

Advancing Cancer Genomics in Public Health

Date: Nov 05 2013 | **Policy Number:** 201317

Key Words: Genetics, Cancer, CDC Centers For Disease Control And Prevention

Relationship to Existing APHA Policies

APHA Policy Statement 7708 – The role of health professionals in promoting active measures of prevention

APHA Policy Statement 8310 – Guidelines for genetic testing in industry

APHA Policy Statement 9105 – Cervical and breast screening

APHA Policy Statement 20005 – Effective interventions for reducing racial and ethnic disparities in health

APHA Policy Statement 2002-1 – The role of genomics in public health

APHA Policy Statement 2004-12 – Support for community-based participatory research in public health

APHA Policy Statement 2005-11 – Colorectal cancer screening

APHA Policy Statement 201012 – Strengthening genetic and genomic literacy

Abstract

This policy statement addresses cancer genomics and public health at a time when Healthy People 2020 has included cancer genetic testing in its objectives and federal agencies have renewed efforts to translate cancer genomic developments for population use. APHA lacks a unified policy document in this emerging arena. In remedying this gap, the present policy statement addresses conditions that strike large numbers of people and are at the heart of many ongoing efforts by state health departments, in terms of both surveillance and education: hereditary breast/ovarian cancer, hereditary nonpolyposis colorectal cancer (Lynch syndrome), and prostate, lung, and bladder cancer. Areas covered include technical (genetic testing, gene expression profiling, genome-wide association studies) and humanistic (cost and availability, disparities, education) concerns as they relate to traditional public health efforts (e.g., cancer disease registries and family health histories). The policy recommendations developed encourage inclusion of BRCA1/2 and Lynch syndrome incidence and testing data in state surveillance efforts and integration into electronic data systems. Cascade screening for Tier 1 (validated) cancer genetic tests and ongoing weighing of associated ethical, legal, and social issues are encouraged. The recommendations of the US Preventive Services Task Force and the Evaluation of Genomic Applications in Practice and Prevention Working Group on cancer genetic diagnostic and predictive testing are becoming a part of state health department assessment and educational programs; there is a need for further harmonization between existent policies. Disparities remain in major cancer categories and in oncogenomic services for racial-ethnic minorities and the uninsured, and these disparities must be addressed through federal initiatives and attention to the needs and concerns of vulnerable populations. Public health practitioners can be active agents in these efforts.

Problem Statement

While the incidence of several types of cancer has been reduced over the past decade, in part as a result of public health initiatives, mortality disparities still remain in those cancers that are most frequently screened.^{1,2} Individuals need to be apprised of the importance of cancer screening, and health providers and consumers require information on available technologies, including family health history instruments and cancer genetic testing, that have been evaluated and found to be accurate and useful. In some instances, consumers have actually preferred genetic techniques to standard options such as colonoscopy,³ but not all consumers are aware of cancer genetic testing, and many fear that cancer genetic services will not be a viable option for them.⁴⁻⁶ The American Public Health Association has a longstanding commitment to the health of the entire population, including the underserved, especially in cases in which disease can be caught at an early stage or prior to manifestation. APHA policy 2002-1 (The Role of Genomics in Public Health) recognizes that new genetic tests may emerge onto the market with relatively unknown reliability, sensitivity, and specificity. At this point, however, systematic evidence-based reviews have been published on a number of types of oncogenomic tests, and public health practitioners are in a position to inform consumers and health care providers of their current status.

APHA has also covered genetic and genomic literacy (Policy No. 201012); these recommendations can now be extended to the cancer genomics area. Genetic workforce development was adequately covered by policy 201012. APHA duly recognized the persistence of disparities in colorectal cancer (CRC) screening and mortality in policy 2005-11, but the statement was produced before the validation of genetic testing strategies for mainstream CRC use. It is important to bring objectives cited by Healthy People 2010 up to date in public health policy recommendations, as the 2020 revision includes genetic testing objectives for CRC and hereditary breast/ovarian cancer.⁷ State health departments are beginning to recognize the importance of including genetics in their cancer surveillance and educational efforts.⁸⁻¹⁰ Public health is uniquely able to reach a large number of health providers and consumers regarding cancer family history and validated predictive and diagnostic cancer genomic (oncogenomic) testing and to receive input from communities. As discussed in a 2013 Healthy People 2020 progress review webinar on cancer and genomics, public health at the federal level has already played a central role in the evaluation of widely used oncogenomic tests. Public health has an important focus on the needs of diverse racial-ethnic and socioeconomic groups conducive to maximizing benefits and minimizing harms and ensuring the culturally appropriate use of burgeoning genetic technologies. The policy gaps to date and new developments call for a guiding set of policy recommendations for the public health community.

This policy statement adopts as examples cancers of public health and community-based interest (<http://www.champhealth.org/projects.html>) as opposed to strictly clinical concern, with a principal focus on hereditary breast/ovarian cancer and colorectal cancer and additional attention given to prostate, lung, and bladder cancer. Thematically, it walks a middle line between overspecialization (e.g., dealing only with cancer genomics education) and overgeneralization (e.g., moving into technological vistas that are clearly more clinically oriented than population oriented). The objectives are to review the intersecting areas of public health, genomics, and cancer; note consensus documents where they exist as well as areas of disagreement among existing policies; cite current gaps in research and policy; and develop needed recommendations. Problem areas covered relate to cancer genetics surveillance, family health history, diagnostic and predictive testing, gene expression profiling, genome-wide association studies, direct-to-consumer genetic testing, cost, availability, disparities, and education. Disparities and health information awareness are linked because underserved groups are disproportionately uninformed about the existence of cancer genetic testing, which touches on public health's mission.⁵ Any attempt to formulate relevant oncogenomic policies must take into account the most burning social and ethical issues (e.g., privacy and information sharing, equity, informed use) coupled with the latest scientific developments.

