2007 Program Review

National Office of Public Health Genomics
Centers for Disease Control and Prevention

Table of Contents

1.0 National Office of Public Health Genomics

Public health genomics is a multidisciplinary field concerned with the effective and responsible translation of genome-based knowledge and technologies to improve population health. Public health genomics uses population-based data on genetic variation and gene-environment interactions to develop evidence-based tools for improving health and preventing disease.

Through the National Office of Public Health Genomics (NOPHG), the Centers for Disease Control and Prevention (CDC) provides national and international leadership in public heath genomics, while building partnerships with other federal agencies, state health departments, public health organizations, professional groups, and the private sector.

1.1 Vision, Mission, and Goals

The vision, mission, and goals of NOPHG have evolved over time in response to ongoing input from internal and external CDC partners; lessons learned from NOPHG initiatives; priorities of CDC agency-wide initiatives, including the Goals Process and the Futures Initiative; and the changing identity and location of the office within CDC's organizational structure. The central tenet upon which NOPHG's vision, mission, and goals is based is the role of public health in translating human genome discoveries into population health benefits.

Although fundamental to many CDC programs, legislation has not been the primary influence in directing specific NOPHG activities. Instead, priorities are continually shaped by NOPHG leadership, input from internal and external CDC partners, the roles of other government agencies and the private sector, availability of funding, and the state of the science. NOPHG's research and program portfolios are dedicated to closing the gap between genome discoveries and public health impact.

Vision:
To use genomic knowledge to improve the lives and health of all people.

Mission:
To integrate genomics into public health research, policy, and programs.

Goals:
To improve public health interventions of diseases of major public health importance, including chronic, infectious, environmental, and occupational diseases, through population-based genomic research, assessment of the role of family history in determining risk and preventing disease, and the evaluation of genetic tests.

1.2 Major Initiatives

Evaluation of Genomics Applications for Practice and Prevention
The Evaluation of Genomic Applications in Practice and Prevention (EGAPP) initiative was launched by NOPHG to establish and test a systematic, evidence-based process for evaluating genetic tests and other applications of genomic technology that are in transition from research to clinical and public health practice.

Family History Public Health Initiative
NOPHG started the Family History Public Health Initiative in 2002 to increase awareness of family history as an important risk factor for common chronic diseases such as cancer and diabetes, and to promote its use in programs aimed at reducing the burden of these diseases in the U.S. population.

Human Genome Epidemiology Network
NOPHG established the Human Genome Epidemiology Network (HuGENet™) in 1998 to help translate genetic research findings into opportunities for preventive medicine and public health by advancing the synthesis, interpretation, and dissemination of population-based data on human genetic variation in health and disease.

NHANESIII Collaborative Genomics Project
In 2002, NOPHG formed a multidisciplinary working group with members from across CDC to develop a proposal to measure the prevalence of selected genetic variants of public health significance in a representative sample of the U.S. population and to examine the associations between the selected genetic variants and disease outcomes available in NHANES III data.

Public Health Genomics Capacity Building
Since 2005, NOPHG has funded Centers for Genomics and Public Health within schools of public health at the Universities of Michigan and Washington to provide expertise in translating genomic information into useable public health knowledge, to provide technical assistance to state and community public health agencies, and to integrate genomics into programs and practice.

Since 2003, NOPHG has supported genomics programs in four state health departments (Michigan, Minnesota, Oregon, and Utah) to integrate genomics knowledge (e.g., genetic risk factors) and tools (e.g., family history assessments) into chronic disease prevention programs and core public health functions.

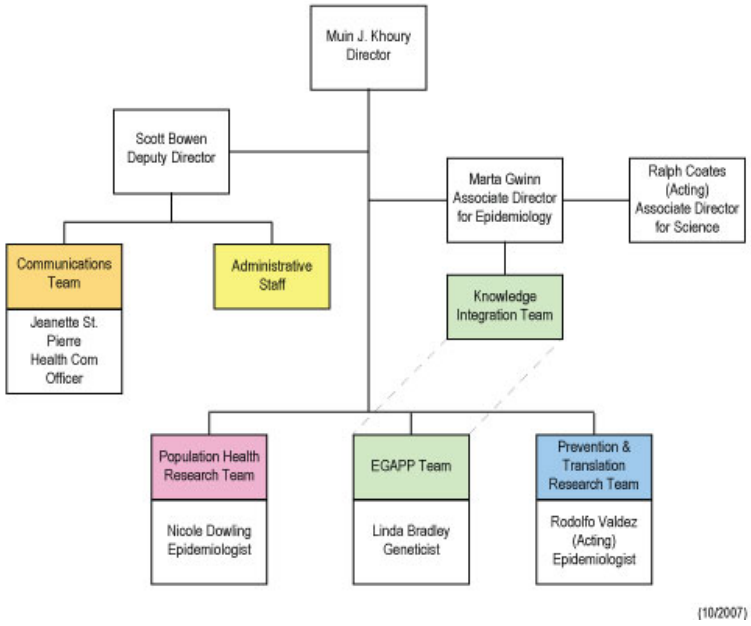
Public Health Investigations
NOPHG and the National Center for Influenza and Respiratory Diseases developed the Influenza Public Health Genomics Initiative in 2006 to investigate the role of population genetic variation in the epidemiology of influenza morbidity and mortality and the effectiveness of public health interventions.

In 2006, NOPHG provided seed funding for 11 innovative CDC projects, focusing on infectious disease, chronic disease, birth defects, pharmacogenomics, and environmental exposures, to integrate genomics into their research and programs. Nine of these initiatives were funded in 2007, for a second year, with anticipated completion date of April 2008.

