.[6] Habits started at younger ages and a family-centered approach might provide greater benefit and consistency, although the transition from parent-led change to child-led change needs to be explored. Evidence is needed that treatment in childhood alters the course of chronic diseases in adulthood, especially for

interventions involving drug therapy. Furthermore, the availability of presymptomatic diagnosis and treatment does not ensure benefit to the child. This is illustrated by the examples of early screening and surgery for neuroblastoma, which created morbidity in patients whose lesions might have been benign, and the recommendation for children at risk for sudden cardiac death to avoid sports, which puts these children at risk for obesity and its attendant health problems.[12,13]

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Research Challenges in Demonstrating the Utility of Family History in Obstetrical and Pediatric Settings

Siobhan M. Dolan, M.D., M.P.H.

Family history captures the collective influences of inherited genetic susceptibility, shared environmental factors, and common behaviors within families. Throughout the reproductive continuum, pediatricians, obstetricians, family practitioners, genetic counselors, and other clinicians work with families to elicit relevant family history information and factor it into risk assessment calculations and, when appropriate, decision making. To date, mechanisms for collecting family history information have focused on understanding the risk for single-gene disorders, chromosomal conditions, and teratogen exposures during the preconception, prenatal, and interconception periods.[1,2] Research is needed to understand how to link this information at the appropriate points between the pediatric and obstetric settings. In addition, more research is needed to understand how family history influences risk for a wide variety of more common complex birth outcomes such as preterm birth, stillbirth, and many birth defects.[3] With a better understanding of the impact of family history on the full spectrum of adverse birth outcomes, tools for the collection of a broader set of pertinent family history information must be developed in order to improve birth outcomes, setting the stage for better lifelong health.

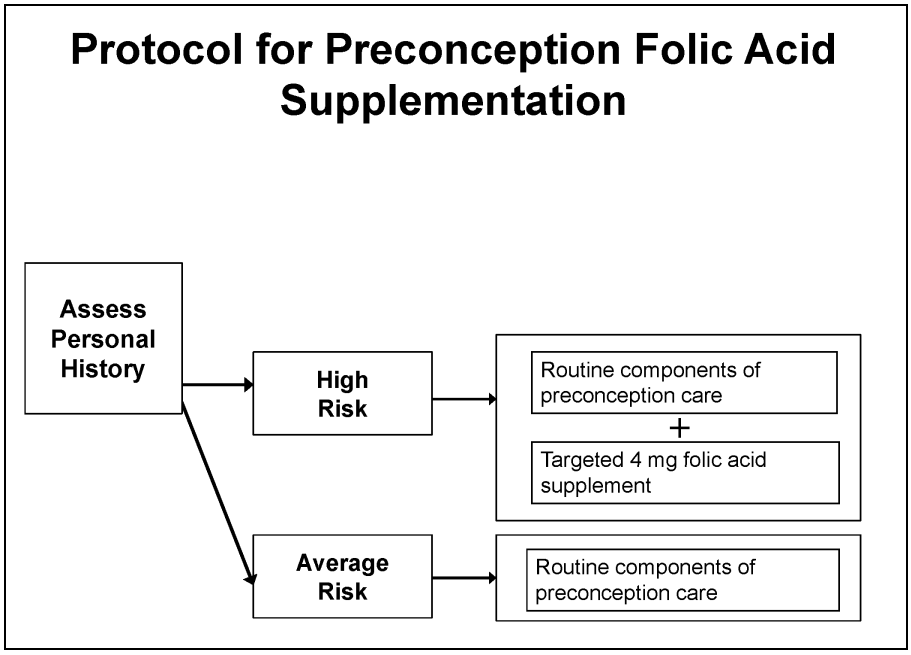
Linking family history elicited in pediatric care with preconception and prenatal care in the obstetric setting is an important clinical challenge and research avenue.[4] For example, a survey of families regarding the diagnosis of a child with Fragile X syndrome revealed that delay in diagnosis of an older child meant many families had additional children with Fragile X without knowing their risk.[5] At the other end of the spectrum from delayed diagnosis, expanded newborn screening will provide families with information about their children in the first few days of life that immediately constitutes a family history which is relevant to the care of older siblings, as well as reproductive planning for subsequent pregnancies.[6] In the case of medium-chain acyl-coenzyme A dehydrogenase deficiency (MCADD), information regarding an infant diagnosed via newborn screening has immediate ramifications for an older sibling who might have been born prior to expanded newborn screening and who warrants immediate testing and anticipatory guidance. Lastly, broader guidelines for preconception and prenatal carrier screening for conditions such as cystic fibrosis,[7,8] hemoglobinopathies,[9] Jewish genetic diseases,[10,11] and spinal muscular atrophy[12] will provide additional information for families during the preconception and prenatal period that will not only influence reproductive planning and prenatal care but may also be relevant to the pediatric care of siblings.

How to optimize the flow of family history information back and forth between the obstetrical and pediatric setting presents a research challenge. What is the best mechanism for collecting family history information? How can providers share relevant information at the appropriate times while protecting patients' privacy? In which clinical setting is time available for providers and/or patients to collect family history information? Is the information accurate? Electronic medical records will likely provide additional options for sharing family history information,[13,14] but such electronic medical records must capture information on multiple family members and be available in several distinct clinical disciplines, including pediatrics, obstetrics, and family practice. Excellent tools, such as the Surgeon General's Family History tool,[15] will need to be expanded to include collection of information regarding family history relevant to obstetric and pediatric care, and the complete list of data elements that are relevant to obstetric and pediatric care will need to be determined. Finally, the optimal way to integrate newborn screening results

into the clinical care section of an individual child's electronic medical record, as well as the family history section of his or her relatives' medical record, is an important area currently under investigation.

