SAMHSA
Substance Abuse and Mental Health Services Administration

CLINICAL ADVISORY

DECEMBER 2024

CONSIDERATIONS FOR GENETIC TESTING IN THE ASSESSMENT OF SUBSTANCE USE DISORDER RISK

Introduction

Substance use disorders (SUDs) are chronic relapsing health conditions characterized by continued substance use despite negative consequences. Deaths arising from these disorders have reached epidemic levels in the United States – in 2023, 48.5 million people aged 12 or older met criteria for SUD in the past year.[1] According to the National Survey on Drug Use and Health, in 2023, 5.3 million people misused prescription pain relievers, and 3.9 million people misused prescription stimulants.[2]

The potential for SUDs to occur is multifaceted – SUDs are products of genetic, biologic, and environmental influences. SUDs occur in individuals from all educational and socioeconomic backgrounds, and long-term vulnerability is mediated by a complex interplay of genes, environmental impacts, and biopsychosocial factors. Childhood trauma, mental illness, reduced access to resources, lack of opportunity, and social isolation can all raise one's susceptibility.[3] On the other hand, access to education, employment, housing, substance use prevention and recovery support services, and mental health services can foster resilience and reduce risk.

Research shows that some people who misuse prescription medications go on to develop a SUD.[4] This can be curtailed through patient-centered care that includes comprehensive screening and shared decision-making prior to the first prescription being issued. Prior to prescribing medications with potential for misuse, guidelines[5] recommend that practitioners use validated screening tools, many of which are freely available, to assess for potential risk factors. It is also recommended that practitioners combine information from screening tools with Prescription Drug Monitoring Program (PDMP) data and toxicology screening, as appropriate, to assess for concurrent substance use that might place patients at higher risk for use disorders or harms such as overdose.[6] Practitioners should also provide specific counseling on increased risks for harm when prescribed medications are combined with other drugs or alcohol, as well as ensuring that patients have access to naloxone or other opioid overdose reversal medications and receive effective treatment for SUDs, if needed.

Studies have demonstrated that SUDs have a hereditary component, with genetic risks accounting for 40-70% of vulnerability.[7] Based on this, there is growing interest and research on genetic tests that may predict vulnerability to developing an SUD. Such tests represent a growing awareness of the potential for personalized medicine within the addiction space, with important questions arising about their role and use.

Key Messages

- Substance use disorder risk reflects an interplay of genetic, environmental, and psychosocial factors, highlighting the need for comprehensive, multidimensional risk screening and whole-person care.
- In the absence of appropriate clinical guidelines and safeguards to ensure responsible and equitable use, SAMHSA recommends against routine use of genetic testing as the sole indicator of substance use disorder risk in clinical practice.
- While genetic testing provides useful insights, it is potentially most effective when used alongside established tools to support multidimensional risk assessment.
- Privacy protections, informed consent, and careful implementation are essential to ensure genetic testing is used responsibly and equitably.
- Integrating genetic testing with validated tools and biopsychosocial evaluations ensures patient-centered care and informed clinical decisions.
- Ongoing research and clear guidelines are critical to responsibly incorporating genetic testing into SUD prevention and treatment.

The Substance Abuse and Mental Health Services Administration (SAMHSA) improves access to reliable and valid information on evidence-based practices, including information on the strength of evidence associated with such practices. This Advisory reviews evidence underlying the practice of genetic testing in assessment of vulnerability to SUDs and discusses the practice of using such tests in clinical practice. In the absence of appropriate guidelines and safeguards to ensure responsible and equitable use, SAMHSA recommends against routine use of genetic testing as the sole indicator of SUD risk in clinical practice. This Advisory reiterates the importance of patient-centered care that includes comprehensive and multidimensional screening, shared decision-making, and regular follow-up. A single test or screen should not constitute the sole piece of information in decision-making, and care should be taken to avoid harm to patients or to exacerbate existing disparities in access to treatment.