2.0 Organization and Staffing

Dr. Muin J. Khoury, NOPHG director, and Scott Bowen, deputy director, provide strategic leadership for NOPHG with support and input from the associate director for epidemiology, Dr. Marta Gwinn, and the associate director for science, Dr. Ralph Coates, and the other senior staff. Day-to-day operations are supported by management and operations staff.

NOPHG has dedicated teams to support its major projects and communication functions. These teams include: the Knowledge Integration Team; the Population Health Research Team; the EGAPP Team; the Prevention and Translation Research Team; and the Communications Team. Each team has a designated lead staff member and support staff. The organizational structure, depicted in the figure below, includes personnel who possess a wide array of professional disciplines and skills. Currently, NOPHG supports a total of 45 staff, including 18 federal full-time employees (and four vacancies).



3.0 Strategic Accomplishments in FY2007

Advances in genomics have led to mounting expectations for the translation of genomic research into applications for health care and disease prevention. A comprehensive agenda for translation research and surveillance is needed to move human genome discoveries into health practice in a way that maximizes health benefits and minimizes harm to individuals and populations. Currently, hundreds of thousands of genetic variants are being evaluated for association with common, chronic diseases. Research is accelerating the use of new biomarkers derived from gene expression, proteomic, and other “omic” technologies. The number of genetic tests used in clinical practice and research is increasing. In addition, family medical history is receiving renewed attention as a genomic and public health tool for disease detection and prevention.

3.1 External Peer Review

In the past decade, NOPHG has established public health genomics as an interdisciplinary field and developed strong collaborations to begin closing the gap between gene discoveries and population health benefits. To obtain scientific review and assessment of NOPHG research and public health initiatives, NOPHG held an external peer review panel in August 2007. Public health experts Deborah Klein Walker, EdD, Norman Kahn, MD, Joann Boughman, PhD, Charles Rotimi, PhD, and Alan Guttmacher, MD participated in the review panel. NOPHG presented an overview of CDC's work in public health genomics during the last 10 years, summaries of the current major NOPHG initiatives, and NOPHG's vision for the next decade. Directors and management staff from CDC's Coordinating Center for Health Promotion, the National Center for Chronic Disease Prevention and Health Promotion, and other CDC centers participated in this event.

The external peer review panel developed the following program recommendations to strengthen NOPHG's strategy, goals, and initiatives:

- Focus on activities that help move genomics from research to practice.
- Continue and expand the current seed grant program.
- Expand the family history project by adding a translational research dimension.
- Undertake a specific proof-of-principle study to illustrate the value of genomic-based education among providers and patients.
- Investigate ways to incorporate translational research initiatives into existing practice-based research networks.
- Continue the Evaluation of Genomics Applications in Practice and Prevention (EGAPP) initiative to ensure appropriate evaluation of newly available genetic tests.
- Sustain the HuGENet project.
- Partner with existing provider groups and end-users of genomic data to determine the utility of specific types of genomic data and activities.
- Continue work on the Beyond Gene Discovery initiative using NHANES III data.
- Focus on communicating CDC's unique role in the field of genomics.
- Develop logic models to help elucidate program effectiveness over time.
- Expand efforts to educate other CDC units about the field of genomics.
- Continue leadership in infusing genomics into public health practice at the state and local levels.
- Reposition NOPHG within existing organizational structure of CDC.
- Continue to collaborate on international genomics initiatives.

NOPHG is making strides to ensure that these recommendations are incorporated into its current strategic plan, focusing on genomics initiatives that are most critical for public health and clinical practice, and developing new ways to increase investment in public health genomics at CDC.

3.2 Strategic Plan for Translation Research

In 2007, NOPHG continued to develop its portfolio for translation research and surveillance activities to advance knowledge about the validity, utility, utilization and population health impact of genomic applications and family history for improving health and preventing disease in well-defined populations or practice settings. The objective is to address key questions along the translation continuum, from 1) the initial development and evaluation of candidate genomic applications, to 2) thorough evaluation of the genomic applications and development of evidence-based clinical practice guidelines for the use those applications, to 3) the dissemination and implementation of recommended applications in clinical and public health practice, to 4) the evaluation of the extent and fidelity with which recommended applications are implemented in community settings and the effect of implementation on population health.

4.0 Scientific Highlights in FY2007

This section provides a summary of NOPHG's major scientific highlights in FY2007. References to scientific publications by NOPHG are provided.

4.1 Evaluation of Genomic Applications in Practice and Prevention (EGAPP)

EGAPP activities are focused around the independent, non-federal EGAPP Working Group established in May 2005. The roles of this multidisciplinary panel include optimization of methods and processes for evidence review to deal with complex and rapidly emerging technologies; identification, prioritization and selection of topics; participation on technical expert panels that guide conduct of evidence reports; and development of recommendation statements for clinicians based on the evidence.

In FY2007, four CDC-funded evidence reports were completed for the EGAPP Working Group by Evidence-Based Practice Centers (EPCs), through an interagency agreement with the Agency for Healthcare Research and Quality (AHRQ):

- *Genomic Tests for Ovarian Cancer Detection and Management* (www.ahrq.gov/clinic/tp/genovctp.htm)
- *Testing for Cytochrome P450 (CYP450) Polymorphisms in Adults With Non-Psychotic Depression Treated With Selective Serotonin Reuptake Inhibitors (SSRIs)* (www.ahrq.gov/clinic/tp/cyp450tp.htm)
- *Hereditary Nonpolyposis Colorectal Cancer: Diagnostic Strategies and Their Implications* (http://www.ahrq.gov/clinic/tp/hnpcctp.htm)
- *Impact of Gene Expression Profiling Tests on Breast Cancer Outcomes* (pending release by AHRQ)

Another non-EPC report, *Can UGT1A1 Genotyping Reduce Morbidity and Mortality in Patients with Metastatic Colorectal Cancer Treated with Irinotecan?,* and a supplemental report, *DNA Testing Strategies Aimed at Reducing Morbidity and Mortality from Lynch Syndrome*, will be released in early 2008.

