



# Health Services Advisory Council

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Minutes — February 11, 2016  
3:00 – 5:00 p.m.  
DHS Andersen Building, St Paul

## Members Present

Timothy Sielaff (chair), Don Brunquell, Amelia Burgess (by phone), Andrea Hillerud, Patrick Irvine, Chris Johnson, Jim Miner (by phone), Tamiko Morgan (by phone), Jeff Schiff (non-voting), Cedric Skillon

## Members Absent

Howard Fink

## DHS Staff Present

Ellie Garrett, Dave Hoang, Cindy Marihart, Sarah Rinn

## Others Present

Mike Jablonski (Assurex Health), Alison Martinez (Oklahoma Health Care Authority; by phone), Jim Pollard (Assurex Health), Molly Sajady (University of Minnesota), Charleton Smith (Assurex Health), Kristine Willey (Assurex Health)

## I. Welcome, introductions, updates and minutes

Timothy Sielaff welcomed everyone, and introductions were made around the room. Alison Martinez joined by phone. Martinez is a geneticist with the Oklahoma Health Care Authority, and DHS staff asked that she participate in order to respond to members' questions today.

Ellie Garrett stated that the meeting minutes needed to be corrected to reflect the date, time and location of the January meeting (January 14, 3:00 – 5:00 p.m., DHS Andersen Building). **On motion made and seconded, the members voted unanimously to approve the January meeting minutes as corrected.**

Jeff Schiff provided brief updates from DHS: The Institute of Medicine's *Vital Signs* report is catalyzing national discussions about improving quality measurement, discussions of which DHS is a part. HSAC member Chris Johnson has been named chair of DHS' Opioid Prescribing Work Group. A request for information will be issued soon regarding the next iteration of integrated health partnerships. The behavioral health homes program is scheduled to launch in July. A request for proposals has been issued in connection with a legislatively mandated report on using social risk factors as a consideration in health care payment models.

## II. HSAC membership update

DHS has interviewed candidates for the two HSAC vacancies, and invitations have been extended to two superb candidates, conditioned upon the Commissioner's approval.

## III. Pharmacogenetic testing and GeneSight Psychotropic

### A. Presentation – Ellie Garrett

Ellie Garrett summarized the evidence pertaining to GeneSight that she'd presented at the last HSAC meeting:

- There are no published studies of the GeneSight algorithm in use today. Both genes and drug lists have expanded since studies were conducted.
- All studies were authored or co-authored and funded by the manufacturer or patent-holder.
- All studies have high risk of bias.
- The manufacturer's claims about effectiveness hinge on two, small open-label studies and one small, partially blinded randomized controlled trial with statistically insignificant results and a meta-analysis of same, all of which call for more study.
- Published cost-effectiveness/resource utilization analyses rely either on the above effectiveness studies, or are otherwise limited (a retrospective analysis of one psychiatrist's practice in one case; reliance on pharmacy data alone without adding in the cost of the intervention in another).
- There are more studies underway.

Garrett also updated members on Medicare's decision-making process regarding lab tests such as GeneSight. Pursuant to [CMS' Medicare Managed Care Manual, Chapter 4, Section 90.4.1](#), a favorable decision of a single Medicare regional contractor will bind all other regional contractors and have national impact when, as is the case with GeneSight, there is only one provider for the proprietary lab service. DHS staff recommends that HSAC members adopt and apply the National Human Genome Research Institute's three questions to evaluate a genetic test pertaining to analytical and clinical validity and clinical utility and add a fourth consideration pertaining to algorithmic validity:

- Is the test accurate and reliable? (Analytical validity)
- Is the test result medically meaningful? (Clinical validity)
- Does the test improve healthcare? (Clinical utility)
- Has the algorithm's utility and scientific basis been clearly established? (Algorithmic validity)

### B. Clarifying questions

No questions were asked at this time.

### C. Public comment

Garrett drew members' attention to the written comments and disclosures that were in their folders and distributed electronically in advance of the meeting. In response to a question from Jim Pollard, Garrett stated that comments submitted after the meeting would likely be too late to influence HSAC, since HSAC was scheduled to make its recommendations during the meeting. Schiff added that comments would be welcome at any time for the Commissioner's consideration.