The Landscape of Substance Use Disorders

According to data from the Centers for Disease Control and Prevention (CDC), over 75% of the nearly 108,000 drug overdose deaths in 2022 involved an opioid.[8] Synthetic opioids (primarily illegally made fentanyl) continue to be the principal driver of overdose deaths, increasing 55 percent from 2019 to 2020 and further increasing 26 percent from 2020 to 2021.[9] Overdose deaths involving stimulants increased by 32 percent from 2020 to 2021, and the rate in 2022 was 12.3% higher than the rate in 2021.[10] These deaths are often linked to co-use or mixing (by illicit producers) of cocaine or methamphetamine with illegally made fentanyl or heroin.[11]

A recent analysis by the CDC demonstrates high rates of overdose among Black or African American, American Indian, and Alaska Native communities over the course of the last few years, particularly during the COVID-19 pandemic.[12] While these trends existed long before the COVID-19 pandemic, this study highlights that overdose death rates rose 44% in 2020 for Black or African American people and 39% for American Indian and Alaska Native people, compared with 22% for White people. Black or African American youth aged 15 to 24 saw an 86% increase in overdose deaths, the largest spike of any age or racial and ethnic group, while Black or African American men 65 and older were nearly seven times as likely than White men 65 and older to die from an overdose. A separate study found that Black or African American people were less than half as likely as White people to have received SUD treatment. [13]

Research has also demonstrated that people of color are more likely to be viewed and treated with suspicion when it comes to pain management and being prescribed opioids when clinically indicated.[14] A recent systematic review found that minoritized racial and ethnic groups prescribed opioids for chronic non-cancer pain were subject to more scrutiny and monitoring and were more likely to have prescription opioids discontinued in response to positive drug tests compared to White groups.[15] Whether across SUDs or pain management and opioids, these disparities are driven by the inequitable distribution of resources due to historical and ongoing structural inequities, stigma, inadequate education at professional and medical schools, practitioner hesitancy, and, in some cases, restrictive state laws. It also amplifies the importance of allocating limited resources toward broadening the reach of existing, evidence-based interventions and avoiding interventions that further clinical disparities and stigma.

The Limitations and Risks of Genetic Testing

Estimates from some genetic epidemiology studies indicate that genes may account for between 40-70% of the vulnerability to SUD, including opioid use disorder (OUD).[8, 15, 16] However, identifying specific genetic variants for increased vulnerability to SUD has been difficult, which likely reflects the fact that SUD, similar to other psychiatric disorders, is a disease that involves multiple, interacting genes. Furthermore, vulnerability to use disorders is not reliant on genes alone. Widely available and validated screening tools for opioid and other substance misuse are more robust and comprehensive than a single genetic risk test result, since they are based on self-reporting of multiple risk factors, such as personal and family history of substance misuse and use disorders, age, presence of psychiatric disorders, and history of preadolescent sexual abuse, among other factors.

At the same time, predictive tools that use genetic samples to identify at-risk individuals for prevention and early intervention are being developed or have received FDA approval for use.[17] Gene variants (for example, those impacting dopamine and serotonin regulation) are routinely used in prediction tools for addiction vulnerability, despite scientific consensus regarding the weaknesses inherent to selection of candidate genes for complex traits.[18, 19, 20] To this end, OUD is a chronic disease with a large number of variants of small effect contributing to its inheritability. One of the largest genome-wide association studies of OUD to-date (15,756 OUD cases and 99,039 controls) identified only one variant with a significant association to OUD.[21] This study also demonstrated that the effect size associated with this variant was 11%, putting a limit on overall predictive ability. As a result, researchers have suggested that the addition of polygenic risk scores to existing non-biologic screening tools may add little clinical benefit to a clinical/environmental risk approach for SUD.[22] Genetic risk assessment for SUDs is still in the early stages of development, and testing has not yet been widely incorporated into clinical practice. Individuals and their providers face other potential hurdles:

- **Potential For Racial or Ethnic Bias and Disparities**: When markers used by genetic tests exhibit substantial frequency differences across populations, these could bias results. Individuals with SUD may be protected under Federal disability nondiscrimination laws when the drug addiction substantially limits a major life activity.[23] In addition, Section 1557 of the Affordable Care Act prohibits discrimination on the basis of race, color, national origin, sex, age, or disability through the use of patient care decision support tools.[24] If practitioners are basing their prescribing decisions solely on the results of such genetic tests, certain racial or ethnic groups could be unjustly denied necessary treatment or, conversely, be overprescribed due to these genetic differences.