Based on consideration of the availability and quality of evidence and clinical and social contextual issues, the Working Group develops recommendation statements that summarize current knowledge, provides guidance on appropriate use, and defines key gaps and needed research. In FY2007, the first in a series of EGAPP Working Group recommendation statements, on CYP450 testing in patients with depression treated with SSRIs, was accepted for publication in *Genetics in Medicine* (December 2007 issue).

Other EGAPP accomplishments for FY2007 include the establishment, with NOPHG support, of the EGAPP Stakeholders Group, and the independent website (www.egappreviews.org), which hosts products of the EGAPP Working Group.

4.2 Family History Public Health Initiative

Family History Analyses

To assess the risk of common chronic diseases and conditions in the U.S. population attributable to family health history, NOPHG analyzed data collected through the National Health and Nutrition Examination Survey (NHANES). NOPHG stratified the U.S. population in three levels of familial risk (average, moderate, and high) and examined the association between risk and the prevalence of specific diseases.

NOPHG found that several studies indicate that the risk for type 2 diabetes or cardiovascular disease is detectable in childhood, although these disorders may not emerge until adulthood. A simple way to detect risk for either diabetes or cardiovascular disease is to examine the family history. Numerous studies have shown that adults who have one or more first- or second-degree relatives affected with diabetes or cardiovascular disease are at high risk of having or developing these diseases. Although there are currently no overall screening strategies recommended for either disease among children or adolescents, family history should become part of prevention campaigns aimed at reducing the burden of these diseases and their risk factors in children.

NOPHG found that family history of diabetes has a significant, independent, and graded association with the prevalence of diabetes in the U.S. population. Independently of sex, race/ethnicity, age, BMI, hypertension, income, and education, people in the moderate and high familial risk categories for diabetes were 2.3 and 5.5 times more likely to have diabetes, respectively, than people in the average risk category.

In another study of the U.S. population, NOPHG found that a positive family history of osteoporosis was present in 19.8% of women aged 20 years or older. Women aged 35 years or older with a positive family history of osteoporosis were 2.3 times more likely to have the disease. The association grew stronger (to 8.4 times) when two or more close relatives affected with osteoporosis had a family history of the disease.

Publications:

Valdez R, Greenlund KJ, Khoury MJ, Yoon PW. Is family history a useful tool for detecting children at risk for diabetes and cardiovascular diseases? A public health perspective. *Pediatrics* 2007;120 Suppl 2:78-86.

Valdez R, Yoon P, Liu K, Khoury MJ. Family history and prevalence of diabetes in the U.S. population: The 6-year results from the National Health and Nutrition Examination Survey (1999-2004). *Diabetes Care* 2007;30:2517-2522.

Manuscript in clearance:

Robitaille J, Yoon PW, Irizarry-Delacruz M, Liu T, Moore CA, Looker AC, Khoury MJ. Prevalence, Family History, and Prevention of Reported Osteoporosis in U.S. Women.

Family Healthware™

In October 2007, three NOPHG-sponsored research centers at the University of Michigan School of Medicine, Evanston Northwestern Healthcare Research Institute, and Case Western Reserve University School of Medicine completed data collection for an evaluation study of the Family Healthware™ tool. This web-based tool provides users with a familial risk assessment for six chronic conditions (breast, colorectal, and ovarian cancer, coronary heart disease, diabetes, and stroke) and a "prevention plan" containing personalized recommendations for lifestyle changes and screening recommendations. Researchers of the Family Healthware™ study are currently developing manuscripts on the study methodology and health risk perceptions of family history and chronic diseases. NOPHG is currently collaborating with NIH to test Family Healthware™ in a longitudinal clinical trial as part of a new effort to combine Family Healthware™ with the U.S. Surgeon General's tool "My Family Health Portrait."

4.3 Human Genome Epidemiology Network (HuGENet™)

HuGENet™ Collaboration

HuGENet™ has continued to grow as an open collaboration of individuals and organizations from around the world. In FY2007, a HuGENet™ Short Course was offered in the United Kingdom and a HuGENet™ Workshop on the Assessment of Cumulative Evidence on Genetic Associations was held in Italy.

HuGE Publications

HuGENet™ has a leadership role in promoting study approaches and methods that lead to synthesis and translation of population-based genomic research data. In FY2007, HuGENet™ collaborators published 14 articles on these topics in scientific journals, including the *American Journal of Epidemiology,* the *International Journal of Epidemiology,* and *PLoS Medicine.*

Publications:

Ioannidis JPA, Boffetta P, Little J, O'Brien TR, Uitterlinden AG, Vineis P, et al. Assessment of Cumulative Evidence on Genetic Associations: Interim Guidelines. *Int J Epidemiol* 2007;Sep 26 [Epub ahead of print].

Yu W, Yesupriya A, Wulf A, Qu J, Khoury MJ, and Gwinn M. An open source infrastructure for managing knowledge and finding potential collaborators in a

domain-specific subset of PubMed, with an example from human genome epidemiology*. BMC Bioinformatics* 2007;8:436.