Mike Jablonski, a neuroscientist with Assurex Health, the manufacturer of GeneSight, offered these comments:

- FDA drug labels increasingly contain dosage limits or suggestions based on genotype, and 29 of the drugs in GeneSight’s panel have such language on their labels. FDA is now looking at the combined effects of various genes, as well as enzymes.
- The analytical validity of GeneSight’s labs is confirmed by an extensive laboratory testing and inspection process.
- Consistent outcomes from all studies of GeneSight in comparison to treatment-as-usual groups establish clinical validity. Patients in treatment-as-usual groups who are taking red-binned drugs consistently show worse outcomes than those taking green or yellow-binned medications.
- With regard to clinical utility, improved patient outcomes make the GeneSight test quite useful.
- With regard to the suggested algorithmic validity consideration, it is important to differentiate between a single gene analysis and a panel of genes. Assurex’ algorithm considers the effect of multiple enzymes, the phenotypes based on them and then how the drugs are metabolized.
- With regard to the studies’ risk of bias, all of the articles were accepted and published in peer-reviewed journals, with designs based on real-world trials.
- Future studies are progressing the technology and evidence behind it. To date, though, GeneSight has already been studied sufficiently to demonstrate beneficial outcomes for patients with major depression.

The chair opened the floor up to questions from members. A member asked about the estimated lifetime savings, and Jablonski clarified that the savings were from reduction in total health care visits, which would be reduced if a patient were taking a green or yellow-binned drug compared to a red one. Garrett added that the article in question described results of an economic model that relied on the effectiveness assumptions from three small pilot studies (two open-label studies and one partially blinded RCT with statistically insignificant results).

A member asked how new genes are selected for addition to the panel. Jablonski stated that Assurex has strict criteria to add genes to the GeneSight panel. The criteria are based on literature, including large scale meta-analyses and reproducible genetic effects.

In response to a question from a member, Jablonski stated that Assurex’ studies have not confirmed with blood tests that medication levels indicate that drugs are being metabolized as predicted by GeneSight’s results.

In response to another question, Jablonski clarified that the test provides information about gene/drug interactions, not interactions between two or more drugs.

Jablonski also clarified that the manufacturer recommends using the test for treatment response-resistant patients, because half of treatment-naïve patients already respond well to therapy and do not need the additional test. He stated that in treatment resistant groups, the test works better than current trial-and-error approaches.

## **D. Discussion and recommendations:**

### **1. Coverage criteria for pharmacogenetic testing generally**

Members discussed the proposed criterion regarding algorithmic validity at length, with some members commenting that it is unnecessary because clinical utility criterion is sufficient. Others suggested that it’s a useful criterion for tests reflecting a proprietary algorithm. **A member moved to recommend the**

**first three criteria (analytical validity, clinical validity and clinical utility) and add the fourth criterion (algorithmic validity) as a subset of clinical utility. The motion was seconded. Brief discussion ensued. The motion carried, with one vote opposed.**

## **2. Coverage of GeneSight Psychotropic**

Applying the coverage criteria to GeneSight Psychotropic, a member suggested the following to frame the discussion:

- Assurex' laboratory is certified by the applicable accreditation body, so the analytical validity criterion is satisfied.
- Clinical validity is satisfied, recognizing that the literature shows that people with differing gene phenotypes have different responses to medications.
- The clinical utility criterion (health care improvement) is not satisfied, given the dearth of evidence supporting GeneSight's effectiveness and cost-effectiveness. The studies conducted thus far are insufficient to support a conclusion that health care is improved by use of GeneSight.

Discussion ensued. Some members questioned whether GeneSight satisfied the clinical validity criterion. In response to a question, Martinez suggested that the clinical validity criterion was satisfied, given that there is a relationship between a genotype and some biochemical marker. But it does not give one enough information to be useful clinically—one needs to know not just whether a mutation is present, but whether there is enough information to be measurable in a body. **A motion was made and seconded that the first and second criteria were satisfied with regard to GeneSight. The motion carried with two votes opposed.**

Brief discussion ensued with regard to the clinical utility criterion. Consensus emerged that the published studies are insufficient to establish the test's clinical utility. **A motion was made and seconded that coverage of GeneSight not be recommended because the test did not meet the clinical utility criterion. The motion carried unanimously.**

Schiff thanked members for their recommendation and stated that staff will be sharing the recommendation internally to inform DHS policy making for the fee-for-service program. In response to a question, he clarified that contracted managed care plans are free to establish more expansive policy if they wish.

