

CT Primary Care Payment Reform

Design Group Capabilities Skeleton: *Genomic Screening for CDC Priority Conditions* *This Draft: 08-28-2018*

Feedback from August 3, 2018 DESIGN GROUP Meeting:

The Design Group discussed how genomic screening should be incorporated into primary care. Meeting notes from the design group are attached to this document.

Design Group Recommendations:

- Include genomic screening in primary care bundle for all adults ages 18-65 for three CDC priority conditions
- Provide resources at network level (e.g., referrals to appropriate subspecialists, access to genetic counselors)
- Train practice level clinical staff to assist with educating patients about screening and results

Consumer Input, Questions and Concerns for Implementation:

Consumer representatives at the Design Group meeting added to the initial list of Consumer Needs (see [Consumer Input, Questions and Concerns for Implementation](#)):

- Importance of population health data showing screenings reduce death
- Importance of education for primary care physicians to understand these are screening tests
- Need to understand lessons learned from Geisinger pilot program and how they would apply to CT
- Need to ensure primary care practice capacity to provide sufficient infrastructure for patient education, counseling and support (and their genetic relatives who may also need to be screened), including appropriate, timely assistance interpreting results
- Concern about the cost of testing
- Need for secure data management and privacy protections
- Need for additional medical surveillance and counseling/support for those who are “screened in”

Design group meeting notes are attached at the end of this document

Understanding the Need

The Problem:

Screening in healthcare is used to identify pre-symptomatic health risks which would otherwise go unrecognized until it was too late. Blood pressure screening followed by blood pressure control has been effectively used to lower the incidence of stroke. Newborn screening has existed for over 50 years as a method of finding the 1 in 300 newborns with risk for serious health problems related to approximately 30 different conditions that can be identified prior to any symptoms in the first few days of life and then managed pre-emptively.

A conservative estimate is that, unbeknownst to them and their healthcare providers, between 1-2% of the U.S. population has an identifiable genetic risk for cancer or heart disease that could be detected and clinically managed via a genomic screening approach. These risks in 1-2% of the population are associated with three conditions that the CDC's Office of Public Health Genomics (OPHG) has labeled as "Tier One" conditions (see table below). CDC Tier 1 Conditions are conditions where clear and accepted strategies to diminish the disease risk can be applied once an at-risk case is identified. The list of conditions that meet these Tier One criteria are expected to grow in the decades ahead as our genomic knowledge grows.

CDC Office of Public Health Genomics - Tier One Genomics Applications		
Condition	Genes	Disease Risk
Hereditary Breast and Ovarian Cancer Syndrome (HBOC)	<i>BRCA1, BRCA2</i>	Cancer of the: breast, ovary, prostate, pancreas, other
Lynch Syndrome (LS)	<i>MSH6, MSH2, MLH1, PMS2, EPCAM</i>	Cancer of the: colon, uterus, other
Familial Hypercholesterolemia (FH)	<i>LDLR, APOB, PCSK9</i>	Heart attack, stroke, other

Until recently two issues have been stumbling blocks to genomic screening implementation for these three conditions: the cost of DNA sequence testing and limitations to DNA sequence variant interpretation. For instance, in 2015 it cost between \$3,000-4000 to sequence just two of the 10 genes (*BRCA1/2*), however in 2018 laboratories can sequence all 10 genes for between \$300-400. In this same period, investments by the federal government (i.e. the NIH) have made available a robust public database (ClinVar <https://www.ncbi.nlm.nih.gov/clinvar/>) containing verified "pathogenic" variants in these genes which allows for more uniform data interpretation.

Prior to these favorable recent changes in cost and variant data interpretation tools, the healthcare system had defaulted to the weak proxy of family history to identify who is eligible for the expensive testing. Recent data demonstrates that for one of these three conditions, namely *BRCA1/2* associated cancer risk, over 80% of those identified through genomic screening had not been otherwise identified in the course of their normal healthcare (i.e. through family history or other strategies). Genomic screening of adults is a safe, effective, and efficient way to identify the at-risk population.