Beyond single-gene disorders, family history is a relevant risk factor for many adverse birth outcomes, such as birth defects,[16] preterm birth,[17] stillbirth,[18] and recurrent miscarriage. These conditions, which follow a complex disease model in which both genetic and environmental factors contribute, will likely be akin to adult chronic diseases such as cardiovascular disease and cancer, in which family history has been shown to be a valuable screening tool.[19,20] Progress has been made in the prevention of neural tube defects (NTD) following a personalized risk assessment model in which all women follow a universal recommendation to supplement their well-balanced diets with a 400 microgram folic acid supplement, but women with a personal or previous history of NTD follow a targeted recommendation for a higher-dose folic acid supplement of 4 milligrams.[21] This strategy of risk stratification and targeted evidence-based intervention illustrated in figure 1, as well as the fortification of grains, has led to a substantial reduction in the incidence of NTDs.[22] If such a model could be expanded to include family history of NTD as a risk factor warranting higher-dose folic acid and the model were validated, perhaps additional progress could be made in prevention.

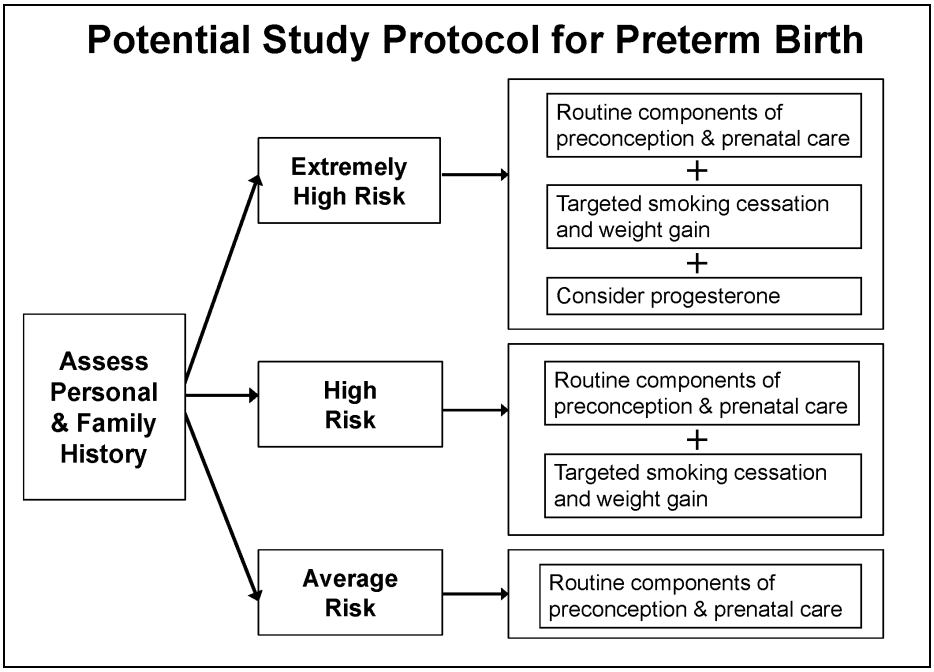
Figure 1. Targeted Intervention for Preconception Folic Acid Supplementation



Another important obstetrical outcome which follows a complex disease model is preterm birth. Preterm birth is a major public health concern internationally, with rates of preterm birth high and rising in many parts of the world. In 2006, 12.8% of all births in the United States were preterm, defined as delivery before 37 completed weeks gestation.[23] Preterm birth is the second-leading cause of infant mortality and the leading cause of infant mortality among black infants in the United States, as well as the major contributor to worldwide infant mortality and morbidity.[24] Children born preterm may suffer lifelong morbidities, including lung disease, vision and hearing deficits, and other neurosensory impairments, as well as predisposition to

hypertension and diabetes in adult life.[25] While clinicians largely recognize that a personal or family history of preterm birth increases a woman's risk for preterm birth, a standard tool for collecting such family history information in obstetric care and validated algorithms that interpret familial risk are needed. Research could then be carried out to test interventions on women of various risk groups and the evidence base for targeted prevention messages and clinical interventions could be tested. A potential research protocol is proposed in figure 2, with targeted interventions for average-risk women, including routine care; targeted interventions for high-risk women, including weight gain guidance and smoking cessation; and targeted interventions for extremely high-risk women, including progesterone supplementation.[26]

Figure 2. Potential Study Protocol for Targeted Interventions To Prevent Preterm Birth



Family history will certainly be a powerful tool for assessing risk relevant to improving obstetric outcomes, thereby setting the stage for improved childhood and lifelong health. A robust research agenda aimed at identifying the appropriate information to collect in the obstetric setting, developing useful and practical tools to collect such family history information, validating algorithms that interpret familial risk, and demonstrated evidence-based prevention messages and interventions in the obstetric setting will lead to the full realization of its potential.

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Family History and Those Providing Care for Patients With Genetic Disorders: The Customer's Perspective

Sharon F. Terry, M.A.