HuGE Reviews

HuGE Reviews are systematic, peer-reviewed assessments of gene-disease association studies conducted by health researchers affiliated with the Human Genome Epidemiology Network (HuGENet™). HuGE Reviews typically point to gaps in existing epidemiologic and clinical knowledge, thus stimulating further research in these areas. These reviews are published in partnership with 10 scientific journals. In FY2007, 11 HuGE Reviews were published by authors affiliated with institutions in the U.S. and five other countries, reflecting the global reach of HuGENet™. Through special agreements with the journals, HuGE reviews are available free of charge on the HuGENet™ web pages of NOPHG's website (www.cdc.gov/genomics/hugenet/reviews).

HuGE Navigator

In September 2007, NOPHG launched the HuGE Navigator, which is an up-to-date online knowledge base on human genome epidemiology, including information on the population prevalence of genetic variants, gene-disease associations, gene-gene and gene-environment interactions, and the evaluation of genetic tests. HuGE Navigator is intended primarily for researchers in public health genomics and other related disciplines and includes the following applications:

- *HuGE Literature Finder*, a database curated by NOPHG that includes abstracts from approximately 30,000 published articles on human genome epidemiology, extracted from PubMed. These articles reference about 3,000 genes and 3,500 diseases and conditions.
- *HuGE Investigator Browser*, which allows users to identify investigators in a particular field of human genome epidemiology.
- *GeneSelectAssist*, a search engine for finding possible candidate genes based on the NCBI Entrez Gene, PubMed and HuGE Pub Lit databases.
- *HuGE Risk Translator*, a tool for calculating the expected predictive value of genetic markers.
- *HuGE Watch*, a tool for tracking the evolution of published literature in human genome epidemiology.
- *HuGEpedia,* an online encyclopedia of human genetic variation and health information that is currently in development.

HuGE Navigator can be accessed at (www.hugenavigator.net/).

Publication:

Yu W, Yesupriya A, Wulf A, Qu J, Gwinn M, Khoury MJ. An automatic method to generate domain-specific investigator networks using PubMed abstracts. *BMC Med Inform Decis Mak* 2007; 20:7:17.

4.4 NHANES III Collaborative Genomics Project

Determination of the prevalence of genetic polymorphisms of public health importance in the U.S. population, and in subgroups of the population, is a critical first step in evaluating the genetic epidemiology of complex diseases. Such data would be an invaluable resource for: 1) investigations into U.S. population structure; 2) calculations of population attributable fraction(s) of the U.S. burden of disease associated with genetic variation and gene-environment interaction; and 3) assessment of the potential for screening population subgroups for genes that confer susceptibility to disease. In addition, population-based allele and genotype prevalence data would also serve as a reference for researchers to use in designing future association studies.

Genotyping of Gene Variants of Public Health Importance

In FY2007, NCI and CDC laboratories completed the genotyping of 90 variants in 50 genes, and successfully deposited the results at the National Center for Health Statistics (NCHS). Statistical analysis for each of the approximately 35 genotype-phenotype correlation studies is in progress at NCHS.

CDC/NCI NHANES Working Group

The CDC/NCI Working Group has written the first manuscript entitled “Prevalence in the United States of Variants in Genes of Public Health Importance: Third National Health and Nutrition Examination Survey (NHANES III), 1991-1994.” NOPHG statisticians and analysts are also preparing a second manuscript describing the statistical methods that have been developed for use in complex surveys including genetic data. The CDC/NCI Working Group are reviewing their preliminary data analyses and finalizing their analytic plans for genotype-phenotype association analyses of the NCHS genotype-phenotype correlation studies.

Manuscript in clearance:

Chang M, Lindegren ML, Butler MA, Chanock SJ, Dowling NF, Gallagher M, Moonesinghe R, Moore CA, Ned RM, Reichler M, Sanders CL, Welch R, Yesupriya A, and Khoury MJ. Prevalence in the United States of Variants in Genes of Public Health Importance: Third National Health and Nutrition Examination Survey (NHANES III), 1991-1994.

Beyond Gene Discovery (BGD) Working Group

In FY2007, NOPHG established a Beyond Gene Discovery (BGD) Working Group, with representation from all centers at CDC, which will use a whole-genome approach (approximately one million SNPs and copy number variants) to assess the prevalence of genetic polymorphisms in the NHANES III DNA Bank. Completion of this project will enhance the value of many ongoing gene discovery studies, helping to translate their findings into new targets for prevention, diagnosis, and treatment of common diseases, and will provide the basis for estimating the number of people who may benefit from particular genotype-based screening or diagnostic tests, drugs, or other preventive or therapeutic interventions.

4.5 Other NOPHG Scientific Highlights

National Surveys of Direct-To-Consumer Nutrigenomic Tests

In 2006, NOPHG utilized two national surveys—HealthStyles and DocStyles—to assess U.S. consumer awareness and use of direct-to-consumer (DTC) nutrigenomic tests (HealthStyles), and to assess knowledge of and experiences with these tests among U.S. physicians (DocStyles). NOPHG found that 14% of consumers were aware of nutrigenomic tests, and 0.6% reported using them. 44% of physicians were aware of these tests, and of those, 41% had never had a patient ask about such tests, and 74% had never discussed the results of a nutrigenomic test with a patient.

Until now, no national baseline information has been available regarding public awareness, interest in, or use of DTC nutrigenomic tests. Likewise, information is scarce regarding health care providers' knowledge, attitudes, and experiences with DTC nutrigenomic tests. This information provides insight into the public demand for such tests and the potential for harm and, as additional information is collected over time, will provide a historical reference of trends in awareness and use. In addition, baseline information can be tracked longitudinally to assess the impact of policies, efforts at public and provider education, and the evolution of the availability and demand for such test.

