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## The need for vigilance in the marketing of genomic tests in psychiatry

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### Keywords

Genomic; Genetic testing; Ethics; Policy; FDA

Recently, several for-profit companies have been developing and marketing genetic tests to psychiatrists, yet the clinical utility of these is not always clear, posing several concerns. Important genomic research is continuing, and genomic tests potentially can help with both the diagnosis and treatment of many patients. Yet it is important that clinicians be aware of potential limitations of tests that may be marketed to them.

Different types of genomic tests are becoming available – from chromosome microarrays and single gene tests, assessing particular polymorphisms, to whole genome and whole exome sequencing. Research has sought to identify genetic markers associated with both various diagnoses and likelihoods of effectiveness and serious side effects of medications. Chromosome microarrays have identified markers associated with DiGeorge syndrome and schizophrenia, and deletions and duplications associated with approximately 1% of autism (Betancur, 2011). Over time, these and other tests can potentially be useful for a small group of psychiatric patients. Some markers, such as the DRD2 gene, which codes for the dopamine D2 receptor, affects antipsychotic medication efficacy. Yet though a particular variant has been found to lower drug response substantially, the sensitivity and specificity of this array are insufficient for clinical use (Zhang et al., 2010; Serretti et al., 2007).

In general, the development of psychiatric tests in psychiatry has faced several limitations. While the Clinical Laboratory Improvement Amendments Act (CLIA, 2015) focuses on ensuring quality control in laboratories, the Federal Drug Administration (FDA, 2015) only approves tests that have proven sufficient clinical utility. To date, only one psychiatric genetic test has received such approval – AmpliChip CYP450 Test (F. Hoffmann-La Roche Ltd., 2015) which assesses alleles of the CYP2D6 and CYP2C19 genes – though the FDA did not approve any specific clinical claims for it, and evidence that the test has clinical benefit is limited (Thomas and Chau, 2015).

Laboratories can also develop and market tests directly to clinicians, even if these assays do not have FDA approval or any demonstrated clinical utility. The policy that permits

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marketing of such tests has raised controversy, in part because federal agencies do not ordinarily undertake post-marketing surveillance of these tests (Malhotra et al., 2012).

In assessing genetic tests, the CDC's Office of Public Health Genomics has supported the Evaluation of Genomic Applications in Practice and Prevention (EGAPP, 2014), based on the ACCE Model – the acronym based on four components of analytic validity, clinical validity, clinical utility, and associated ethical, legal and social implications. EGAPP has listed recommendations concerning several diseases, of which only one is psychiatric – depression. Regarding adult testing for cytochrome P450 polymorphisms for depression, EGAPP concludes, “insufficient evidence to recommend for or against use, but use discouraged pending further research. (EGAPP, 2014)”

Not only polygenetic influences, but life circumstances, and interpersonal and environmental interactions can shape many mental health conditions. Several tests are now being marketed to psychiatrists, based on reports of genetic markers found to be associated in various samples of patients with a range of psychiatric conditions. But the replicability and clinical utility of these have been limited (Burmeister et al., 2008). Nonetheless, Assurex Health, for instance, markets GeneSightRx ADHD and other tests (AssureRx.com, 2012). Genomind sells the “Genecept™ Assay” to understand “genetic and biological markers that best inform responses to different psychiatric treatments (Genomind.com, 2015).” Proove Biosciences markets a test to determine the risk of abuse of narcotic pain killers, and another test purports to predict patients' perception of pain (proove.com, 2015). Sundance Diagnostics plans to market a genetic test that predicts suicidality (PR Newswire, 2013).

Though companies marketing genetic tests have tended to claim that their tests have clinical utility (Dolgin, 2012), systematic reviews have concluded that the data supporting these claims generally remains relatively weak (e.g., with non-replicated findings, and no p values <.05). Overall, well-designed studies should have sufficient sample sizes, and p values for genome-wide significance, and be replicated – especially since a study may assess thousands of potential markers, leading to type II errors. Other challenges include lack of prospective studies (Malhotra et al., 2012), and inclusion of patients with co-morbid conditions, chronic mental illness, and poor responsiveness to prior treatment. For use of antidepressant pharmacogenomic tests, for instance, evidence is lacking due to the polygenic nature of psychiatric disorders and treatment response, small numbers of studies and effect sizes, and lack of controls for other genetic and non-genetic factors. Observers have thus not supported incorporating these tests into clinical guidelines (Singh et al., 2014). The Sundance test purporting to predict suicidality, for instance, is based on a study of only 32 patients with treatment emergent suicidal ideation (TESI) vs. 365 other patients. The researchers assayed over 400,000 single nucleotide polymorphism (SNPs), and identified 79 that had a 91% probability to classify TESI in a replication sample – though none of the SNPs achieved genome-wide significance (Menke, 2012).

The utility of these tests may also be limited in particular patient's treatment, since a patient's specific responses to a medication (e.g., benefits, side effects or non-response) should, arguably, guide the psychiatrist's decisions more than genetic markers alone.