Family health history (FHH) information used in a clinical setting is useful for diagnosis, disease management, and treatment. Indeed, family history can even be more predictive of diseases or disorders than genetic variants.[1–4] Furthermore, family health history as a tool allows patients to be a direct partner in the management of their own care. Yet there has been little study of whether FHH tools used by individuals, families, and communities inspire measurable changes in behavior and communication, within the family or with a healthcare provider.[5,6]

The Health Resources and Public Administration (HRSA)–funded Community Centered Family Health History Project began with the idea that accessible tools produced by the community for the community would promote conversations among family members about health and would translate knowledge of FHH into healthy lifestyle choices. Genetic Alliance worked with seven different communities across the country to customize and measure the utility of the "Does It Run in the Family?" toolkit. This set of two booklets explains the importance of family health history, how to collect the FHH, and basic genetics concepts that can run in families. Each community recruited 25 families of at least 2 blood relatives. Participants discussed booklet content with family members and friends within the study cohort and without. From pre- to posttoolkit use, the participants showed positive changes in communicating about family history of disease risk ($p<0.01$) and in communicating with providers about health risk ($p<0.05$).

For individuals and families with genetic conditions, communication is essential for disease and risk management as well as care. Empowering the participant to be the steward of his or her own FHH information facilitates the job of the healthcare provider and creates an informed public capable of and comfortable with dialoguing around genetics and health.

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Research Challenges in Affecting Behavioral Change With Family History Information: Patients and Providers

Colleen M. McBride, Ph.D.

Family-history-based risk assessment is a well-established clinical tool widely used by healthcare providers. Informed by genetic discovery, new standards have been set to improve the precision of family history assessment (e.g., collecting disease incidence and death for three generations of blood relatives; frequent updates). In the same timeframe, several interactive Web-based tools (e.g., Centers for Disease Control and Prevention's [CDC's] Family Healthware) have been developed and advertised directly to the public via national marketing campaigns (Surgeon General's Family History Day). This new generation of tools and campaigns encourages individuals and families to collect their personal family history assessments, with the objective to increase the accuracy of the information collected and presented to healthcare providers. Moreover, the Family Healthware™ tool includes customized prevention recommendations based on individuals' self-reported risk behaviors. This presentation will highlight emerging research findings derived from these efforts and the evidence to support changes in reported health habits, related disease outcomes, and healthcare use. In particular, ongoing research from the three studies funded by the CDC to evaluate the Family Healthware™ will be featured. Additionally, insights gained from other ongoing community- and clinic-based research published or in press in 2009 also will be presented. Conclusions to be drawn from these findings and future research directions will be suggested.

The Potential Costs of Screening for Risk With Family History

James E. Haddow, M.D.

Little information is available about harms that might be associated with asking family history questions in primary care settings. In April 2009, an Agency for Healthcare Research Quality (AHRQ) report indicated that "there is insufficient evidence to assess whether FHx-based personalized risk assessment directly causes adverse outcomes."[1] More meaningful data in relation to possible harms must come from documenting associated tests and actions recommended as a result of family history-based risk assessments (rather than limiting assessment of possible harm to how an individual reacts to risk interpretations). While most family history questionnaires (FHQs) have focused on a single disease (most often, a cancer), one group has postulated that a broadly inclusive "generic tool" might be more effective in primary care, simultaneously suggesting that disease-specific FHQs may have limited applicability.[2] Whichever approach is chosen, the intent would be to replace the traditional assessment of family history in medical practice with a more formal standardized screening questionnaire, suitable for target populations. This presentation does not consider the global, generic FHQ option, because proper assessment of its performance would be a virtual impossibility. Instead, a conceptual framework is described for studying and evaluating individual, targeted FHQs that might focus on a specific medical disorder.

The dilemma at present is that use of a structured FHQ has been advocated in primary care as a component of "personalized medicine," but specific evidence for its validity and utility is lacking. Expert review groups have been set up at the national level, charged with responsibility for reviewing the evidence for validity and utility of tests being introduced into medical practice and then making recommendations, with emphasis on tests which might be widely applied (e.g., screening tests). Two such groups are the AHRQ-supported United States Preventive Services Task Force (USPSTF) which oversees a wide variety of general practice interventions,[3] and the Centers for Disease Control and Prevention (CDC)-funded Evaluation of Genetic Applications in Practice and Prevention Working Group, focused on genomic applications with potentially broad use in general populations.[4] Reviews and recommendations from both groups are dependent upon availability of the type of information that would be collected using the framework presented here. Often, enthusiasm for introducing a screening test outpaces the accumulation of data to define its performance. When that happens, a test with merit may unfairly fall into disuse due to unrealistic initial expectations, or the test may continue being used, even though subsequent studies show little, or no, value. Against this background, it is particularly timely to advise caution in deploying FHQ for general use until documentation of performance is assured.

In 1989, Wald and Cuckle described a systematic approach for evaluating the performance of screening and diagnostic tests.[5] More recently, the CDC has sponsored the development of the Analytic Validity, Clinical Validity, Clinical Utility, and ELSI (ethical, legal, and social implications) (ACCE) process, which builds upon this preexisting work and incorporates terminology recommended by the Secretary's Advisory Committee on Genetic Testing.[6,7] Using guidance of this type not only to assess, but also to design, strategies for assessing harms from family history screening offers the best prospect for avoiding pitfalls that are expressed by the axiom: "You can't repair by analysis what you've bungled by design." Initially, the medical disorder being sought needs to be characterized, because success of the family history screening process is to be measured by its health impact, over and above existing medical practice. While

this first step might appear obvious, a number of historical examples exist in which the medical problem has been commonly misperceived (e.g., What disorder is sought by measuring blood pressure?). Critical performance characteristics of the FHQ designed for improving the health outcome of the designated medical disorder should be understood, including the detection rate and the false positive rate. Then, the target population can be chosen (based on such characteristics as age or gender, depending on the condition being sought). Finally, the odds of being affected given a positive result (OAPR) can be calculated, based on the frequency of the disorder in the target population. The OAPR is equivalent to the positive predictive value. The FHQ ought to contain only pertinent questions, be field tested for ease of use, and contain a standardized interpretive algorithm developed for recommending actions, based upon risk assignment. Once recommended actions have been decided upon for individuals with positive screening-test results, it will be possible to gather data on both benefits and harms. When effective actions are taken to prevent a serious medical problem following high-risk identification, it is not unusual for harms to occur as well. Such harms may be found acceptable when weighed against the benefits.