Publication:

Goddard KAB, Moore C, Ottman D, Szegda KL, Bradley L, Khoury MJ. Awareness and use of direct-to-consumer nutrigenomic tests, United States, 2006. *Genet Med*. 2007 Aug;9(8):510-7.

Public Health Genomics Seminar Series

During FY2007, NOPHG organized a public health genomics seminar series, "Public Health Genomics: Closing the Gap Between Human Genome Discoveries and Population Health," in partnership with the National Cancer Institute, the National Human Genome Research Institute, the National Institute for Child Health and Development, and the Office of Behavioral and Social Sciences Research. The goal of this seminar series is to educate health researchers and practitioners in public health genomics. The series explores various topics at the intersection of genetics, medicine, and public health, and the contributions of the multidisciplinary field of public health genomics to the translation of gene discoveries into population health benefits.

From January to October 2007, eight seminars were conducted on these topics:

- What is public health genomics and why should we care? An overview of the series
- How do we assess the contribution of complex genotypes and gene-environment interaction to the population burden of common diseases?
- What is the role of behavioral and social sciences in translating genetic research into population health benefits?
- Knowledge integration in public health genomics: evaluation of the epidemiologic evidence

- Knowledge integration in public health genomics: evaluation of genetic and genomic tests
- But how do we translate new genetic knowledge into practice?
- How do we actually translate guidelines into action?
- How do we monitor the impact of genomics on population health?
- Can we use family history as a tool for disease prevention and public health?
- Can Genomics help heal the schism between medicine and public health?

The last seminar is planned for November 29th, 2007, and will focus on "Genomics and the schism between basic sciences, medicine and public health."

This seminar series is conducted at NIH and broadcast live at CDC. Videocasts and slides of the presentations and selected articles are available as a resource on NOPHG's website: (www.cdc.gov/genomics/events/special1.htm)

Influenza Public Health Genomics Workshop

In January 2007, NOPHG and National Center for Immunization and Respiratory Diseases held a workshop to discuss opportunities for public health research on the role of human genomics in influenza disease and vaccine response. More than 100 participants from diverse fields—including immunology, virology, epidemiology, medicine and public health—working in government, academia, and private-sector research organizations attended the workshop. The workshop concluded by proposing priorities for genomics research on determinants of influenza disease severity and vaccine response and side effects.

5.0 NOPHG-Funded State Achievements in FY2007

The following are examples of achievements in FY2007 of the state genomics programs in Michigan and Minnesota.

5.1 Michigan Department of Community Health

Public Health Issue

Sudden cardiac death (SCD) is defined as an unexpected sudden death due to a cardiac cause and occurring within one hour of the onset of symptoms in an individual who had been in his/her usual state of health, without any known life-threatening condition. SCD can be especially devastating when it occurs in children, youth, or young adults in the prime of life who were previously thought to have been in good health. The Michigan Department of Community Health (MDCH) Genomics Program has identified sudden cardiac or unexplained death of the young (under age 30) as a potentially preventable condition, due to the heritable nature of certain cardiac disorders. Specific causes of SCD in younger adults and children are more likely to have genetic determinants than similar conditions in older persons. These include etiologies such as inherited arrhythmias, hypertrophic cardiomyopathy, undetected congenital heart defects, and early atherosclerotic heart disease.

Program Example

In an effort to learn more about the burden of SCD of the young in Michigan, the MDCH Genomics Program, in collaboration with MDCH Cardiovascular Health

Section and Michigan State University, initiated a pilot mortality review system in early summer 2007. The goal of this project is to reduce the burden of SCD of the young in Michigan by identifying health care system changes and family-based interventions for increasing awareness and prevention among individuals at increased risk. The mortality review system utilizes multiple avenues to gather information; mortality data are obtained from MDCH Division for Vital Records and Health Statistics. The SCD case definition includes decedents who were Michigan residents, aged 1-29 years, who died outside of the hospital or in an emergency department, and had specific cardiac or ill-defined causes of death recorded as the underlying cause of death on their death certificate.

For select cases who died between October 2006 and March 2007, medical records for the day of death and for the year prior to death were requested from providers and health care facilities. Selected decedents' next-of-kin were contacted and asked to participate in an interview regarding the events surrounding the death. Four anonymized case summaries were prepared and an advisory panel of 13 members, with varied genetics, cardiac, and medical expertise, was convened in October 2007 to review the cases and provide feedback on the etiologic nature of the deaths, implications for family members, and the mortality review process.

Implications and Impact

In 2006, a total of 83 deaths met the SCD case definition, translating to an estimated mortality rate of 2.1 per 100,000 for individuals 1-29 years of age. Black men were disproportionately affected. Almost one-third of the total cases died of cardiomyopathy. About half of the total cases died in an emergency department, while the other half died elsewhere. The SCD advisory panel found several implications for immediate family members of three out of the four cases that were reviewed during the panel meeting. Recommendations made by the advisory panel will be used to modify the case definition, improve the review process, and guide ongoing efforts to develop evidence-based public health recommendations for preventing SCD of the young in Michigan. This project is expected to increase knowledge of factors that contribute to SCD and feasibility of using mortality data to identify family, public, and provider needs regarding SCD.

Public Health Issue

In 2006-2007, the MDCH Genomics Program partnered for the first time with the MDCH Division of Environmental Health to integrate genomics and family history principles into a project called Health Homes University (HHU). This projects aims to positively affect the knowledge, attitudes, and behaviors of families to reduce asthma triggers and potential injury sources within their homes, to reduce emergency-care events related to asthma and injury, and to reduce school absenteeism. To date, more than 200 families have enrolled in the program. Family history is an important known risk factor for asthma. A family history of asthma has also been associated with asthma severity.