Proposed Recommendations Statement

Cancer Surveillance

Problem: limited number of state cancer genetics surveillance systems, along with unfulfilled opportunities to apply the information gained.

Opposing viewpoints: Public health authorities have used surveillance to track the epidemiology of various cancers, use of cancer genetic testing, and program impact, including consumer trends. Room exists for cancer genetic surveillance to expand to a larger collection of states than the current number. While it might be argued that state health departments are set up only for standard forms of surveillance—contagious disease, birth defects, and cancer as a whole—the presence of newborn screening in every state shows that genetic surveillance is feasible and can be performed through a variety of means. Integration of cancer genetic surveillance with electronic health record systems may seem futuristic but is now in progress in several states. Some of the data being accumulated are actionable in the sense that they can be directed to strengthen services for high-risk individuals, racial-ethnic minorities, and the uninsured.

Issues and strategies: The Association of State and Territorial Health Officials' 2010 State Public Health Genomics Resource Guide lists 4 modalities for incorporating genomics into surveillance practices: maximizing existing data, integrating genomics into existing systems, developing new systems to address data gaps, and improving the quality of existing data.⁸ Multiple states (Connecticut, Michigan, Minnesota, Oregon, Utah, Washington, and Wisconsin) have included questions about family history of chronic disease, knowledge of genetic tests, perceived health risks, and related topics in their Behavioral Risk Factor Surveillance System (BRFSS) surveys. Utah's Breast and Cervical Cancer Program has combined mining of its longstanding family health history data set with the distribution of tools to educate the public and health care providers on family history, an example dual program that could be followed in other states.

A long-term Finnish trial of systematic colon cancer surveillance reported a 62% reduction in risk based on the number of incident cases among high-risk relatives who received colonoscopy and mutation testing for Lynch syndrome.¹¹ Michigan and Oregon have incorporated incidence data for heritable cancers into their cancer disease registries and detected significant between-state differentials (with incidence rates of 4.9 per 100,000 women in Michigan and 8.2 per 100,000 women in Oregon).¹⁰ Several states, including Michigan, Minnesota, and Utah, have analyzed clinical data on cancer family health history by accessing doctors' office chart reviews, electronic medical records, and information from local public health encounters.⁸ More could be done with this information than just assessment. Oregon has used deidentified genetic services data to ascertain the number of people visiting genetics clinics for cancer-related reasons, but this information could alternatively be fed back to reporting institutions to alert individuals at high risk for Lynch syndrome (e.g., females diagnosed at an early age with endometrial or ovarian cancer). Surveillance operations could also be used to inform state policies on adequacy of services for racial-ethnic minorities and the uninsured. Programs are generally in the early stages of integrating genomic information and services into electronic health record systems (e.g., the eMERGE system of the National Institutes of Health [NIH]) and decision support systems (e.g., the Body Talk initiative of the Centers for Disease Control and Prevention [CDC]).

Family Health History

Problem: incomplete validation of comprehensive cancer family histories, call for cascade screening of heritable cancer conditions.

Opposing viewpoints: Family health histories are often considered the “first genetic test.” They can have great value in suggesting the need for additional action in both individual cases and among family members through individualized risk assessment, a goal of personalized medicine. Validation of their sensitivity in identifying cancer risk, however, particularly to inform early screening, is still lacking. Family health histories can ultimately lead to cancer predictive testing of additional family members through cascade screening, but further validation is needed when external risk factors are also being considered.

Issues and strategies: A 2009 NIH state-of-the-science conference report showed high specificity but a large sensitivity range (33% to 95%) for identification of cancer risk in family members through family histories, which especially applies to their use in early screening for conditions such as colorectal cancer.¹² A distinction exists between family history for chronic conditions with complex etiologies and that representing single-gene disorders (e.g., hereditary breast/ovarian cancer and Lynch syndrome).¹³ Heald and Eng found that family history had greater clinical accuracy than direct-to-consumer personalized genomic testing in identifying individuals at high risk for breast and colorectal cancer.¹⁴ The evidence generally suggests that family histories can motivate healthy behaviors, but further data are needed to conclude that routine use in primary care populations leads to improved health outcomes.¹² The reluctance of some individuals to share personal health information with other family members is a factor that must be taken into account.

A number of risk assessment tools are available that rely on family history, such as CDC’s Family Healthware and Your Disease Risk, developed by the Harvard School of Public Health.^[13] The utility of risk assessment tools that use family history in combination with other lifestyle and environmental risk factors has not been fully explored. Evaluations must lead to practical guidelines for those found to be at elevated risk.¹³

The use of family history can ultimately benefit family members through predictive genetic testing. Cascade screening involves a chain process of using one relative who has tested positive to identify another at risk. Several recent public health reports have called for cascade screening of cancer conditions that achieve Tier 1 status (high validity based on a systematic evidence review).^{13,15,16} Contact tracing of family members for other genetic conditions has been estimated to yield upward of 20 additional tests per family.¹⁷ It is projected that cascade screening for hereditary cancers could reach thousands of people in the United States each year.¹⁵ The ethical-legal-social and health service (e.g., privacy, accessibility, follow-up) implications of such expanded screening have not been fully mapped out.¹⁵

Diagnostic and Predictive Testing

Problem: need for clear-cut guidelines for cancer diagnostic and predictive genetic testing services that allow wider use in public health.