Applying an FHQ as a screening test for identifying individuals (or families) at risk for carrying a BRCA mutation is a good example of how studies might be structured to obtain information about benefits and harms. These mutations are associated with breast and ovarian cancer, accounting for about 2% of breast cancer overall, and 10% of breast cancer in younger women. Availability of genetic testing offers the prospect of identifying carrier women before cancer occurs, allowing well-defined actions to be chosen aimed at early diagnosis, chemoprevention, or risk-reducing surgery. Family history is necessary, here, because mutations are relatively rare (1 in 300 to 1 in 450 in the general population), the cost of mutation testing is high, and genetic variants of unknown significance are occasionally identified, leaving the person being tested without a clear answer. Although information on FHQ performance characteristics for BRCA detection is incomplete, enough is available to begin constructing a rationale for pilot studies which are capable of yielding data on screening performance, as well as benefits and harms. In recommending that BRCA testing be used in practice, the USPSTF has indicated that no more than about 2% of screened women in the general population (<55 years of age) should be recommended BRCA testing as a result of FHQ screening.[8] Satisfying those guidelines requires understanding how an FHQ designed for this purpose performs in the primary care setting. This example is to be explored in greater depth at the conference.

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Perspectives on the Clinical Applications of Family History as a Screening Tool Across Multiple Populations

Chanita Hughes Halbert, Ph.D.

Despite previous efforts, members of ethnic and racial groups continue to experience poorer outcomes from several chronic diseases.[1,2] Family history plays an important role in many chronic health conditions (e.g., cancer, cardiovascular disease). For instance, individuals who have a family history of breast or prostate cancer have an increased risk of developing these diseases compared to individuals without a family history. However, previous research has shown that ethnic and racial minority groups may lack awareness about their family history of disease and, perhaps more importantly, may not understand the implications of their family history for their personal disease risk.[3,4] To improve comprehension about the implications of family history of disease, risk counseling and education programs have been developed specifically for members of ethnic and racial minority groups.[5] It is important to determine if these programs are beneficial in terms of improving risk comprehension. Because the recruitment process for risk counseling programs is likely to involve an assessment of family history, it is also important to evaluate whether or not those at risk are likely to use these services.

The available data suggest that participation in risk counseling programs is highly variable among ethnic and racial minority groups. In a series of studies that evaluated participation in genetic counseling and testing for inherited breast cancer risk among African-Americans, Halbert and colleagues[6,7] found that about 50% of women who had a personal and family history of cancer that was suggestive of hereditary disease participated in genetic counseling; however, only about one-fourth received BRCA1 or BRCA2 genetic test results. Similar results were obtained in recent research that evaluated participation in genetic testing among breast cancer survivors; when compared to white women, African-American women were significantly less likely to receive BRCA1/2 test results.[8] However, among African-American women, being recently diagnosed with cancer was associated with an increased likelihood of utilization.[8]

Substantial empirical data are lacking on the effects of risk counseling that includes an assessment of family history among ethnic and racial minority groups. In one study that evaluated the effects of individualized risk counseling among women who had a family history of breast cancer, African-American women appeared to benefit more from this approach compared to white women.[9]. However, results from a recent randomized trial with African-American women at increased risk for hereditary breast cancer suggest that genetic counseling that includes a pedigree or family history assessment is likely to have mixed effects on cancer work and perceived risk. Additional research is needed to evaluate the effects of applying family history information in clinical interactions with members of ethnic and racial minority groups.

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Research Challenges in Assessing the Economic Costs of Using Family History as a Screening Tool in Primary Care

Scott D. Ramsey, M.D., Ph.D.

Several expert groups now advocate family history screening (FHS) as an approach to identify persons at increased risk for disease, but the clinical and economic implications of programs to improve FHS have not been established. The economic implications of implementing populationwide family history assessment programs are likely to be substantial. Although the costs of assessing family history will be small at the individual level, the societal costs of assessing millions of individuals could potentially be very large. Implementing family history programs would greatly impact primary care physicians, specialists, and public and private healthcare payers. Moreover, the initial family history screen could result in a number of downstream interventions, with potentially high costs. Because the impact of FHS and FHS-based care on outcomes are at present uncertain, understanding the economic costs involved with FHS is an important endeavor. This presentation outlines the conceptual issues involved in economic evaluation of FHS, and some challenges to measuring its economic impact.