- **Ethical Concerns**: Any test that has potential biases can lead to unjust practices in healthcare. If certain groups are more likely to test positive due to inherent biases in the genetic markers used, they could be unjustly denied opioids for pain relief or stimulants

for Attention Hyperactivity Deficit Disorder based on an inaccurate assessment of addiction risk. This can lead to ethical dilemmas in providing equal and fair treatment to all patients.

- **Privacy Concerns**: While the Genetic Information Nondiscrimination Act (GINA) protects individuals against discrimination based on their genetic information in health coverage and in employment, people with SUDs are frequently stigmatized. Outside of current privacy protections, any information pertaining to SUDs and vulnerability is sensitive, and there is always a risk genetic test results could be misused or misinterpreted. This can lead to further stigma, particularly for those identified as "high risk," despite GINA and other privacy protections.
- **Predictive Limitations**: Based on the limitations of a test and the complex nature of addiction, overreliance on single genetic risk assessments might offer a false sense of security. Given the current understanding of SUD genetics, a test that includes relatively few markers cannot solely and definitively predict vulnerability for SUD. Misplaced confidence in such a test can lead to inadequate risk assessment and possibly detrimental clinical decisions.
- **Lack of Large, Well-Controlled Studies**: The existing research for genetic testing for SUD risk is mostly based on small, non-randomized studies with significant variability in results. Therefore, these results should be interpreted with caution and may benefit from being validated in larger and more diverse populations.[25]
- **Lack of Comparative Studies**: Current, non-biologic screening tools are based on self-reporting of factors, such as personal and family history of substance misuse and use disorders, age, presence of other psychiatric disorders, and history of preadolescent sexual abuse, among other factors. These screening tools have undergone study and validation. Testing genetic evaluations of vulnerability to SUDs against these established tools in large, randomized controlled trials will be important to scientifically assess clinical utility and how they impact clinical decision-making, as well as potential drawbacks.
- **Cost and Accessibility**: The cost of genetic testing can range from $100 to more than $2,000, depending on the nature and complexity of the test.[26] The cost of current pharmacogenetic testing may limit access and potentially contribute to existing disparities in care.[27]
- **Lack of Standardized Guidelines**: There are no universally accepted clinical guidelines for applying genetic test results in the primary prevention of SUDs, posing challenges for healthcare providers.[28]

Safeguards and Additional Research Are Needed

While emerging approaches like genetic tests for vulnerability to SUDs may enhance risk prediction, several ethical and practical safeguards must be addressed before widespread clinical adoption is warranted. Given the interplay of genetic, biological, and environmental factors on development of SUDs, test results should only comprise one part of a comprehensive risk assessment. Using any screening tool in isolation could produce misleading results and lead to misguided clinical decisions. Appropriate informed consent processes are also essential to ensure patients understand limitations and potential consequences prior to testing. For example, risk scores indicating higher genetic susceptibility for OUD should not automatically preclude pain treatment with opioids, if deemed medically necessary. Until further evidence and

guidelines emerge, test integration into care plans should focus on providing additional risk information rather than restricting options.

Perhaps most crucially, demonstrating that use of genetic tests improves patient outcomes remains imperative. Analyses should seek to confirm that clinical benefits outweigh any unintended harms, such as further stigmatization or displacement of resources from evidence-based practices. If such technologies are implemented cautiously with necessary safeguards, they may support prevention and early intervention efforts. More rigorous comparative effectiveness studies are needed within representative clinical settings to truly gauge real-world utility.[29] Ongoing scrutiny of ethical, legal, and social implications also warrants consideration moving forward.