Opposing viewpoints: The public health focus in cancer diagnostic and predictive genetic testing has tended to be on hereditary breast/ovarian and colorectal cancer, which together with lung and prostate cancer (these conditions generally being amendable to more conventional forms of testing) contribute the greatest number of cancer deaths in the United States. While standard guidelines provide suitable criteria to identify many of those at risk, the cost-effectiveness of cancer predictive genetic testing, which begins with conventional screening, has been demonstrated. The clinical diagnostic guidelines themselves show inconsistencies needing attention. Healthy People 2020 now includes criteria for utilization of cancer genetic testing and family history.⁷ Problems exist, however, with respect to provider appreciation of risk levels based on family history and public health dissemination of cancer assessment guidelines incorporating genetics. Public health clinics are far from finished with the incorporation of cancer genetic testing into their arsenal, which should be seen as a call to action rather than a deterrent.

Issues and strategies: A number of professional guidelines using the Amsterdam and Bethesda criteria have been developed for judging the likely presence in at-risk individuals of a heritable colorectal cancer syndrome and whether a screened index case should go on to genetic diagnostic testing. Cost-effectiveness data indicate that screening using age and risk score based on family pedigrees followed by genetic testing “could improve health outcomes in a cost-effective manner,” achieving \$26,000 per quality-adjusted life-year gained, well below the standard \$50,000 threshold.¹⁸ The Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Working Group, however, noted the variable performance of existing standards in identifying cases of Lynch syndrome.¹¹

EGAPP examined several different molecular screening strategies used on tumor tissue to indicate need for genetic testing and was ultimately unable to find sufficient evidence to recommend one strategy over another.¹¹ Only one population-based study was identified that assessed the clinical validity of microsatellite instability (MSI) testing and none for immunohistochemical (IHC) testing. An intensive 104-study evidence review concluded that 3 clinical predictors—age of less than 50 years at diagnosis, cancer history in a first-degree relative, and the presence of multiple colorectal or endometrial cancers in the index case—combined with a positive result from MSI or IHC testing would be just as efficient (i.e., testing at least 7% fewer patients while missing at most 22% more true positives) as other, more complex strategies.¹⁹ Given the latitude in such findings, these reviews suggest that the field is still converging on an optimal molecular screening strategy.

Once preliminary testing on the patient has led to confirmatory genetic testing for relevant Lynch syndrome mutations, the National Comprehensive Cancer Network (NCCN) practice guidelines recommend predictive testing in at-risk relatives.¹⁹ Studies suggest that the level of participation among relatives is sufficient to justify routine genetic testing strategies (about half receive counseling, almost all of whom accept mutation testing), but comparison with Scandinavian countries, where pretest counseling rates can be as high as 85%, underscores the importance of consumer education to increase acceptance in the United States.^{19,20} Many public health departments have early breast, cervical, and colorectal cancer detection programs; cancer genomics can be customized into these services. Some degree of system-level coordination is needed, though, given that relative notification cannot possibly be conducted by single practitioners for all family members, many of whom are geographically dispersed. Authorities have suggested that the administrative structure evolved for regional cancer registries can be used for this task.

As with colorectal cancer, a number of molecular diagnostic tests, some using immunohistochemical markers, are available for preliminary triage of patients into low-, moderate-, and high-risk groups for breast cancer spread. Test kits (e.g., MammaPrint, Oncotype Dx) utilizing gene expression profiling (see below) can be used to provide definitive diagnosis and prognosis. Women in families with a history of breast cancer may wish to be worked up for the possibility of carrying a gene associated with hereditary breast cancer. While a large proportion of public health practitioners are chiefly concerned with primary prevention as opposed to symptomatic diagnosis, those involved with direct care will need a basic knowledge of the available diagnostic technologies.

Clinical practice guidelines have evolved that provide criteria by which to judge whether referral for hereditary breast/ovarian cancer (BRCA1/2) predictive genetic testing and counseling is warranted. Several state public health departments (e.g., Connecticut, Michigan) are already incorporating US Preventive Services Task Force (USPSTF) guidelines and Healthy People 2020 objectives into their genomics education programs,⁷ which should be emulated by other states. A CDC survey suggested that many providers unfortunately may not correctly recognize the increased-risk family history patterns in the USPSTF guidelines or be able to distinguish them from low-risk patterns, indicating the need for provider education.²¹ A health professional group at Harvard University and the Dana-Farber Cancer Institute undertook a comparative analysis that showed good agreement between the 2005 USPSTF and 2007 NCCN guidelines but poor agreement between these guidelines and the 2007 informally updated New York State/American College of Medical Genetics criteria.²² The lack of consensus suggests the need for further harmonization taking into account the latest revisions (updated USPSTF guidelines appeared in 2013) and, more fundamentally, for providers to be aware of the specific criteria in the guidelines they are using.

Gene Expression Profiling

Problem: lack of knowledge among public health practitioners of the appropriate, risk-related use of gene expression profiling (GEP), ongoing validation of GEP for different cancer types.