Traditionally, economic analysis of medical interventions is referred to as cost-effectiveness analysis (CEA). CEA studies are estimates of value for money spent on an intervention of interest. The most common metric is the incremental cost effectiveness ratio (ICER), expressed as a ratio of the difference in costs over the differences in outcomes between two treatments *A* and *B:*

$$ICER = \frac{Cost_A - Cost_B}{Outcome_A - Outcome_B}$$

When one measures costs—the numerator of the ICER equation—one is measuring the cost of the intervention and comparator group and all costs that stem from the intervention and comparator over the time horizon of interest. In the case of FHS for susceptibility to chronic diseases, the relevant time horizon is usually a lifetime. Costs are divided into two general components, (1) direct medical care costs and (2) direct nonmedical care costs. Direct medical care costs include the costs of tests, drugs, supplies, healthcare personnel, and medical facilities. Direct nonmedical costs are those consumed as a result of the intervention but are not medical costs *per se.* In the context of FHS, the clinician's evaluation of the family history is considered a direct healthcare cost, while the value of patient time spent in the office and the transportation costs associated with getting to the office are considered direct nonmedical costs. Several reference texts discuss methods to evaluate costs for CEA, and thus they will not be reviewed in detail here.[1,2]

Measuring costs directly associated with assessing a family history can be broken down into the value of the clinician's time and the value of the patient's time, plus transportation costs traveling to the clinic for evaluation. Clinician's time can be estimated as the proportion of an office visit used to assess family history multiplied by the value of that time. The amount of time needed can be estimated indirectly (e.g., asking clinicians how long they take for family history) or directly using time and motion studies. The value of that time is commonly estimated by relative value units (RVUs), a measure used by Medicare to determine payments for clinicians

for office visits and other services. Of note, if it is anticipated that the family history requires periodic updates over time, these costs should be included in the economic evaluation.

The other costs associated with FHS are medical interventions that stem from the family history assessment. Measuring these costs can be difficult depending on whether the FHS directly influences care or is part of an overall assessment of multiple risk factors that influence care. As an example of the former, evaluation of a 40-year-old man's family history for colorectal cancer could lead directly to a screening colonoscopy if it revealed that one or more first-degree relatives developed colon cancer at a young age. On the other hand, a family history of coronary artery disease may lead to an intervention (e.g., cholesterol-lowering drugs) only if other risk factors are present, such as high cholesterol and smoking. Thus, an important methodological challenge when evaluating the economic impact of FHS is identifying the interventions that occur as the result of an FHS evaluation.

To address the problem of identifying costs attributable to FHS, one can utilize expert panels or gather empirical data. Expert panels can be useful for identifying healthcare use stemming from "positive" and "negative" FHS evaluations, but one has to be careful to identify problems inherent when using experts, such as discounting or ignoring adverse impacts of the intervention or describing care that is not representative of usual clinical practice.

Perhaps most difficult in FHS is measuring the cost-effectiveness of assessing a particular aspect of the family history as part of a comprehensive evaluation. For example, several clinical practice guidelines recommend that persons meeting colorectal cancer family history criteria should begin colorectal screening at an earlier age than the general population.[3–6] It is desirable to evaluate the cost-effectiveness of FHS screening programs, which may include FHS and earlier intervention (e.g., screening colonoscopy) among those identified at increased risk. Assessment of a colorectal cancer family history, however, is usually done in the context of comprehensive FHS, which may identify other disease areas where the person has increased risk. Because FHS is a "joint product," should the positive and negative consequences of detecting risk for *other* diseases be counted when considering the cost-effectiveness of evaluating colorectal cancer family history? Economists have not yet determined how this issue should be resolved.

In conclusion, FHS screening warrants economic evaluation due to the large number of persons potentially affected; the total potential costs of screening programs, including the cost of the screening evaluation itself; and the downstream healthcare and nonhealthcare expenditures that may be incurred as a result of the screening program. While measuring the cost of screening is relatively straightforward, evaluating the resulting healthcare use that results from screening—particularly in the context of evaluating the cost-effectiveness of screening—can be challenging. More research, both on the conceptual aspects of FHS and empirical evaluations of the economic implications of screening programs, is needed.

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A Summary of the Use of Family History in Primary Care From Across the Pond(s)

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While the United Kingdom and Australia have not had the benefit of a national-policy-driven effort to promote the use of family history in primary care, there have been several studies in both countries that have examined how to encourage greater clinical application of family history. Broadly speaking, one can consider these in terms of interventions aimed at the level of the consumer or practitioner, the former based on the assumption that increased consumer demand for advice about their family history will drive primary care practitioners to alter their clinical behaviors.

Consumer awareness campaigns have been developed in both Western Australia[1] and New South Wales (NSW).[2] The NSW campaign included promoting use of a paper-based Family Health Record and a Start the Conversation campaign driven through a variety of different media. The results of a formal evaluation of the NSW campaign have recently been analyzed, which suggest small but important effects on discussions about family health history within the family and with their family practitioner.[3] Family practitioners were supportive of the campaign but emphasized the need to focus it on conditions for which there are clear preventive strategies available.

Family history remains a neglected part of medical history in British and Australian primary care. Three main factors are at play: time, tools, and technology. Average consultations in both countries in family practice last approximately 10 minutes and remain predominantly reactive rather than proactive. Although the Quality Outcomes Framework in England has created a much greater emphasis on proactive disease management and prevention, it has not recognized any role of the family history in tailored prevention. The fee-for-service model of Australian general practice, and a weaker culture of proactive disease prevention, limit the potential to spend time discussing family history in the context of symptomatic consultations. Adult health checks have recently been introduced in both countries for people in their 40s; these may provide opportunities to raise awareness and use of family history in preventing common chronic disease(s).