## **IV. Other business/next steps**

There was no other business. The meeting was adjourned.



# Health Services Advisory Council

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Minutes — January 14, 2016  
3:00 – 5:00 p.m.  
DHS Andersen Building, St Paul

## Members Present

Timothy Sielaff (chair), Don Brunquell, Amelia Burgess, Howard Fink, Andrea Hillerud, Patrick Irvine, Chris Johnson, Tamiko Morgan, Jeff Schiff (non-voting), Cedric Skillon

## Members Absent

Jim Miner

## DHS Staff Present

Ellie Garrett, Dave Hoang, Robert Lloyd, Cindy Marihart, Sarah Rinn

## Others Present

Melissa Geyer (Assurex Health), Tamara Graziano (psychiatric nurse) Jim Pollard (Assurex Health), Amber Soukkala (University of Minnesota), Joel Winner (Assurex Health), Kristine Willey (Assurex Health)

## I. Welcome, introductions, updates and minutes

Timothy Sielaff welcomed everyone, and introductions were made around the room. **On motion made and seconded, the members voted unanimously to approve the November meeting minutes with no corrections.**

Jeff Schiff provided brief updates from DHS: Governor Dayton appointed Emily Johnson Piper as the new Commissioner of Human Services. The Opioid Prescribing Work Group (OPWG) is meeting monthly, having convened for the first time in November. Chris Johnson represents HSAC on the OPWG. The legislative session will be short this year, since it's a bonding and not a budget year. Work has begun to plan for the 2017 session.

## II. HSAC membership update

Ellie Garrett introduced Chris Johnson, who was attending his first HSAC meeting in person. (He participated by phone in November.) HSAC has two vacancies, strong candidates for which have been identified.

### III. Principles for prioritizing existing quality measures

Robert Lloyd summarized ongoing work at DHS to reduce the burden of quality measurement and prioritize measures that better reflect health outcomes and health status. A copy of his presentation is available upon request from [HSAC staff](#). The proposal builds on the [Institute of Medicine's \*Vital Signs\*](#) report as a basis for rethinking quality measurement. Schiff observed that the challenge is to bridge health care and population or public health. Members discussed the *Vital Signs* report's domains and elements. A member asked for context about quality measures. Perspectives about a measure's utility will vary depending on whether it's being used for quality improvement or accountability, for example. Another member observed that some of the higher level measures, like injury and violence are too broad; a more finely tuned approach would discern between different causes and interventions. Another member observed that measurement is costly, and if measurement results are not well used, then those dollars that could otherwise be directed to patient care are wasted.

A member discussed measurement of value (expressed as cost and quality combined) and of equity. Another asked about resources to act on problems identified through measurement and of connecting measurement to outcomes. Discussion concluded, and the chair opened the floor up to public comments. There were no comments offered regarding this topic.

### IV. Pharmacogenetic testing and GeneSight Psychotropic

Garrett summarized the federal regulatory environment for pharmacogenetic testing and the published studies pertaining to GeneSight Psychotropic. According to the National Human Genome Research Institute (NHGRI), which is part of the National Institutes of Health, these tests are largely unregulated at the federal level. NHGRI suggests evaluating a genetic test's usefulness based on three criteria:

- Is the test accurate and reliable? (Analytical validity)
- Is the test result medically meaningful? (Clinical validity)
- Does the test improve healthcare? (Clinical utility)

The GeneSight product analyzes various genes and then groups drugs for the patient's individual genetic profile into three categories according to a proprietary algorithm:

- Green: use as directed
- Yellow: use with caution
- Red: use with increased caution and with more frequent monitoring

Garrett reported that the scientific evidence supporting GeneSight Psychotropic's usefulness for the treatment of depression or major depression is scant and flawed:

- The GeneSight product being marketed today is not the one that was studied. Both the number of genes and drugs have expanded since the studies were performed.
- All studies were authored or co-authored and funded by the manufacturer or patent-holder and have high risk of bias due both to study design and to unmanaged conflicts of interest.
- The manufacturer's claims about effectiveness hinge on two, small open-label studies and one small, partially blinded randomized controlled trial (an RCT with statistically insignificant results) and a meta-analysis of same. The published articles call for more study.