Program Example

The MDCH Genomics Program integrated questions into the HHU baseline survey and interviews given to families participating in the project, which inquired about the

number of family members in the household and those who had asthma, severity of asthma, and knowledge of asthma triggers. Family history information from 162 families showed that 65% of probands (affected child) had at least one first-degree relative who had ever been diagnosed with asthma. When expanded to include second-degree relatives, this number rose to 77%.

The results from the baseline interview showed a significant trend of an increasing number of affected first-degree relatives associated with increasing days reported with asthma symptoms (e.g., shortness of breath, wheezing). Children with one or more first-degree relatives ever diagnosed with asthma had more days with symptoms on average than children without a first-degree family history.

Implications and Impact

By identifying households with multiple family members with asthma and educating these family members about asthma triggers in the home, the number of persons with asthma and/or the frequency and severity of asthma are expected to decline in these households.

5.2 Minnesota Department of Health

Public Health Issue

The integration of genomics into public health requires an educated and skilled workforce capable of interpreting and applying relevant genomic and family history information to research and practice settings and policy development.

Program Example

The Minnesota genomics program collaborated with the University of Minnesota's School of Public Health to organize three new courses and a roundtable session on public health genomics as part of the 6th annual Summer Public Health Institute from May 21 to June 8, 2007. Courses on "Genomics in Public Health," and "Application of Genomics to Public Health Part 1, and Part 2" provided an overview of basic human genetics and genomics, and a survey of the opportunities and challenges for using these disciplines in public health research and practice. The roundtable session focused on "Genes and the Environment: The Emerging Role of Genomics in Public Health." Muin Khoury, MD, PhD, director of the National Office of Public Health Genomics at the Centers for Disease Control presented on gene-environment interactions and the emerging role of genomics in public health during this session. More information about the Summer Public Health Institute is available at http://cpheo.sph.umn.edu/cpheo/institute/home.html, and more information about the roundtable session is available at: http://www.sph.umn.edu/cpheo/events/roundtable/Roundtable_060807.html.

Implications and Impact

The Public Health Institute courses were nationally advertised and over 300 participants attended from 28 states and five countries. Total enrollment for the genomics courses was 27, and included participants from Illinois, Michigan, Minnesota, North Dakota and Oregon. An additional 100 public health practitioners, health care providers, faculty, students, and other professionals attended the roundtable and there were over 325 "hits" recorded on the roundtable website. Participant evaluations of the courses and roundtable were overwhelmingly positive.

6.0 Future Directions

Our vision for public health genomics at CDC in the next decade is to accelerate the evaluation and appropriate integration of new genomic knowledge into CDC goals and actions. During the past two years, CDC has developed new goals for achieving greater health impact in the U.S. These goals are framed in the context of life stages, places, preparedness, and global health. Progress toward this vision will be accomplished in two overlapping phases over the next 10 years:

Phase I: During the next five years, NOPHG plans to accelerate research and development of new information and tools for use by the public and the health care community. Specific approaches and products will include a human genome profile of the U.S. population, family history tools, genetic test evaluations, and dissemination of translational materials to the public and providers. CDC will fund intramural and extramural research on genomics and population health.

Phase II: During the following five years, NOPHG envisions a phased approach for integrating genomic information into public health programs that promotes health and prevents disease. When evidence-based recommendations are developed, NOPHG will work with CDC programs to integrate them into guidance and programs conducted by CDC and its partners in the public health and clinical communities.

NOPHG will spearhead an ongoing assessment of CDC's public health genomics capacity (laboratory, informatics, training, etc). With additional resources, we will try to fill gaps in infrastructure in order to meet the challenge of public health genomics in the next decade.

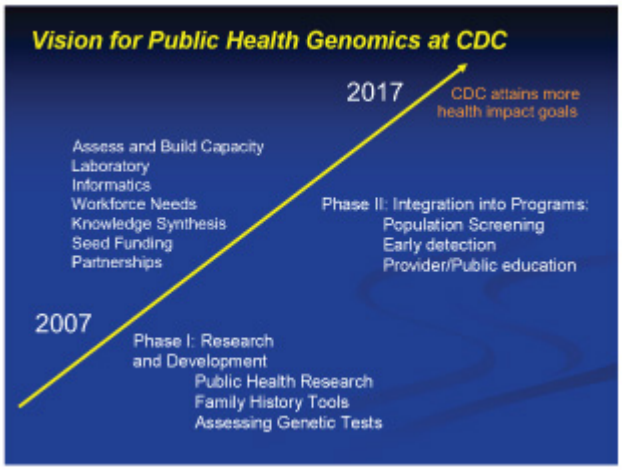
Expansion of Collaborative NOPHG Initiatives

The next 10 years of public health genomics at CDC will focus on:

- Accelerating the process of translation to close the widening gap between basic research and application,
- Synthesizing and integrating knowledge for better decision making,
- Engaging, educating, and empowering consumers and providers,
- Expanding and leveraging partnerships to enhance the integration of genomics across all areas of health and health care, and
- Expanding international collaborations in public health genomics.

The following section describes proposed NOPHG collaborative initiatives for the next 10 years that build on the success and achievements of ongoing initiatives. The diagram below shows how these initiatives are designed to begin to close the gap between gene discoveries and population health.