Opposing viewpoints: Gene expression profiling, which involves the simultaneous measurement of a vast array of genes or genetic variants, can be used for classifying cancerous tissue for prognostic purposes and predicting individual response to chemotherapy. Arguments against public health attention to GEP include the technology's use for secondary as opposed to primary prevention, the contention that it does not apply to public health patients, and the general absence of training in its use among many health practitioners. However, other major areas of public health, such as newborn screening and screening for hypertension, are also concerned with secondary prevention. Many oncology authorities argue that GEP should be universally applied to all estrogen-receptor-positive breast cancer patients, which represents a population-level approach. For this reason, public health evaluative bodies such as EGAPP (the United States), the Public Health Genomics European Network (PHGEN), and the PHG Foundation (Europe) have examined GEP technologies, and the Michigan Department of Community Health includes GEP in its educational efforts, an example that deserves repeating in other states.²³ From the public health perspective, it would be especially useful to have a means of identifying patients with low-risk tumor subtypes and in less progressed stages (I or II) who might be responsive to less aggressive operative procedures or adjuvant therapy (complementing chemotherapy and surgery) and, conversely, to identify individuals who might be unresponsive.

Issues and strategies: Colorectal cancer is the second leading cause of cancer-related deaths in the Western world.²⁴ A number of investigative teams have used GEP with DNA microarrays to discriminate between patients with a favorable versus poor prognosis independent of therapy and to identify individuals at risk for CRC tumor recurrence. These arrays have been reported to have a clinical accuracy between 75% and 90%.^{24,25} Some tests, such as KRAS (a gene involved in regulating cell division) mutational analysis for CRC, have shown predictive value for response to therapy but mixed prognostic capability in terms of outcome, and they require further study.²⁶ The EGAPP Working Group found that genotyping to avoid adjuvant toxicity can have a clear clinical benefit in terms of reducing side effects but that final decisions must be balanced with the effects of lowering drug doses.^{24,27} The data are in evolution as to whether the MammaPrint GEP assay is superior to clinicopathological prognostic indicators for breast cancer; Oncotype Dx has shown clinical utility in women at high risk for breast cancer recurrence. The EGAPP group found differing levels of evidence for the 2 techniques in directing women to tamoxifen chemotherapy.²⁸ They lack validation for women with early-stage breast cancer and a low risk of recurrence, a distinction that should be included in national practice guidelines. Clinical trials assessing both techniques are ongoing.²⁸

Continued pooling of initial and validation study data through comprehensive evidence reviews is necessary to highlight shortcomings of GEP assays bound for the market. The above examples represent a subset of those pharmacogenomic regimens that tailor cancer drug therapy for the individual via genetic testing, some of which

target cancer proteins in novel ways.²⁹ While the public health community is divided on the centrality of these personalized medicine developments for population health,¹⁶ safety assurance through bodies such as EGAPP on those assays that have been widely marketed is quite valuable. In the future, use of genome expression profiling can be expected to compete with conventional forms of risk assessment for a variety of cancers of public health concern, including non-small cell lung cancer and prostate cancer. Environmental influences (smoking, dietary nitrites, and industrial aromatic amines) might one day be taken into account via use of microarrays to check for epigenetic effects on key genes marking cancer progression.³⁰ Public health departments can be instrumental in increasing provider awareness about EGAPP recommendations on the use of GEP assays for cancers relevant to public health,²³ but a direct chain for translating this information is yet to be established.

Genome-Wide Association Studies

Problem: replication of genome-wide association studies in diverse racial-ethnic groups, need for provider awareness of when associated testing is ready for mainstream use.

Opposing viewpoints: Chronic disease genome-wide association studies (GWAS) constitute major collaborative activities to identify susceptibility genes that confer risk not fully explained by familial history of disease or individual genes with major impact (e.g., BRCA1/2 and hereditary breast/ovarian cancer). It can be argued that the major cancer mutations have already been identified, but for many cancer conditions 75% of familial cases remain unexplained. As GWAS explore the genome agnostically, without a priori knowledge of single nucleotide polymorphism (point changes in DNA occurring in more than 1% of the population) function, they are ideal for detecting common, low-risk variant disease susceptibility markers. These variants can have a cumulative effect, and the public health community needs to be reminded that the several cancer predictive genetic tests that predominate cannot completely fulfill public health's assessment goals. Opponents of participation argue that informational propriety is needed for innovation, but it is precisely the large-scale pooling of data from different population sources that enables the discovery of genetic markers associated with low to intermediate risk.

Issues and strategies: As of 2008, more than 9 genetic loci had significant and consistent low- to moderate-risk associations with breast cancer, 16 with prostate cancer, and 5 with colorectal cancer.³¹ Added to this list is a collection of new risk variants from the multicenter Collaborative Oncological Gene-environment Study (COGS).³² GWAS of postmenopausal female participants detected significant associations between the FGFR2 locus and cases of breast cancer without a family history.³³ Multicenter studies of BRCA1 and 2 carriers can uncover polymorphisms that can act as risk modifiers for these major genotypes. GWAS in African American men have been useful in detecting prostate cancer risk variants more common in men of African than European descent.³⁴ Recent GWAS of colorectal cancer, largely conducted in Europeans, identified 14 chromosomal regions associated with cancer risk.³⁵ To date, replication studies have confirmed some of the associations in Japanese, Swedish, and African American populations, but given CRC's worldwide impact, further studies are needed to explore the generalizability of these findings for cancer risk in additional populations.³⁶

A 5-country multicenter, multistage genome-wide association study confirmed 4 and identified 3 novel regions associated with bladder cancer and interactions between specific mutations and smoking in 2 additional regions.³⁷ Indeed, more than 90% of bladder cancer is associated with smoking and environmental exposures, calling for studies that clarify which regions vary in their association with such exposures.³⁵ Likewise, GWAS of lung cancer have been useful in corroborating gene-environment associations with nicotinic acetylcholine receptor gene loci and lung cancer risk,³⁸ although the degree of association with smoking behavior is inconsistent between studies. Several recent studies have looked at lung cancer risk in nonsmoking populations.³⁹ These studies need to continue, especially in cultures where air quality is compromised on a daily basis.