Given the time constraints family practitioners face, a variety of patient-centered family history questionnaires (FHQ) have been developed for use in primary care.[4] Several of these have been disease- or even cancer-site-specific; researchers from Nottingham and London have published an FHQ which was generic and attempted to obtain sufficient information to create a full pedigree.[5] Many of these tools have undergone only very limited assessment of their clinical validity. There are several important unanswered questions about FHQs: In the generalist setting of primary care, do we need generic or disease-specific FHQs for our patients to complete? Should we attempt to obtain sufficient information from an FHQ to build a pedigree covering all conditions, or should we focus only on those for which primary care practitioners can offer some form of “intervention”? Furthermore, should FHQs aim simply to collect family history data for assessment by a practitioner, or should they act as the initial screening tool, aiming to categorize risk? Currently, an FHQ designed as a screening tool for several common chronic diseases is being evaluated in a collaborative study in Cambridge and Western Australia to test its clinical validity prior to future trials of clinical utility.

An alternative approach to encouraging use of family history has been the development of electronic family history risk-assessment tools. A cluster randomized controlled trial in the United Kingdom of the GRAIDS software, aligned to a new service model of a lead clinician in each family practice, demonstrated improvements in risk assessment and referrals to cancer genetics clinics.[6] An Australian Family History Tool based on the GRAIDS software has been developed to cover a wider range of diseases. A major challenge, however, to wider application of this type of software is its integration into family-practice clinical software. The vast majority of British and Australian family practices use some form of electronic health record. Currently, none of the commercial providers of these electronic health records has been convinced of the business case for integrating, or developing their own, family history tool. Until this technological hurdle is breached, electronic family history tools are likely to remain of academic interest only.

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Family History and Healthcare: The Experience of the National Council of La Raza

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In what has frequently been called one of the most significant discoveries of our time, 56 years ago James Watson and Francis Crick identified the DNA double helix. The discovery of DNA has led to numerous advances in science and medicine, and in 1990, it led to the creation of the Human Genome Project. While all of the Human Genome Project goals have been accomplished, there is much to be done, including how to apply the knowledge we have generated to health education and disease prevention efforts.

The knowledge gained by sequencing the human genome should expand beyond the realm of scientific research and specialized treatment. It can and should be used to encourage behavior change and to maximize health benefits. For this to happen, all populations should have access to easily understandable genomics literature that assists them in identifying their own inherited risk factors and encourages them to engage in preventive behaviors. Unfortunately, this is not the case for many communities, particularly Hispanics.[1]

Latinos represent 15.4% of the total U.S. population (not including residents of Puerto Rico) and are the fastest growing population in the country. [1] Hispanics are also a young population. The median age of Latinos in the United States is 27.7 years versus 36.8 years for the population as a whole.[1] In fact, 25% of children under the age of 5 years and 22% of children under the age of 18 years are Latino.[1] The Latino population will continue to grow and is projected to reach 29% of the country's population by the year 2050.[2] The tremendous growth of the population necessitates a more proactive approach to address the health disparities the community faces. The field of genomics can be one tool to help do so.

Hispanics are disproportionately affected by many diseases, such as diabetes, certain cancers, and cardiovascular disease. Reasons for these disparities include language, education, and a lack of health insurance and bilingual healthcare providers.[3] Add to these reasons the lack of knowledge and awareness regarding inherited risk factors[4] and Latinos may be at greater risk for developing diseases with a genetic component. To address this, the National Council of La Raza (NCLR), in collaboration with the National Human Genome Research Institute at National Institutes of Health (NIH), tested the effectiveness of using a *promotores de salud* (lay health educators) model to increase the genetic literacy of Latinos using a family health history (FHH) approach.

[1] The terms "Hispanic" and "Latino" are used interchangeably by the U.S. Census Bureau and throughout this document to refer to persons of Mexican, Puerto Rican, Cuban, Central and South American, Dominican, Spanish, and other Hispanic descent; they may be of any race.

As part of the project, NCLR conducted formative research to determine the knowledge, attitudes, and behaviors of Latinos related to genetics and genomics and to develop materials and approaches to meet their information needs. A total of eight focus group discussions (FGDs) were held in collaboration with two community-based organizations (*La Clínica del Pueblo* in Washington, DC, and *La Clínica de la Raza* in Oakland, California). FGDs were held with community members and *promotores* (two of each group at each location).

Questions touched on the following topics: heritage and health; FHH; awareness of the Human Genome Project; understanding of genetics, genetic conditions, and genetic testing; seeking genetic-related information; rumor or misinformation about genetics; philosophical and religious perspectives; comfort level with the topic; barriers to learning about genetics; and hopes and fears for the future of the science.

Key findings included the following:

- There is a general lack of knowledge about genetics, genetic conditions, and genetic testing among community members. *Promotores* had a little more knowledge about the subject matter. Misinformation regarding genetics existed among participants. Many participants mentioned myths related to cloning and stem cell research.

- There is little access to credible, scientific, and culturally competent information on genetics. Both groups had a great interest in such information. Participants expressed concerns about accessing information because of literacy, fear, and stigma.

- Most participants trusted their physician and/or local clinic to provide them with information on a specific condition or on where to find help. Very few individuals mentioned the Internet as a mechanism to find information, although *promotores* mentioned it more frequently than community members.

- Conversations about FHH occur most often during funerals or when someone becomes ill.

- The Human Genome Project was unknown to FGD participants.

- Participants in all groups felt that using *promotores de salud* was an effective strategy to provide information on genetics to the Latino community.

Based on this information, NCLR developed a toolkit for *promotores* to use in their outreach. The toolkit included a flip chart, training manual, and the U.S. Surgeon General's *My Family Health Portrait. Promotores* were trained on the use of the materials and the implementation of *charlas* (community education sessions) by NCLR staff and experts in genetics. *Promotores* conducted eight *charlas* with 86 community members.

Evaluation results showed that community members found the information provided during the *charlas* useful, with 100% of participants stating that the topic was "Very Important" or "Important." Additionally, 95% of participants stated an intent to share the information they received with family and friends.