Beyond Gene Discovery (BGD)



With the completion of the Human Genome Project and the emerging availability of genomic technologies to measure human genetic variation, CDC and the CDC Foundation are launching a new initiative, BGD. In collaboration with public, private, and academic partners, the initiative will assess population genetic variation in the U.S. in relation to health and disease and develop strategies for using genetic information to impact health and eliminate disparities among population groups. NHANES provides a unique national resource for investigating the effects of genetic variation on health and will serve as the initial focus of BGD. Genetic samples are available for nationally representative probability samples of approximately 15,000 persons enrolled in two NHANES (about 7,000 participants in NHANES III from 1991 to 1994 and 8,000 participants in NHANES 1999–2002). The survey over samples the two largest race/ethnic minority groups, non-Hispanic blacks and Mexican Americans along with other subgroups of the population. Information on multiple aspects of health obtained through interview, laboratory tests, and direct examinations is also available for the NHANES participants. BGD is the first large-scale effort in the U.S. to support comprehensive identification of the associations among variations in genotype, phenotype, and risk factors in a representative sample of the population, laying the groundwork for understanding the relation between human genome variation and health status.

BGD has the following overarching, three-year goals:

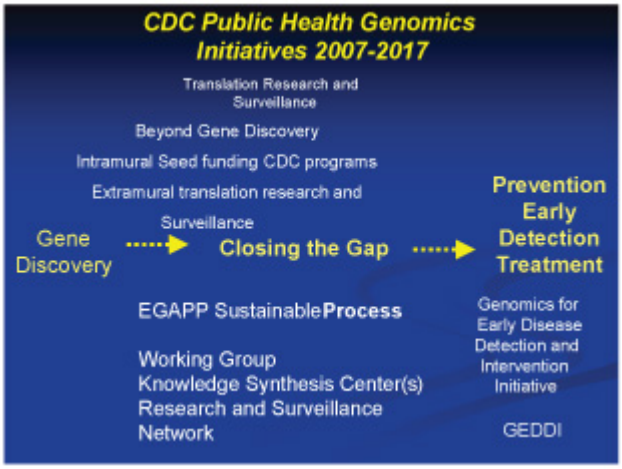
- Produce the first comprehensive report of the “Genome Profile of the United States” population, a summary of the prevalence of common genetic variants in the U.S., including racial and ethnic population groups.
- Support the development of a searchable, online information system of human genome variation (allele, genotype and haplotype frequencies at individual and multiple genetic loci) that is readily accessible to researchers, health care providers and policy makers. Access to these data will comply with federal requirements that ensure the protection of survey participant confidentiality.
- Develop and disseminate a comprehensive agenda for population research to fill the gaps between gene discoveries and health benefits of genetic information. The agenda will identify potentially fruitful analyses to be conducted by researchers on genotype-phenotype correlation, gene-gene and gene-environment interaction and various health outcomes.
- Enhance CDC’s informatics and analytic capacity to develop research datasets that link relevant genetic test results and NHANES interview, examination, and laboratory measurements. Such an enhanced capacity is needed for data management, review, quality control, editing, and documentation, production of research datasets, developing access modalities that protect confidentiality, support of proposed research activities, and disclosure review to maintain confidentiality of NHANES participants.

Accelerate Translation Research and Surveillance

NOPHG will accelerate its initiatives and activities in the areas of translation research and surveillance to advance knowledge about the validity, utility, utilization and population health impact of genomic applications and family history for improving health and preventing disease in well-defined populations or practice settings. The diagram below shows how these translation research and surveillance activities are designed to begin to close the gap between gene discoveries and the population health goals of prevention, early detection, and treatment.

Intramural Seed Funding for Public Health Genomics Research

To build on the successes of the current seed funding initiatives, NOPHG intends to accelerate the process of integrating genomics into public health investigations (e.g., infectious, environmental, occupational, injury, MCH and chronic diseases) by funding additional initiatives through CDC and its partners. These initiatives will demonstrate the utility of public health genomics research throughout CDC programs and will help plant the seeds of growth and development across these programs.



Sustainable EGAPP Process

NOPHG continues to support the evolution of the EGAPP initiative to meet the growing challenges of evidence-based synthesis of knowledge on emerging applications of genomic technology and the dissemination of that information. With guidance from the HHS interagency EGAPP Steering Committee (http://www.egappreviews.org/committee.htm), NOPHG will continue to support the independent EGAPP Working Group and the newly formed EGAPP Stakeholders Group, as well as survey stakeholders to obtain feedback on EGAPP products and process, and continue efforts to enhance partnerships and collaborations with similar efforts in the U.S. and globally.

Genomics for Early Disease Detection and Intervention Initiative (GEDDI)

NOPHG will work with CDC programs and other partners to develop and evaluate genomic applications that use clinical and genomic information, such as familial risk assessment, signs and symptoms recognition, and genetic testing to promote the prevention and early detection of both traditional genetic disorders and common diseases.

For many years, integration of genomic applications into clinical practice has been focused on genetic testing for individually rare single gene disorders. More recently, we are seeing the introduction of genomic applications for common chronic diseases—e.g., by using genetic markers in early identification of cancer, or targeting therapies based on genotype that optimize response and avoid adverse drug reactions. We can expect increasingly rapid development of new genetic tests—including those that test multiple genetic markers concurrently using microarray technologies (multiplex testing)—that will be used to help

refine diagnoses, improve risk prediction, and target therapies for both traditional genetic disorders as well as common chronic diseases.

In the meantime, genomic applications already being used in clinical medicine can be evaluated at the population level for assessing disease risk, influencing early disease detection, and providing guidance for disease prevention or management. These applications—including familial risk assessment, signs and symptoms recognition, and genetic testing—when used as public health strategies, could contribute to improved population health. Family history is an important tool for identifying individuals and families with genetic susceptibility to common chronic diseases such as coronary heart disease, stroke, diabetes and most cancers, as well as the rare single gene disorders like cystic fibrosis, sickle cell anemia, hereditary forms of breast and colorectal cancer. As an integral part of primary care and preventive medicine, familial risk assessment has the potential to identify individuals at risk of disease, those with sub-clinical disease, and those who may already be affected but are undiagnosed.