Commercial companies are currently marketing bladder cancer susceptibility tests online to consumers without due attention to the environmental contribution to risk. Professional and consumer education on when a test is ready for commercialization, the value of taking a smoking and occupational history, and maintenance of a healthy lifestyle to reduce background risk are paramount. In the noncommercial setting, COGS has proposed population screening based on polygenic (multi-gene) common risk variants, which could lead to more accurate risk stratification for those in the highest and lowest risk groups. Ethical challenges include consideration of screening in younger age groups, the social impact of knowledge of disease susceptibility, and lack of preliminary data in diverse racial-ethnic groups.³²

Direct-to-Consumer Genetic Testing

Problem: uninformed use of direct-to-consumer genetic testing and need for protective legislation.

Opposing viewpoints: Direct-to-consumer (DTC) genetic testing has taken off since BRCA1/2 mutation testing was first marketed by Myriad Genetic Laboratories directly to consumers in 2002.⁴⁰ While it is not the centerpiece of public health genomics, this new trend has managed to affect the wider population and has garnered attention from public health authorities and policymakers. Suggested benefits of DTC marketing of genetic tests include a possible increase in patient autonomy (one characteristic of personalized medicine), increased genetic literacy and awareness of genetic issues, and promotion of disease prevention. Arguments against DTC genetic testing and advertising include concerns over premature release of genetic tests with questionable validity (e.g., limited predictive value) and utility, exaggerated claims over the tests' capabilities, and nonexistent to limited counseling services and means of consumers becoming more informed. The central problem is thus one of potential benefits versus risks associated with the DTC services being offered.

Issues and strategies: CDC studies of the Myriad campaign via telephone surveys and the BRFSS have shown that consumers in the pilot cities were substantially more likely to have heard of the test and shared the results with their health care provider, although perceived knowledge about testing and ability to interpret test results were not increased.⁴⁰⁻⁴² Increases in provider ordering of genetic tests and making referrals to genetics and oncology clinics were also noted. Enhancing caregivers' knowledge of cancer testing guidelines—what criteria qualify for the ordering of a genetic test—and of their own institution's ordering policies would be one way to regulate the purchase of online genetic tests. Providers being approached also have an opportunity to offer consumer education regarding such tests.⁴¹

Safety concerns have taken 2 major directions: test related and media related. 23andMe offers DTC tests for each of the major genome-wide association study cancer categories mentioned above. To offer a test before the genetic variants being assessed are fully investigated makes little sense. A US Government Accountability Office investigation of companies conducting DTC genetic testing revealed significant variability in the reporting of results between and within companies and reporting that was incomplete for the ethnicity information provided.⁴³ In the case of leukemia and prostate cancer, 4 companies reported results reflecting disparate risk levels across a 3-point scale. Conflicting results may in part be due to variable laboratory test quality. The Centers for Medicare and Medicaid Services has not yet issued any new genetic testing specialty rules under the Clinical Laboratory Improvement Amendments (CLIA), and potentially helpful legislation (e.g., the Laboratory Test Improvement Act and the Genomics and Personalized Medicine Act) has not yet passed. The advertisements on breast/ovarian cancer genetic testing missed the opportunity to address relevant lifestyle factors and the value of genetic counseling and were potentially stigmatizing (e.g., BRCA mutations as "Jewish genetic conditions"). Studies have demonstrated that balanced information squarely discussing the risks posed by DTC genetic testing has a leveling effect on enthusiasm for such services and can prompt women to seek clinic-based testing.⁴⁴ Public health departments in California, New York, and other states, because of their health policing authority and the existence of DTC-related statutes and regulations, have played and can continue to play a decisive role in the in-state availability of DTC genetic tests.

Disparities

Problem: system-level and sociocultural barriers to the equitable use of oncogenomic testing in diverse racial-ethnic groups.

Opposing viewpoints: Health disparities for multiple cancer sites are well documented and persist despite adjustment for income and timing of diagnosis.⁴⁵ African Americans suffer increased mortality from early-stage premenopausal and early-stage postmenopausal breast cancer, advanced-stage ovarian cancer, and advanced-stage prostate cancer.² While genetic and other biological factors (e.g., greater prevalence of deleterious BRCA2 mutations and of aggressive triple negative [hormone-receptor-negative] breast cancer) may be partly responsible, systemic causes have been well researched and should be a part of policy approaches. The Institute of Medicine report *Unequal Treatment* counts patient preferences, health care system differences, discrimination, and genetic or biological differences among the factors responsible for such lingering gaps.⁴⁶ Analysis of the contributors is somewhat hampered by most of the studies not being controlled for racial differences in disease severity or presentation. The data nonetheless indicate the need for action to resolve the disparities on multiple fronts, educational and provisional.

