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EDITORIAL

Response to the SAMHSA Clinical Advisory: Considerations for Genetic Testing in the Assessment of Substance Use Disorder Risk

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Introduction

Substance Use Disorders (SUDs) are a public health crisis affecting over 20 million individuals annually in the United States, with profound social, economic, and health impacts.[1] Addressing this crisis requires innovative approaches that integrate advances in genetic research and technology. Genetic testing offers a pathway to personalized medicine, enabling clinicians to predict addiction risk, tailor treatments, and challenge stigmatizing views of SUD as a moral failing rather than a neurobiological condition.

The December 2024 SAMHSA Clinical Advisory provides valuable guidelines but also highlights the complexity of SUD as a multifactorial disorder influenced by genetic, environmental, and psychosocial factors. This paper expands upon the advisory, addressing critical methodological gaps, refining the role of genetic testing, and advocating for a more robust and equitable framework for integrating genetic insights into SUD care.

Genetic Testing as a Tool Against Stigma

Stigma remains a pervasive barrier to effective SUD treatment. Societal misconceptions that addiction is a moral failing perpetuate shame and discourage individuals from seeking help. Genetic testing provides compelling evidence that addiction is a brain disease influenced by genetic and neurobiological factors.[2] By demonstrating a clear genetic component, testing can transform perceptions among patients, families, and the broader public, fostering a compassionate, science-based understanding of addiction.

Addressing Denial in Patients

One of the most transformative applications of genetic testing lies in its ability to address denial, a hallmark of addiction. Many patients resist acknowledging their condition due to stigma or misconceptions. Genetic evidence offers objective proof of predisposition, helping patients understand that their condition is not a moral failing but a genetically driven brain disease.[3] This clarity often fosters acceptance, reduces shame, and opens the door to effective treatment.

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Educating Families

Families play a crucial role in supporting individuals with SUDs. However, they often struggle to reconcile addiction with moral or behavioral judgments. Genetic testing serves as a powerful educational tool, helping families grasp the biological basis of addiction. By shifting the narrative from blame to understanding, families are better equipped to provide compassionate, informed support.[4]

Fighting Legal Stigma

The misconception that addiction is a moral failing rather than a neurobiological condition has profoundly influenced the legal system, contributing to the widespread incarceration of individuals with SUDs. Genetic testing is the most potent tool for reframing addiction as a genetically driven brain disease, undermining the rationale for punitive legal approaches. By demonstrating the biological underpinnings of addiction, genetic testing provides critical evidence that supports treatment-focused interventions over incarceration.[5] This shift is essential for dismantling the legal-industrial complex's reliance on punitive measures and advancing a public health approach to addiction.

Challenges With Current Comparative Frameworks in Addiction Research

Limitations of Comparative Populations

A fundamental limitation in addiction genetics research is the choice of comparative populations. Current studies often compare individuals diagnosed with SUD against the general population. This approach underestimates genetic contributions to addiction, as it includes individuals who may not have been sufficiently exposed to addictive substances or environmental stressors to activate their genetic predispositions.[6] These groups include:

1. Individuals who have not been exposed to addictive substances.
2. Individuals with insufficient exposure to trigger addiction.
3. Individuals who, despite genetic vulnerabilities, have benefited from protective environmental factors.

By failing to control these variables, such frameworks dilute findings and lead to an underestimation of addiction heritability. For instance, the inclusion of undiagnosed individuals who may later develop SUD further confounds results.[7]

Over-Diagnosis and Diagnostic Noise

Additionally, diagnostic criteria for SUD, particularly in mild and moderate cases, often lack precision and objectivity. There is a well-documented trend toward over-diagnosis, influenced by subjective assessments and treatment-provider biases.[8] This issue disproportionately affects studies comparing diagnosed populations, where individuals with minimal genetic burden may inflate variance estimates.

The DSM-5-TR categorizes SUD into mild, moderate, and severe. For genetic studies, only severe cases—those most likely to reflect neurobiological underpinnings—should be included to establish meaningful associations between addiction and genetic risk.[9]

Reward Deficiency Syndrome: A Framework for Understanding Addiction

Reward Deficiency Syndrome (RDS), a term coined by Blum et al, provides a robust neurobiological framework for understanding addiction. RDS describes dysfunctions in the brain's dopamine reward system, contributing to conditions like SUDs, ADHD, and impulse control disorders.[10] This framework emphasizes the role of hypodopaminergic function in addiction risk, integrating genetic, neurochemical, and environmental factors.

Genetic Markers and RDS

Genetic testing targeting RDS-related markers has identified polymorphisms in dopamine receptor genes (eg, DRD2 Taq1A) as significant predictors of addiction risk. Studies demonstrate that individuals with these genetic variants are at heightened risk for SUDs, particularly when exposed to high-stress environments or addictive substances.[11]

Genetic Addiction Risk Score (GARS™) and Opioid Use Disorder Testing

The Genetic Addiction Risk severity (GARS®) test is a predictive tool developed to assess genetic vulnerability to addiction. GARS evaluates variations in genes involved in the brain reward cascade, focusing on dopaminergic function and its role in behavioral regulation.[12] By analyzing a simple cheek swab, GARS provides clinicians with actionable insights for tailoring prevention and treatment strategies.[13]

Opioid Use Disorder Genetic Testing

While potential infringement of GRAS patents, Advertd's Opioid Use Disorder (OUD) test represents another advancement in personalized medicine. This test identifies genetic markers associated with opioid addiction, enabling early intervention for individuals at risk. Studies have shown it has potential to improve treatment outcomes and reduce relapse rates among high-risk populations.[9,13–15]

Breaking Through Denial and Enhancing Treatment

One of the most transformative applications of genetic testing is its ability to address denial, a hallmark of addiction.[16] Patients often resist acknowledging their condition due to stigma or misconceptions. Genetic evidence demonstrating a biological predisposition can foster acceptance and reduce shame, encouraging engagement in treatment.[17,18]

Conclusion

Genetic testing represents a pivotal advancement in SUD care, offering insights that challenge stigma, improve diagnostics, and enable personalized interventions. By demonstrating the genetic basis of addiction, these tools foster acceptance among patients, understanding among families, and compassion in societal attitudes. Furthermore, genetic testing is the most powerful tool available for shifting the narrative away from punitive legal approaches toward treatment-focused solutions. By reframing addiction as a chronic, genetically driven brain disease, genetic testing provides the foundation for a public health response to the addiction crisis. However, the integration of genetic testing must be guided by ethical considerations, rigorous validation, and equitable access. As the science evolves, clinicians, policymakers, and researchers must collaborate to harness the potential of genetic testing in transforming addiction treatment. Finally, with due respect, the SAMHSA Clinical Advisory: Considerations for Genetic Testing in the Assessment of Substance Use Disorder Risk, should be more rigorous and thoughtful in promoting unsound messages to the field at large.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

RPG reports personal fees from Precision Recovery, outside the submitted work. KB owns both domestic and foreign patents related to GARS testing (a patent 10,894,024 licensed to SYNAPATAMINE, a patent 10,072,284 licensed to SYNAPATAMINE, a patent 3,187,080 licensed to SYNAPATAMINE, a patent 20718485.4 pending to SYNAPATAMINE). He also reports licensing to VNI, personal fees for consultancy from PEAK LOGIC, SUNDER FOUNDATIION, SPINE CLINICAL ARIZONIA; CEO genetic testing for TRANSPLICEGENE HOLDINGS, during the conduct of the study. The authors report no other conflicts of interest in this work.

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