But despite the lack of sufficient evidence demonstrating clinical utility, companies are currently continuing to market these tests to physicians, who often have limited understandings of genetics (Klitzman et al., 2013), and may thus accept, rather than question these companies' claims. Among psychiatrists, 14% have ordered a genetic test in the past 6 months; 41.6% have had patients ask about genetic testing in the last six months; 28.6% had received advertisements from genetic testing labs; but only 23.9% had a geneticist/genetic counselor to whom to refer patients (Salm et al. 2013).

These issues need fuller discussion and examination. Most importantly, it is critical that clinicians and researchers be as aware as possible of potential limitations concerning genetic tests in psychiatry. These issues deserve consideration both to help advance science, and to ensure that clinical care is based upon scientific evidence and benefits patients as much as possible.

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## References

- AssureRx Health Launches Personalized Medicine Test for ADHD. May 7. 2012 cited 15 June 2015) Available from: <http://assurexhealth.com/assurerox-health-launches-personalizedmedicine-test-for-adhd/>
- Betancur C. Etiological heterogeneity in autism spectrum disorders: more than 100 genetic and genomic disorders and still counting. *Brain Res.* 2011; 1380:42–77. [PubMed: 21129364]
- Burmeister M, McInnis MG, Zöllner S. Psychiatric genetics: progress amid controversy. *Nat Rev Genet.* 2008; 9:527–540. [PubMed: 18560438]
- Clinical Laboratory Improvement Amendments (CLIA). 2015. modified 5 March 2015; cited 15 June 2015) Available from: <https://www.cms.gov/Regulations-and-Guidance/Legislation/CLIA/index.html?redirect=/clia/>
- Dolgin, E. Clinical efficacy data on gene tests trails marketing in psychiatry. Aug 6. 2012 cited 15 June 2015 Available at: <http://www.nature.com/nm/journal/v18/n8/full/nm0812-1161.html>
- Evaluation of Genomic Applications in Practice and Prevention (EGAPP). 2009. updated 25 November 2014; cited 15 June 2015) Available from: <http://www.egappreviews.org/default.htm>
- The Federal Drug Administration. 2015. updated 12 June 2015; cited 15 June 2015) Available from: <http://www.fda.gov/>
- Genomind. 2015. updated 12 June 2015; cited 15 June 2015) Available from: <http://genomind.com/>
- F. Hoffmann-La Roche Ltd. The AmpliChip CYP450 Test. 2015. cited 21 May 2015 Available from: <http://www.roche.com/products/productdetails.htm?type=product&id=17>
- Klitzman R, Chung W, Marder K, Shanmugham A, Chin LJ, Stark M, Leu CS, Appelbaum PS. Views of internists towards uses of PGD. *Reprod Biomed Online.* 2013; 26(2):142–147. 2013. [PubMed: 23276655]
- Malhotra AK, Zhang JP, Lencz T. Pharmacogenetics in psychiatry: translating research into clinical practice. *Mol Psychiatry.* 2012; 17:760–769. [PubMed: 22083729]
- Menke A, Domschke K, Czamara D, Klengel T, Hennings J, Lucae S, Baune BT, Arolt V, Müller-Myhsok B, Holsboer F, Binder EB. Genome-wide association study of antidepressant treatment-emergent suicidal ideation. *Neuropsychopharmacology.* 2012; 37(3):797–807. [PubMed: 22030708]
- Proove Biosciences. 2015. updated 20 May 2015; cited 21 May 21, 2015) Available at: <https://proove.com/>

- PR Newswire. [Accessed June 15, 2015] Sundance Diagnostics Developing Antidepressant Suicide Risk Test. Dec 12, 2013 cited 21 May 2015 Available from: <http://www.prnewswire.com/newsreleases/sundance-diagnostics-developing-antidepressant-suicide-risk-test-235558151.html>
- Salm M, Abbate K, Appelbaum P, Ottman R, Chung W, Marder K, Leu CS, Alcalay R, Goldman J, Curtis AM, Leech C, Taber KJ, Klitzman R. Use of genetic tests among neurologists and psychiatrists: knowledge, attitudes, behaviors, and needs for training. *J Genet Couns*. 2014; 23(2): 156–163. [PubMed: 23793969]
- Serretti A, Kato M, De Ronchi D, Kinoshita T. Meta-analysis of serotonin transporter gene promoter polymorphism (5-HTTLPR) association with selective serotonin reuptake inhibitor efficacy in depressed patients. *Mol Psychiatry*. 2007; 12:247–257. [PubMed: 17146470]
- Singh AB, Bousman CA, Ng C, Berk C. Antidepressant pharmacogenetics. *Curr Opin Psychiatry*. 2014; 27:43–51. [PubMed: 24270480]
- Thomas RE, Chau SB. The AmpliChip: a review of its analytic and clinical validity and clinical utility. *Curr Drug Saf*. 2015; 10(2):113–124. [PubMed: 24809462]
- Zhang JP, Lencz T, Malhotra AK. D2 receptor genetic variation and clinical response to antipsychotic drug treatment: a meta-analysis. *Am J Psychiatry*. 2010; 167:763–772. [PubMed: 20194480]