Issues and strategies: Access to and utilization of predictive genetic testing varies by race. A Harvard/MGH Center on Genomics review of claims data showed that Whites were almost twice as likely as African Americans to have received BRCA1/2 breast/ovarian and MLH1/MSH2 colorectal cancer predictive testing.⁴ African American women are also significantly less likely to undergo genetic counseling for BRCA1/2 testing than White women.⁴⁷ Referral for genetic testing and counseling is often "an individual luxury more common among insured patients," with uninsured Latino patients expressing more difficulty than other groups in securing appointments.⁶ African Americans are more likely than Whites to have Medicare and/or Medicaid as opposed to private insurance, and Latino individuals are less likely to have private insurance and more likely to have no insurance at all.⁴⁸ As the Boston Cervical Cancer REACH Coalition Project has demonstrated, insurance status is a factor in the successful receipt and follow-up of abnormal screening results.⁴⁹ The data are unclear on the extent to which service differentials are intermingled with cultural obstacles, as Asian patients, despite rates of private insurance coverage exceeding those of other groups, are markedly more likely to indicate difficulty in seeing their primary source of care.⁴⁸

Knowledge gaps also play a part. African American and Latino consumers are less likely than Whites to have heard of cancer predictive genetic testing.⁴⁻⁶ Genetic testing for Lynch syndrome has tended to concentrate in White populations, producing a disparity in collected information. In the InSiGHT database, 73% of reported colorectal MLH1 mutations were from Caucasian populations, but only 3% were from South American and Caribbean registrants and less than 2% from those of African ancestry.⁵⁰ If the research on genetic mutations and more common polymorphisms does not include information from diverse groups, investigators will know less about what variants are present in their members, which could impede construction of accurate risk models and provider offering of testing for specific groups.^{32,50}

Consumer preferences regarding forms of secondary prevention must be taken into account. Studies have shown consumer preference for fecal occult blood testing (approximately 6% more African Americans and Latinos prefer this technique over colonoscopy) and fecal DNA testing (general population), which relates to screening acceptability and policies adopted.³ Further work on group preferences and the reasons respondents choose a particular option for secondary cancer prevention is needed.

The trust factor represents a deep-seated barrier. African Americans and Latinos are more likely than Whites to distrust risk-reducing interventions such as mammography and colonoscopy, to believe that genetic tests may be misused or used for undisclosed purposes, and to distrust their provider in keeping their medical information private.^{48,51} Although policy actions such as the 2008 Genetic Information Nondiscrimination Act and the 2010 Patient Protection and Affordable Care Act provide assurance, not all consumers are informed, and minority concerns, especially regarding equal access and coverage, remain.

Cost and Availability Considerations

Problem: lack of availability of cancer genetic testing in underserved populations and appropriate use by providers.

Opposing viewpoints: It might be argued that cost and availability considerations for cancer predictive and diagnostic genetic testing pose insurmountable barriers for underserved racial-ethnic and socioeconomic groups and rural populations, that conventional forms of screening and testing are less costly and therefore more within reach, and that oncogenomic testing consequently lies outside the province of public health. However, underserved communities may actually display a greater need than the general population for ascertainment of hereditary conditions; cost comparisons must be made considering intermediate (repeat screening) and long-term costs, which could cast a favorable light on cancer genetic testing; and various means such as Medicaid and Medicare might collaborate to reduce the costs to consumers.

Issues and strategies: While the data show that racial-ethnic minorities experience reduced access to oncogenomic testing and counseling,^{4,47} studies demonstrate that slightly more than 80% of African Americans would take a predictive genetic test for breast/ovarian or colon cancer if it were available and offered to them for future risk assessment.^{52,53} Availability and access barriers are important factors in rural populations, where the need is felt but use of cancer genetic testing is low (fewer than half of Appalachian physicians report any patients with genetic testing).⁵⁴ Rurality does not appear to be a variable in providers' ability to identify hereditary cancer, however. Appreciation of a greater incidence of and mortality from hereditary cancers in Appalachian and rural populations and management of family members by the same provider actually increase receptiveness of both provider and consumer toward cancer genetic testing in these locales.^{54,55} Public health has a dual role in these areas in terms of education regarding exposures (e.g., from work in the fields) and screening for familial and environmentally induced cancers.

Tuckson et al. argue that genetic and genomic innovations contribute to overall cost pressures in already unaffordable health care delivery systems.⁵⁰ The current cost for BRCA predictive (Tier 1, validated) genetic testing is roughly \$3,000 but can be reduced to \$650 for targeted mutation testing.⁵⁶ Likewise, prescreening for Lynch syndrome can cost \$1,200 and genetic testing \$1,000 per mutation assessed (3 possible mutations), but the latter can decrease to \$350 once a specific familial mutation is identified.⁵⁷ By comparison, mammogram costs (without insurance) range from \$150 for a basic screening to \$1,000 for a follow-up second mammogram and sonogram. Colonoscopy generally costs \$800 to \$1,200. The use of cancer predictive genetic testing is thus a calculated decision, more costly initially; however, given that it represents primary as opposed to secondary prevention and involves only a one-time charge in contrast to conventional screening, it is potentially cost-saving. In fact, a negative genetic test result can avoid the cost of unnecessary monitoring.