There are many single gene disorders across the life span that could benefit from early disease detection and interventions through a closer partnership between medicine and public health. Many affected persons with genetic diseases such as hereditary hemochromatosis (HH), familial hypercholesterolemia (FH), and primary immune deficiency disorders, for example, are either missed by the health care system or not diagnosed early enough for effective and appropriate interventions to work. Thus valuable opportunities for disease and disability prevention are lost. A public health approach employing public and provider education about symptom recognition, surveillance strategies, screening, and referral to appropriate services, could be used to enhance existing health care practice leading to earlier diagnosis of these disorders.

Under the GEDDI initiative, NOPHG will take results of translation research and evidence based synthesis and use validated information across public health programs. NOPHG will work with CDC collaborators and external partners to identify the genomic applications and diseases that are ready and most appropriate for a public health approach.

7.0 Publication List

This section provides a list of all scientific articles by NOPHG staff published in peer-reviewed journals in FY2007.

1. Goddard KAB, Moore C, Ottman D, Bradley L, Khoury MJ. Awareness and use of direct to consumer nutrigenomic tests, United States, 2006. *Genet Med* (in press)
2. Gwinn M, Bowen S, Khoury MJ. Genomics and public health: tools for the 21st century. *MMWR* 2006;55 (suppl 2):20-21.
3. Hariri S, Valdez R, Moonesinghe R, Khoury MJ. Evaluation of family history as a risk factor and screening tool for detecting undiagnosed diabetes in a nationally representative survey population. *Genet Med* 2006;8:752-759.
4. Khoury MJ, Gwinn M, Little J, Ioannidis JP. On the interpretation and synthesis of consistent but weak genetic association in the era of genome-wide association studies. *Int J Epidemiol* 2006 (epub)
5. Khoury MJ, Romero R. The integration of genomics into obstetrics and gynecology: a HuGE challenge. *Am J Obstet Gynecol* 2006;195:1503-1505.

6. Khoury MJ, Gwinn M. Genomics, epidemiology and common complex diseases: let's not throw out the baby with the bathwater. *Int J Epidemiol* 2006; 35:1363-4.
7. Davis RL, Khoury MJ. The emergence of biobanks: practical design considerations for large population-based studies of gene-environment interactions. *Comm Genet* 2007 (in press)
8. El-Serag H, Khoury MJ, Lewis JD. HuGE reviews and meta-analysis of gene association studies. *Gastroenterology* 2007;132:839-840.
9. Goddard KAB, Moore C, Ottman D, Szegda KL, Bradley L, Khoury MJ. Awareness and use of direct-to-consumer nutrigenomic tests, United States, 2006. *Genet Med*. 2007 Aug;9(8):510-7.
10. Gwinn M, Khoury MJ. Dermatology and the human genome: and epidemiologic approach. *Arch Dermatology* (2007 in press)
11. Janssens ACJW, Moonesinghe R, Yang, Q, Steyerberg EW, van Dujin CM, Khoury MJ. The impact of genotype frequencies on the clinical predictive value of genomic profiling for susceptibility to common complex diseases. *Genet Med* 2007 (in press)
12. Khoury MJ, Gwinn M, Bowen MS. Genomics and public health research. (letter to the editor) *JAMA*. 2007 June;297(21):2347.
13. Khoury MJ, Little J, Higgins J, Ioannidis JP, Gwinn M. The need for high quality systematic reviews and meta analyses of genetic associations. (letter to the editor) *PLoS Medicine* 2007 (April 16) online at: (http://medicine.plosjournals.org/perlserv/?request=read-response&doi=10.1371/journal.pmed.0040147#r1573)
14. Khoury MJ, Little J, Higgins J, Ioannidis JP, Gwinn M. Reporting of systematic reviews: the challenge of genetic association studies. *PLoS Med* 2007 Jun 26;4(6):e211
15. Moonesinghe R, Khoury MJ, Jansenns AJW. Most published research findings are false - but a little replication goes a long way. *PLoS Medicine* 2007 Feb;4(2):e28:218-220.
16. Rebbeck TR, Khoury MJ, Potter JD. Genetic association studies of cancer: where do we go from here? *CEBP* 2007;16:864-865.
17. Seminara D, Khoury MJ, O'Brien T et al. The emergence of networks in human genome epidemiology: challenges and opportunities. *Epidemiology* 2007;18:1-8.
18. Valdez R, Greenlund KJ, Khoury MJ, Yoon PW. Is family history a useful tool for detecting children at risk for diabetes and cardiovascular diseases? A public health perspective. *Pediatrics* 2007; 120 Suppl 2: 78-86
19. Valdez R, Yoon P, Liu K, Khoury MJ. Family history and prevalence of diabetes in the U.S. population: 6-year results from the National Health and Nutrition Examination Survey (NHANES 1999-2004). *Diabetes Care* 2007;30:2517-2522
20. Yu W, Yesupriya A, Wulf A, Qu J, Gwinn M, Khoury MJ. An automatic method to generate domain-specific investigator networks using PubMed abstracts. *BMC Med Inform Decis Mak* 2007 Jun 20;7(1):17
21. Austin H, Key NS, Benson JM, Lally C, Dowling NF, Whitsett C, and Hoopers WC. Sickle cell trait and the risk of venous thromboembolism among blacks. *Blood* 2007;110(3):908-912