Identifying the 3 to 4 million Americans with these risks via screening and then effectively mitigating the potentially life-threatening risk in follow-up care are worthy goals. A programmatic demonstration of this work in action to identify and improve the health of the estimated 30,000 to 40,000 at-risk citizens in Connecticut will provide the exportable model for the rest of the country. Such a program would be in line with the Genomics and Population Health Action Collaborative Population Screening model (from the US National Academy).

Achieving these short-term goals is made even more attractive by the promise of a broader population benefit (beyond the 1-2%) once the stage is set with an established genomic screening infrastructure that stands ready to implement screening for a growing list of genomic conditions in the decades ahead.

A program in genomic screening for the CDC priority conditions could be set up in a manner that allows for participant's initial sample to later be used to generate pharmacogenomic and other screening results at a later date if the funding for this were allocated.

Proven Strategy:

Name: Genomic Screening for CDC Priority Conditions

Definition: Adult patients (ages 18 to 65) will be offered genomic screening through primary care practices. Those who choose to be screened will provide a DNA sample that will undergo DNA sequencing and interpretation of a ten-gene panel looking for evidence of risk for: HBOC, LS, or FH. Those who screen positive will then be offered support to (1) understand their result, (2) take clinical steps to reduce risk, and (3) get at-risk family members screened. A central care support team (composed of geneticists, specialists, genetic counselors, and others) will be created as a single central resource for the state in order to answer questions for patients or providers, guide decision making as needed, carry out consultation (telemedicine or in person) as needed.

Intended Outcomes:

- Identify among patients who are interested in screening those with detectable risk for cancers (including breast, ovarian, prostate, pancreatic, colon, and uterine) and cardiovascular disease (including heart attack and stroke).
- Offer effective interventions to lower the risk of morbidity and mortality in these patients and their families.

Consumer Input, Questions and Concerns:

- Need for optimized preventive care for cancer
- Need for optimized preventive care for cardiovascular disease

Identified by Design Group:

- Importance of population health data showing screenings reduce death
- Importance of education for primary care physicians to understand these are screening tests
- Need to understand lessons learned from Geisinger pilot program and how they would apply to CT
- Need to ensure primary care practice capacity to provide sufficient infrastructure for patient education, counseling and support (and their genetic relatives who may also need to be screened), including appropriate, timely assistance interpreting results
- Concern about the cost of testing
- Need for secure data management and privacy protections
- Need for additional medical surveillance and counseling/support for those who are "screened in"

Health Equity Lens:

- Genomic screening is currently available as a “concierge” opportunity for those who seek it and can self-pay. This screening would be offered to a more diverse and representative population.

Implementing the Strategy

Example Scenario: An adult seen for routine care within a primary care practice in Connecticut will have the opportunity to opt in to genomic screening after reviewing informational materials (e.g. brochures, videos, other). They will give a DNA sample (blood or saliva) which will be sent to a central laboratory for sequencing and analysis. 1-2% will screen positive for a pathogenic DNA variant for one of the three conditions. The result will be returned to both the provider and directly to the patient within 4 weeks time. Patients and providers will be offered detailed support in (1) understanding the result, (2) planning the next clinical steps, (3) informing and supporting at-risk relatives. A central care support team will be available to support patients and providers with phone discussions, telemedicine support, or traditional face to face consultations.

HIT Requirements:

- Secure electronic portals for patient and provider to results and support materials (including provider CME opportunity).
- Capacity to securely deliver “positive result report” and “negative screening message” directly to EHRs, and to default to secure FAX or mail for patients and providers without EHR.
- Secure telemedicine platform for multiparty consultation (e.g. patient, primary care provider, cardiologist, central care support team).

Implementation Concerns:

- False reassurance of a negative screen. Genomic screening does not look for or rule out all risk for cancer or heart disease. Careful messaging to both patients and their providers is needed to not give the false impression that a negative screen rules out all risk.
- Some with risk will not ultimately develop disease. The identified risk is not “a diagnosis”, and not all of those with these risks (or any health risk) will develop disease. The support materials will make this clear to patients and providers.
- Programmatic Costs. In context, total budget is expected to be ≤ two preventive medicine visits for each participating patient:
 - Test costs
 - Central care support team costs
 - Outcomes monitoring costs
 - HIT costs

Impact

Aim	Summary of Evidence
Health promotion/prevention	Patients who choose to participate will have the opportunity to identify an otherwise invisible risk for themselves and their family, and then take actions to moderate that risk.