Given the positive evaluations of the *charlas,* NCLR and NIH decided to study the effectiveness of a *promotores*-led *charlas* intervention against that of a brochure-only intervention to raise awareness and knowledge about FHH. A total of 489 individuals participated in the study. Of those, 312 participated in the *promotores*-led *charlas* and 177 participated in the brochure-only intervention. While interventions were effective in increasing the participant's intent to speak to their families and doctors about FHH and their confidence (self-efficacy) in engaging in these discussions, the participants in the brochure-only intervention felt that they needed additional information to understand genetic diseases. The brochure-only group score on this item was significantly higher than the *charlas* group (p=<.01), indicating that brochure-only participants felt they needed more information to understand genetic diseases when compared to those participants who had received a *charla* from a *promotore*. The aforementioned study has several limitations. Specifically, as is common with community research, it was a convenience sample that led to preintervention differences between both groups. Additionally, the sample size might not have been large enough to detect statistical differences. Lastly, *promotores* reported that intervention participants did not feel comfortable reporting they were unfamiliar with a topic. Notwithstanding these limitations, it is clear that *promotores* have a role to play in increasing Latinos' genetic literacy using FHH and ultimately helping to improve health outcomes for the population.

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Health IT-Based Strategies for Studying the Use of Family History in Primary Care

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In the collection and analysis of family history, as in much of medicine, the Primary Care Provider (PCP) must obtain more information, record it in a usable format, and synthesize that information into actionable medical advice, all within a shorter period of time. In any other industry, this would be a problem crying out for computerized solutions. Simplified data entry by the clinician or patient, and Clinical Decision Support (CDS), are the future.[1] The question remains as to how fast we can get there and whether the current crop of current Electronic Health Records (EHRs) vendors will facilitate or impede that process. The problem is twofold. First, the PCP needs to obtain detailed family history information from the patient and enter that data in a machine-readable format. Second, the PCP must have a working knowledge of over 180 hereditary syndromes,[2] and be able to identify at-risk patients by using memory, guidelines, or algorithms. While most have touted education,[3] the more viable solution requires information technology (IT).

State of the Art in Data Collection and Entry

EHRs are collections of free text documents that describe independent events. There is no attempt to synthesize these disparate pieces of information into a coherent picture of the current state of the patient.[4] Most clinicians record family history as free text which is not machine-readable for pedigree drawing or CDS. Multiple notes contain multiple family histories collected independently by multiple clinicians. Some EHRs contain a structured family history. These data sets are not compliant with the American Health Information Community (AHIC) core data set, are not accessible to patients, are not accessible to clinicians outside the network, and lack useful CDS. Most family history sections do not include the patient.

Few clinicians find it either practical or worthwhile to enter structured family history into an EHR, as interfaces are cumbersome and time-consuming, and there is little return. Thus, structured family history data tables are usually left empty and the family history appears as free text within clinic notes. Personal Health Records (PHRs) and niche software packages have tried to address this gap.

Allowing patient data entry can help alleviate some of the time and cost of data entry, freeing the practitioner to review and analyze the information rather than transcribe it.[5] This problem has been addressed by several niche software applications that allow patient data entry via tablet PC,[6] kiosk,[7] PHRs, and Web site.[8] None have been adopted by existing EHRs.

Clinical Decision Support (CDS): State of the Art

The inclusion of visualizations, clinical guidelines, risk algorithms, and other knowledge into software tools that help clinicians make better decisions and provide better care is known as CDS. Current EHRs contain few CDS capabilities, and essentially none relating to family history. Guidelines exist for some of the more common hereditary syndromes, but many syndromes lack guidelines and many syndromes have multiple sets. The clinician must decide which guidelines to follow, and then must either commit those to memory or refer to a complex

document in the midst of a busy clinic. No current EHR can use the established guidelines to identify high-risk individuals.

Pedigrees are visualizations that help clinicians identify familial patterns.[9] No EHR has a pedigree drawing function. Clinicians can use niche pedigree software, but its use in the midst of a busy clinic is seldom feasible.

Algorithms can be used to determine the risk of having a mutation and/or the future risk of developing disease.[10] Most algorithms must be run by computer.[11] As no EHR can run accepted-risk algorithms, niche software packages have been created to fill the gap (such as CancerGene,[12] BRCAPRO,[13] and Hughes Risk Apps[5]).

Today, EHRs lack CDS and clinicians are left to use paper-based guidelines to draw pedigrees, to use niche software CDS systems external to the EHR, or to depend on their memory.

Solutions

IT is the solution. Every EHR and PHR should adopt the AHIC core data set and be capable of interacting with other family history applications for analysis and CDS.[14] Family history data should reside in a single area within the EHR and be able to use data regarding the patient.

Multiple approaches to entering the family history into EHRs and PHRs must be explored, including, but not limited to, patient data entry by Web site, tablet PC, and kiosk. New approaches to family history must be explored, such as the possibility of partnering with the genealogy community or linking the PHRs or EHRs of multiple family members. There is the potential of multiple family members sharing data via a family history wiki. Obviously, significant privacy issues need to be addressed. As multiple sources of family history are consolidated into a single record, there will be a need for new approaches to conflicting data. We need to develop CDS that consolidates a family history from multiple sources.

Interoperability is critical, most likely achieved by the adoption of the HL7 standard.[15]

Interfaces need to be developed that allow rapid data entry and editing by the clinician. The interface should be specific to the specialty of the viewing clinician. The family history should be able to be presented as a pedigree, perhaps highlighting diseases specific to that specialty, but other visualizations should be developed as well.