Many health plans cover BRCA analysis and counseling, which can drive BRCA testing out-of-pocket costs down to \$100 to \$600.⁵⁸⁻⁶⁰ A FORCE (Facing Our Risk of Cancer Empowered) assessment and published surveys indicate that BRCA predictive testing (primary prevention) is covered by Medicaid in 32 states and nationally through Medicare local coverage determinations.⁵⁹⁻⁶¹ Comparable information for Lynch syndrome genetic testing is available but is not as systematically organized (<http://www.lynchcancers.com/index.php/u.s.-national-resources>, https://www.wellcare.com/WCAssets/corporate/assets/HS154_Genetic_Testing_for_HNPCC.pdf). Follow-up in terms of genetic counseling is also a function of Medicare recognition of reimbursement for this service. Gene expression profiling (secondary prevention) can cost upward of \$4,000 but is capable of saving \$330.8 million annually by avoiding chemotherapy in patients with low risk scores.⁶² Most health plans as well as state Medicaid programs cover GEP for breast cancer treatment and to predict recurrence, although it remains investigational and uncovered for colorectal and prostate cancer owing to limited knowledge of its clinical utility. Oncotype Dx offers GEP assays for all 3 types of cancer, but thoroughgoing coverage will depend on further validation.

Dinh et al. have shown the cost-effectiveness of Lynch syndrome genetic testing for primary prevention to be similar to mammography for the wider population.¹⁸ Polygenic screening of healthy individuals (the COGS report) may reduce costs by decreasing the number of individuals who must be periodically screened, but it lacks empirical support and comparison with other forms of risk stratification such as family history.^{32,63} It is important that acknowledged criteria for the use of cancer predictive genetic testing, starting with personal and family history, be adhered to by practitioners screening for these cancers in the population setting.⁵⁰ Provider understanding of risk stratification, which helps to allocate individuals to conventional as opposed to genetic technologies, and the value of referral are prime areas for future policy. In ordering cancer predictive tests, providers can sometimes order the wrong test or not identify the best person in the family to initially receive testing, which can lead to insurance denials and increase costs. Exploring ways of systematically identifying individuals and families at high risk would help to keep costs down, in addition to the impact of the US Supreme Court decision against gene patents.⁶⁴ The public health workforce, because it consists of a diversity of professionals, can help with educating providers on notions of risk and the practicalities of ordering oncogenomic tests.

Cancer Genomics Education

Problem: lack of provider knowledge of cancer genetic testing, need for expanded public health and community-based educational efforts.

Opposing viewpoints: The CDC Office of Genetics and Disease Prevention (2001), now the Office of Public Health Genomics (OPHG), and the National Coalition for Health Professional Education in Genetics (NCHPEG; 2001 and 2007) organized efforts to develop core competencies in genetics for public health practitioners and health care professionals. Such targets are useful given the repeated finding that medical and public health professionals have demonstrated deficits in knowledge about familial cancer conditions and the tests available to detect them⁶⁵; this knowledge enables more accurate risk assessment by health professionals, and genetic knowledge gives individual consumers the chance to modify their own health practices. Medical practitioners often claim a lack of time to either learn or utilize genetics, but basic genetics training can allow them to refer patients appropriately. Some public health practitioners question the relevance of acquiring knowledge of genetic conditions and resources, yet these days very few fields in public health remain untouched by genetic considerations, and public health is especially suited to dealing sensitively with the assessment needs of particular groups. Even community-based cancer prevention programs often depend on their participants having adequate knowledge of family health histories. Differences must be recognized, however, in the educational modalities suiting health professionals versus consumers, especially in the level of technicality these efforts employ.

Issues and strategies: Surveys indicate that about a third of practicing physicians correctly answer questions dealing with the prevalence and transmission of hereditary breast/ovarian cancer and Lynch syndrome mutations.⁶⁵ Despite these gaps, the HuGEM survey of 3,600 members of various health professional organizations (from hearing specialists to social workers) ranked genetics in common disorders such as cancer, stroke, and heart disease as the foremost topic of interest for professional genetics education; “genetic information and racial/ethnic concerns” ranked fifth.⁶⁶ General practitioners acknowledge their role in taking family histories and in deciding when patients should be referred to cancer genetics centers but consistently report lack of knowledge of referral guidelines and where to refer as barriers.⁶⁷ Public health practitioners in the past have been accustomed to a specific set of duties relating to cancer screening, principally delivering basic services such as mammography, Pap smears, and fecal occult blood tests to low-income patients. A survey of public health educators by Chen and Goodson showed that only half believed it important to integrate genomic components into community-based education programs.⁶⁸ Part of the reluctance relates to shortcomings in basic and applied knowledge about genetic testing,⁶⁸ but as the Secretary’s Advisory Committee on Genetics, Health, and Society indicates, lack of evidence of the health benefit of existing genetic tests and lack of awareness of the evidence that exists also represent barriers.⁶⁹ To the extent that public health practitioners become educated in cancer genomics, they can serve as resources for other health care providers’ needs for information on cancer family histories and evidence-based guidelines on cancer genetic testing.

The OPHG has funded educational projects in California, Michigan, Oregon, and Georgia.⁹ One project at the Department of Veterans Affairs–Greater Los Angeles Healthcare System undertook a multifaceted education program for health care providers to improve and increase the use of family risk assessment for early detection of hereditary breast/ovarian cancer and Lynch syndrome. Collaboration with professional organizations such as NCHPEG has furthered this work. The Michigan “Promoting Cancer Genomics Best Practices through Surveillance, Education, and Policy” program, another CDC translational grant awardee, has promoted the use of USPSTF practice guidelines for BRCA1/2 testing, as well as provider understanding of the validity and utility of Lynch syndrome predictive testing and gene expression profiling for breast cancer. Although the OPHG grants ran only through 2011, some of the projects are still being funded through the CDC Division of Cancer Prevention and Control.