<i>Improved quality and outcomes</i>	Patients have experienced life saving interventions following genomic screening and preventive interventions.
<i>Patient experience</i>	Screening is optional, patient choice is a priority. For those with concerns about cancer and cardiovascular risk there is an opportunity to be proactive.
<i>Provider satisfaction</i>	Improving preventive care in order to reduce morbidity and mortality is a strong driver of provider satisfaction. In addition, most providers do not currently screen their patients for BRCA in compliance with the USPSTF this screening will replace that risk assessment. (https://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/brca-related-cancer-risk-assessment-genetic-counseling-and-genetic-testing)
<i>Lower Cost</i>	Management of cardiovascular and cancer risk and detection of early stage cancer, leads to improved outcomes and lower costs.

**Please complete the survey on this capability [here](#).

APPENDIX

Learning from Others

State and National Scan:

Case Study #1 Genomic Screening within a Large Regional Healthsystem. The Geisinger Healthsystem in Pennsylvania initiated genomic screening on a group of 200,000 health system volunteers in 2015. This screening program was designed and established under the direction of Dr. Michael Murray, and has proven effective at identifying risk and managing care for the three CDC Tier 1 conditions, as well as 24 other conditions where the data is not yet mature enough to suggest for this demonstration project. A number of the references below detail the findings in the Geisinger work.

Case Study #2 Genomic Screening in Individual Practices through a Commercial Testing Company. The InVita Laboratories is a commercial genetic testing company that launched a concierge-style genomic screening effort; namely an effort wherein an informed provider can order a screen for patients who agree to self-pay coverage of the testing. InVita has reported the success of these efforts in the first 1300 patients. Similar to the Geisinger experience, this screening identified individuals with genetic risk for cancer and heart disease that could not have been identified via implementation of existing identification strategies (i.e. family and personal medical history analysis).

Why Demonstrate Genomic Screening in Connecticut:

Connecticut is a small state, however in terms of racial and ethnic diversity it is representative of the country as a whole (see Table below). With a population of just over 3.5 million, Connecticut is approximately 1% of the U.S. population and is representative of country at large. This demonstration project in Connecticut is expected to be valuable for the whole country.

2010 US CENSUS	CONNECTICUT	US
(RACE AND HISPANIC ORIGIN)		

White alone	80.60%	76.90%
Black or African American alone	11.80%	13.30%
American Indian & Alaska Native alone	0.50%	1.30%
Asian alone	4.70%	5.70%
Native Hawaiian, & Other Pacific Islander alone	0.10%	0.20%
Two or More Races	2.30%	2.60%
Hispanic or Latino	15.70%	17.80%
White alone, not Hispanic or Latino	67.70%	61.30%

Additional Reading:

A list of resources such as publications in peer-reviewed journals and articles from respected trade and popular press.

Genomic Screening Models:

1. Genomics and Population Health Action Collaborative of the National Academies of Sciences, Engineering, and Medicine
<http://nationalacademies.org/hmd/Activities/Research/GenomicBasedResearch/Innovation-Collaboratives/Genomics-and-Population-Health.aspx?page=5>
2. Trivedi BP. [Medicine's future?](#) Science. 2017;358:436-40. [PMID: 29074750]
3. The Center for Disease Control and Prevention's (CDC) Office of Public Health Genomics (OPHG) Tier One Toolkit. <https://www.cdc.gov/genomics/implementation/toolkit/tier1.htm>

Genomic Screening Results:

1. Buchanan AH, Manickam K, Meyer MN, Wagner JK, Hallquist MLG, Williams JL, et al. [Early cancer diagnoses through BRCA1/2 screening of unselected adult biobank participants.](#) Genet Med. 2018;20:554-8. [PMID: 29261187]
2. Manickam K, Buchanan AH, Schwartz M, Hallquist M, Williams J, Rahm AK, et al. Ascertainment of BRCA1/2 Expected Pathogenic Variants in 50,726 Adult Biobank Participants. (publication in press).
3. Abul-Husn NS, Manickam K, Jones LK, Wright EA, Hartzel DN, Gonzaga-Jauregui C, et al. [Genetic identification of familial hypercholesterolemia within a single U.S. health care system.](#) Science. 2016 Dec 23;354(6319). [PMID: 28008010]

Disparities in Genomic Screening:

1. Amrock SM, Duell PB, Knickelbine T, Martin SS, O'Brien EC, Watson KE, et al. [Health disparities among adult patients with a phenotypic diagnosis of familial hypercholesterolemia in the CASCADE-FH™ patient registry.](#) Atherosclerosis. 2017 Dec;267:19-26. PMID: 29080546

2. Newman LA. [Consideration of Population-Based BRCA Testing as a Strategy to Reduce Disparities in Genetic Counseling Referrals: The Importance of Stating \(and Proving\) the Obvious.](#) JAMA Surg. 2018 Jul 3. PMID: 29971430

Stories of Patients who tested positive in Genomic Screening for CDC Tier 1 Conditions:

1. BRCA1/2: <https://www.youtube.com/watch?v=An9Z-fEOvgU> and <https://www.youtube.com/watch?v=wT3KaAqvn-s>
2. Lynch Syndrome: <https://www.youtube.com/watch?v=KIHNM0pYmY> and <https://www.youtube.com/watch?v=PkNUhxtipM0>
3. Familial Hypercholesterolemia: http://www.dailyitem.com/news/lifestyles/health/geisinger-study-finds-potentially-fatal-condition-is-underdiagnosed/article_15ee1b8e-ee30-11e6-9f62-db486fab95c5.html

Genomic Medicine Design Group
8/03/2018

Participants: Linda Green, Mike Murray, Polly Painter, Mark Schaefer, John Freedman, Vinayak Sinha, Jafar Razeq, Karen Woodward, Mark Masselli, Amy Taylor, Jason Prignoli, Tekisha Everette, Laura Housman, Velandy Manohar, Lesley Bennet, Tom Agresta

Public Comments

- None

Primary Care Modernization Design Group Process

- Goal: Make recommendation to the Practice Transformation Task Force as to whether this capability should be considered in the payment model

Genomic Screen for CDC Priority Conditions

- Leading killers in the CT mirror those of the US, of particular concern are heart disease, cancer, and stroke, which screenings discussed here have the potential to affect
- Screening is important when the disease being screened for is:
 - An important health problem
 - Not otherwise apparent
 - Screened via an approach that has good tools for finding it
 - Managed well after screening
- *BRCA 1/2* genomic screening of 50,000 patients in Pennsylvania was conducted as a pilot for the program
 - 40% of women meet the criteria for testing based on family history, but do not receive it
 - 40% of women do not meet criteria for testing, but were screened resulting in early detection
- CDC Public Health Genomics office considers familial hypercholesterolemia, hereditary breast and ovarian cancer, and lynch syndrome as tier 1 disease to screen for
 - There are 10 genes to be screened for these diseases, therefore these are the screenings being examined by the model considered for PCM
- Budget would be less than the cost for two preventive medicine visits
 - Range of \$300-\$400 per test
- These risks can be identified, interpreted, and managed now
- The focus is on 10 genes because they drive these conditions, which there is sufficient data on
- CT ethnic and racial diversity generally reflects that of the US and therefore this model may set the stage for understanding the impact these screenings would have nationally

Comments and Questions

- Velandy Manohar: Is there data from a population health point of view that the screening can make a difference? What would be the estimated number of needed screenings in a defined period of time to prevent one death of adverse event?