- The manufacturer’s claims about cost-effectiveness rely either on the small effectiveness studies mentioned above or two studies that are otherwise limited: (1) in one case, a retrospective analysis of one psychiatrist’s practice; and (2) an examination of pharmacy costs alone that ignores the cost of the intervention or of other health care utilization.

A copy of Garrett’s presentation is available upon request from [HSAC staff](#). Members asked several questions concerning the GeneSight studies’ methodology and results. In response to questions, Garrett or Assurex representatives clarified several points, including;

- The randomized controlled trial reported in Winner 2013 was not blinded to the treating physician/prescriber. It was blinded to the patient and investigator.
- The red/yellow/green categories do not purport to predict which drugs work for what patients, but are designed to suggest whether (and if so, the degree to which) more caution or monitoring would be appropriate.
- Joel Winner, an Assurex Health representative and a psychiatrist, explained that drugs prescribed for depression are metabolized by multiple enzymes. The GeneSight approach takes into account the complex response of multiple genes. Winner disclosed that he is Assurex Health’s medical director and as such owns stock in the company.
- Winner explained how control patients were matched for propensity in the drug cost study. Savings were reported for one year of drug costs. The cost of the intervention (GeneSight test) was not reflected. A member commented that one cannot extrapolate based on the study that cost savings would continue into later years.
- Another member questioned whether the studies (or underlying studies) established whether the genotypes in question really predicted phenotypic action.

In response to a question, Schiff clarified that DHS is being requested to cover GeneSight, and there are more such tests on the horizon. Discussion ensued.

The chair opened the floor up for public comments, and Winner drew the council’s attention to several PowerPoint slides. A copy of Winner’s full PowerPoint presentation, which he did not have time to present in whole, is available from [HSAC staff](#). Among other things, he stated that the Food and Drug Administration (FDA) includes pharmacogenomic language in the package inserts for 29 of the 38 medications on the GeneSight Psychotropic test. Questions from members continued during his presentation. He clarified that GeneSight is intended to be used along with medical history, not to supplant patient history and other relevant treatment information. He also clarified that it is for treatment resistant depression, and has not yet been studied in treatment naïve patients. In response to a question, he stated that the Assurex lab provides two-day turnaround for test results.

A member pointed out that achieving a 3-point difference on a 60-point depression scale is not meaningful. Winner drew the council’s attention to his slide showing the current standard of care, with a quote from the American Psychiatric Association, “The effectiveness of antidepressant medications is generally comparable between classes and within classes of medications.” The slide also showed the shrinking return in terms of lowered treatment responses and increased side effects for patients undergoing numerous drug trials.

Tammy Graziano, a psychiatric nurse practitioner from Advanced Practice Solutions and working with Ramsey County Jails, Meridian and NorthPoint, offered public comment. She stated that she has used GeneSight for a year, and her patients have had favorable outcomes. Patients have a voice with this tool, and can see how their genetic profile informs her prescribing practice. At first she used it only with

patients who were not complying with their drug therapy. Now she uses it for every initial diagnostic evaluation, and explains with each patient how their genetic profile guides her prescribing.

Jim Pollard from Assurex clarified that Assurex is currently providing the test at no cost for Medicaid and other low-income patients lacking coverage for the test, but will have to begin billing for the test in the future. Assurex has also obtained a favorable Medicare local coverage decision, the only neurological pharmacogenetic test to have such standing. Pollard stated that he appreciated HSAC's transparency and welcomed input from Minnesota's Medicaid program about what kind of data it needs to support coverage.

A member asked for information about the study designs of the trials currently in progress. Another member asked about the diversity of the populations being studied. Garrett agreed to circulate information about the research protocols.

The chair asked members to remember that its discussions of GeneSight are as a case study, offering an opportunity to derive principles on which new pharmacogenetic tests can be considered.

The meeting was adjourned.