Continued federal support of cancer genomics education is imperative. The Connecticut Department of Public Health, for example, has leveraged Healthy People 2020 support from the US Department of Health and Human Services to develop a guide, *Cancer Genomics Best Practices for Connecticut Healthcare Providers*. Many states—Texas, Oregon, Georgia, Hawaii, North Carolina, and others—have cancer genomics education on their agenda, either exclusively through their public health departments or in conjunction with university centers. The Texas A&M University Genomics Training Program for Health Educators placed cancer genomics education resources on the Internet along with an online genomics education course. This type of program favors providers who live at a distance and has been suggested for rural practitioners. Such efforts depend on continued federal and state support, are most relevant when they address the educational needs of both the clinical and public health workforces, and are most effective when they incorporate evidence-based guidelines into the information being circulated.

The literature is mixed on the use of electronic media to educate consumers on cancer predictive genetic testing. Computer interactive programs have demonstrated efficacy in imparting knowledge but are designed for the computer literate. Participants in a series of focus groups for cancer genetics communication to African Americans in rural Louisiana prioritized reduction of technical detail in visual materials and “personalizing” the information, making it as relevant to the participants and their families as possible.⁷⁰ The community-based participatory research (CBPR) approach supports personalizing efforts, because community members serve in both the design and interventional phases of a study. Community members can also bring the information back to their own providers, who can learn from their patients and offer additional resources. A CBPR effort to reduce breast cancer disparities in South Dallas (48% at poverty level, 95% African American) showed that women in the intervention group employing both community informational sessions and lay health educators were 10.4 times more likely to receive a screening mammogram than those in the control group.⁷¹ These programs need to embrace technologies other than just conventional screening. Nongovernmental organizations have tailored

family history and genetics education materials to ethnic communities (e.g., Hmong and Latino communities, Ashkenazic or Eastern European Jews). Public health providers in locations with large numbers of foreign language speakers (many of whom may be unaware of their cancer risk status, even if their racial-ethnic group is at an elevated risk) should take this disparity into consideration when making decisions about the focus of their educational efforts. Cancer educational efforts tailored to specific racial-ethnic and socioeconomic groups need to spread from these few examples to broader levels of coverage with greater public health involvement.

Action Steps

The recommendations APHA is advancing are consistent with the findings and recommendations of a wide array of public, private, and government organizations, most prominently those concerned with cancer prevention and genetics and health advocacy and education. In light of the fact that the field is both constantly growing and reaching a stage at which many techniques and technologies are ready for or close to public health application, the following recommendations are offered:

1. Health departments, with the support of federal health agencies and health advocacy organizations (e.g., CDC, NIH, Genetic Alliance, Health IT Now), should incorporate data for heritable cancer conditions and related service utilization into statewide surveillance efforts through cancer disease registries and electronic health record systems and disseminate findings to submitting institutions as well as providers and consumers via electronic decision support systems.
2. Federal health agencies, national advocacy organizations, and genetics working groups (e.g., CDC, Genetic Alliance, EGAPP) should promote the use of family health history and cascade screening for (1) Tier 1 (validated by systematic evidence review) cancer conditions, such as BRCA1/2 hereditary breast/ovarian cancer and Lynch syndrome, and (2) research into the use of these techniques for other single-gene and complex cancer conditions that have not yet achieved Tier 1 status, with the aim of evaluating validity and utility.
3. The use of cancer diagnostic and predictive genetic testing should be encouraged through incorporation of cancer genomics testing and education into existing public health cancer programs, awareness raising by public health officials of the value of cancer genetic testing, system-level coordination by state and regional cancer registries of genetic testing of relatives, and efforts by legislators to secure Medicaid coverage of oncogenomic testing and counseling within their home state.
4. Genetics and heritable disorders divisions within state health departments should educate public health practitioners and health care providers about evidence-based findings for predictive genetic testing, gene expression profiling, and genome-wide association studies of cancer conditions relevant to the public's health; apprise them of relevant services and guidelines; and advocate for federal support of population-based and gene-environment-related research into these applications for all communities.
5. Federal agencies (NIH, CDC) and state health departments should further the appropriate use of oncogenomic testing in members of different racial-ethnic groups by (1) supporting research into the alleviation of institutional and cultural barriers hindering the use of cancer genetic testing by members of diverse groups; (2) promoting the equitable gathering of information (e.g., in state and national cancer disease and genetic testing registries and genomic databases) reflecting the cancer risk status of the entire population, including racial-ethnic minorities and the uninsured; and (3) engaging consumers in basic cancer genetics education and dialogue around cancer genetic testing policies and concerns.
6. Members of the public health community in states engaged in cancer genomic surveillance and education activities should promote efforts by professional groups such as the National Society of Genetic Counselors (NSGC), the American College of Medical Genetics (ACMG), the American Society of Clinical Oncology, the American Medical Association, and advocacy organizations (e.g., FORCE, Lynch Syndrome International, Sharsheret, and the Sisters Network) to address disparities in the offering of oncogenomic tests and counseling to individuals of diverse racial-ethnic, socioeconomic, and geographic backgrounds, as well as collaborative efforts between health departments and state legislatures to expand appropriate coverage of oncogenomic services under Medicaid and Medicare.
7. Health departments and health professional societies (ACMG, American Society of Human Genetics, NSGC) should urge oversight of direct-to-consumer oncogenomic testing through congressional inclusion of genetic testing specialty rules within CLIA, along with passage of legislation addressing DTC oncogenomic testing policies in the context of a personalized medicine act, and collaboration between federal agencies and state health departments in the regulation of DTC oncogenomic testing and advertising.

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