- Response – Mike Murray: In the short run, avoidance of a heart attack under the age of 55, ovarian cancer at any age, breast cancer under the age of 55. The impact should be seen in a 5-10 year time period based on what is known of these conditions and management of impact in other settings are important to understand the impact.
- Velandy Manohar: 5% of people with breast cancer and 10% of people with ovarian cancer have this gene, but of these people how many go on to develop breast or ovarian cancer?
 - There is an 85-90% lifetime risk for cancer in women with BRCA 1 or 2
- Tom Agresta: Important to understand impact for patients, particularly management of screenings to manage patient expectations and understanding of risk. Providers need to be given the correct tools for this type of management. There would need to be a thoughtful approach on data.
- John Freedman: If the proportion of breast cancer related to these genes is only 3-5% of all disease cases can we only anticipate a drop in 3-5% of cases?
 - Response – Mike Murray: There is an amount of misattribution associated with BRCA genes. An estimate considers as much as 6-10% attribution to BRCA 1 or 2 genes. It is only a slice of population burden, but focuses on those with risk of morbidity and mortality earlier in life.
 - Mark Schaefer: For the population tested this has significant impact. Rare diseases collectively are a big percentage of the population (~10%). Genomic/precision medicine offers better care for that 10%. Important to create a pathway for precision medicine early as these screenings are further developed.
- John Freedman: Is cost for the test priced in the market place or through a particular center? Would providers need to seek suppliers of this test?
 - Response – Mike Murray: Would want consistency through one supplier. Would be important to look at competition to compare prices. Color Genomics in Silicon Valley conducts these screenings for roughly \$300-\$400, Yale could deliver similarly.
- Laura Housman: Reflex screening after the fact can identify hereditary origin and be an indicator for familial screenings. Will this occur?
 - Response – Mike Murray: There is no reason why this cannot occur and there may be significant benefits from this. Those with the disease could get the screening from either their oncologist or PCP. For each case identified, there are potentially three family members who may be at risk for the gene.
- Laura Housman: Is there support in the form of counselling only or would there be testing provided for at risk members?
 - Response – Mike Murray: This depends on the details of the program, screening could be provided through the same mechanism for family members. Details would be dependent on the way the payments are structured.
- Laura Housman: HIT requirements – is this going to be a technology agnostic EHR framework or one that will be used predominantly?
 - Response – Mike Murray: Details would need to be worked out, but this could be done by mailing results to the provider and interoperability of EHR platforms.
 - Mark Schaefer: If the design group recommends to the task force for adoption, we would work on detailing information exchange.

- Laura Housman: Would be important to ensure consent is received upfront for additional screening programs, particularly important as additional genes are considered for testing.
- Jafar Razeq: Is there data on whether confirmatory testing is conducted after the first test?
 - Response – Mike Murray: There is still debate on whether secondary analysis needs to be done. Most labs consider a first test and secondary test to confirm the result is correct and this is included in the cost mentioned. Setting a high threshold to avoid false positives would be important for the screening program. The number of confirmable true positives is growing and this program could include ongoing analysis.
- Lesley Bennet: Regarding education – one of the problems for newborn screening is for pediatrics physicians to understand that this is a screening test. Is there something that would be done to help PCPs understand this?
 - Response – Mike Murray: Yes, would like to ensure that materials are clear and reviewed by a diverse set of audiences. Materials for patients and families tend to be helpful for PCPs as well. Education and support has to go out to any providers engaged, as well as patients and families.
- Jason Prignoli: What were challenges in the Pennsylvania pilot screening program and how would these apply to CT?
 - Response – Mike Murray: People were initially not convinced in the value of screening and there were concerns regarding implementation being burdensome. Geisinger providers concluded that the risk being identified for patients may not have ordinarily been otherwise. There was early resistance, but later on there was positive feedback on the program.

Next Steps

- Recommendation to task force:
 - Tom Agresta: Worthy to consider, should be prioritized based on other recommendations.
 - Laura Housman: Support for moving forward
 - Karen Woodward: In support and questions helped clarify.
 - Lesley Bennet: In support
 - Velandy Manohar: In support, but support for those tested needs to be focused on as well. Emotional support post diagnosis should be considered.
 - Jason Prignoli: In support