It is obvious that EHRs must be able to provide CDS by suggesting possible syndromes, displaying information in a manner that makes the next steps obvious to both the clinician and the patient, and helping to facilitate the next steps by generating orders, consultation requests, or requisitions for tests or other outputs that decrease workload.

CDS is dependent on the accuracy of the knowledge bases, and it is critical that someone takes responsibility for their creation and maintenance. Most likely a specialty society, the government, an academic medical center, or some combination thereof should take responsibility for the subset specific to their area of expertise. There is significant effort and cost required to undertake this maintenance, and a method to support this function must be developed. In addition, liability issues must be addressed. Updates must be incorporated into extant CDS systems, likely via a Web service approach, but this and other approaches must be explored.

Creative solutions are needed too. It is highly unlikely that over 150 EHR vendors today will each independently develop every possible CDS and data entry system that our clinicians need. For this reason, the best solution has been suggested by AHIC: "Where collection of family health history is performed within the EHR, followed by messaging of this information to a variety of richer family history tools that perform risk analyses…the enhanced family history and results of these algorithmic calculations could then be returned to the EHR…".[16] A modular approach that unlocks the creative potential of academics, entrepreneurs, and small niche vendors seems much more likely to succeed in the short-term future.

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Reconsidering the Use of Family History in Primary Care Revisited

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In our original 2004 paper we reviewed the role of the family history in predictive genetic testing, described how family history taking was currently practiced in adult primary care, identified some of the current barriers to using family history in the primary care setting, and noted some of the potential requirements for a new family history tool to augment its use by adult primary-care clinicians.[1] Much has occurred relevant to these issues in the intervening 5 years, [2–4] and, accordingly, a number of authoritative conferees are providing detailed insights on key developments in the value of predictive genetic testing, the accuracy of patient-reported family history, the development of family history tools, and other efforts to enhance generalist skills. This manuscript will focus on the ongoing barriers to obtaining and using a family history in U.S. primary-care practice, and the potential for policy reforms, practice transformation, and technology enhancement to alleviate these.

The recent policy debate over "personalized medicine" and "comparative effectiveness research" has highlighted the expectation that physicians should carefully weigh each patient's unique personal and genetic characteristics in applying evidence and offering recommendations at the bedside.[5–7] Recent research suggests that reality falls far short of this expectation, however; not only as it relates to using family history[8] but other aspects of personalized primary care. Indeed, several studies indicate that typical primary care physicians already have no time to deliver even basic recommended preventive services to their usual array of patients.[9,10] Not surprisingly, policy makers find the United States suffers from widespread underprovision of proven preventive services and inadequate care of the chronically ill.[11] In discovering there is no time for preventive care, the investigators considered only highly evidence-based and widely accepted guidelines and therefore did not address the potential for additional demands made by future targeted genetic testing in prevention and pharmacogenomics, much less the prospect of personalized interpretation of whole gene scans.[12–14]

Our previous analysis documented the inadequacy of U.S. fee-for-service payments to support the time needed to obtain, review, and interpret a comprehensive family history in primary care.[8] Several authorities have noted more fundamental flaws in the Medicare fees for primary care,[15,16] resulting in the aforementioned impossible demands on primary care physicians, the challenges to an economically viable practice, collapse of U.S. medical student interest in primary care careers,[17] and dissatisfaction of many in these specialties. However, rising healthcare costs and unsustainable increases in Medicare expenditures for physician services[18,19] may render untenable increased fee payments as the long-term solution to poor family history taking, or other underutilized primary care services. Indeed, policy analysts argue that many elements of high-quality primary care (e.g., comprehensiveness, coordination, accountability) are not easily rewarded through payment for office encounters.[19–21] The problems in primary care may now be so severe that greater evidence on the value of the family history, or even family history tools and electronic reminders, will be insufficient to overcome the other challenges to the U.S. primary care infrastructure. To achieve wise development and use of family history in personalized primary care, it is likely that both new technologies and new practice models will be required.

In view of the current shortage of primary care physicians and their present time constraints, proposals for U.S. primary care reform involve both enhanced use of technology and better use of relevant expertise in interdisciplinary teams, often referred to as the "patient-centered medical home."[22,23] In this reform model, practices could earn additional per-patient payments by developing specific new primary care infrastructure (e.g., health information technology, informed decision-making tools, patient educators, etc.) and would be further rewarded by adherence to evidence-based standards as well as delivery of patient-centered (i.e., personalized) care. Clearly, such payment reforms, once implemented, could provide a powerful mechanism to promote the optimal mix of physician skills, practice infrastructure, and interdisciplinary arrangements to efficiently and effectively use family history and predictive genetic testing in primary medical care.

To do so, however, will require timely answers to some key research questions. The following are but a few examples: What healthcare indicator tool (HIT), family history, and other tools are best for supporting genomic and personalized medicine in primary care, and what are the most effective policies to promote their adoption? What is the optimal mix of knowledge and skills across the primary care interdisciplinary team to efficiently deliver the advances of genetic medicine in the medical home and what then is the most effective role of specialized genetics expertise in the "medical neighborhood"?[24] What are the evidence-based standards for use of family history and predictive genetic testing in primary care, and what are the best ways to measure adherence in routine practice?

Updating our conclusions from 2004 "The patient's family history remains a critical element in risk assessment for many conditions, but substantive barriers impede application in primary care practice…," new tools and new payment policies will be required to develop and support the right multidisciplinary primary care team in the efficient and effective application of patient family history in the era of personalized medicine.

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