The integration of genetic testing into clinical settings calls for development of best practices that speak to responsible use. These guidelines must safeguard against overreliance on genetic data, ensuring that genetic testing is used as an adjunct to, not a replacement for, comprehensive clinical assessment.[30] Guideline creation must also include those with lived experience.[31] As this technology advances, it is important to evaluate not only its effectiveness but also its ethical implications. This dual assessment will address issues such as potential biases and the impact of socioeconomic factors on access to testing.[32]

Moreover, there is an urgent need for policies that tread the fine line between preventing misuse and harnessing the benefits of genetic testing. Such policies should aim to protect patient privacy and avoid discrimination while ensuring that genetic testing contributes positively to patient outcomes.[33] To this end, the clinical integration of genetic testing requires clear, evidence-based guidelines that can offer healthcare providers a framework for incorporating test results into a holistic care strategy.[34]

It is imperative for professional societies, practitioners, patients, and those with lived experience to engage in a collaborative effort to ensure that emerging genetic tests are introduced into clinical practice with scientific rigor and ethical integrity, ever mindful of the real and diverse lives they aim to impact. Universal guidelines are required to ensure rigorous patient protections and to promote equitable application of new technologies.

Next Steps

As part of efforts to mitigate the impact of SUDs, genetic testing offers potential for more personalized health care. However, this must be tempered by the substantial limitations that currently exist in the application of this technology. The predictive power of genetic testing for vulnerability to the development of SUDs is still in its infancy, with much of its promise yet to be fully realized. This early stage of development underscores the need for genetic testing to be used cautiously, and as one part of broader and person-centered decision-making. Robust protections against misuse are essential to prevent unintended negative consequences, such as the exacerbation of health disparities or encroachments on personal privacy.[35] As such, genetic testing should be implemented with caution, ensuring that it supports, rather than undermines, the principles of equity and beneficence in healthcare.

To responsibly advance the role of genetic testing in predicting those individuals that may be vulnerable to an SUD, continuing to develop a substantial evidence base is important. It is imperative that the impact of genetic testing be monitored closely through rigorous, long-term studies that can provide a clearer picture of its effectiveness and clinical utility.[36] Only through additional research and a commitment to ethical standards can the healthcare community navigate the complexities of genetic testing, steering it toward becoming a beneficial tool in efforts to overcome the overdose crisis, while safeguarding against potential risks. As the

science evolves, so too must our strategies for implementation, ensuring that genetic testing serves as an additional evidence-based tool in patient care.

While there is substantial interest in personalized medicine, navigating the integration of genetic tests, particularly into efforts to predict SUDs, necessitates a cautious and well-planned approach. A strategy that prioritizes ongoing research, responsible and equitable use, ethical considerations, and robust policy frameworks is crucial to ensure these tests are used appropriately and without harm to vulnerable patients. To achieve this aim, SAMHSA recognizes the important role that stakeholders will play in the following areas:

- **Evaluation:** The validity and clinical utility of a genetic test that indicates vulnerability to SUDs may merit rigorous and longitudinal evaluation across diverse populations and genetic backgrounds.[37] It is essential to understand a test's accuracy in predicting SUD risk, the potential for false positives and negatives, potential inferiority or superiority, and how these may vary with individual differences.[38] Studies exploring effectiveness in guiding preventive measures and treatment decisions are central to establishing clinical utility.

- **Clinical Guidelines:** Health care professionals must rely on clinical guidelines that explicitly direct the interpretation of test results and their integration into patient care.[39] Guidelines should emphasize that genetic tests are only one component of a complex assessment and that they should not be used in isolation.[40] Comprehensive assessments, including environmental and biopsychosocial factors, alongside genetic information, are critical for forming a holistic picture of individual risk and tailoring evidence-based interventions. Additional guidance should be provided on how to counsel patients related to test results and include specific clinical scenarios in which genetic testing for vulnerability to SUDs is appropriate. Ultimately, clinical guidelines should be used to consider acceptable use cases, limit discriminatory practices based on genetic information, and support oversight mechanisms to prevent misuse.

  Healthcare institutions and practitioners need protocols for interpreting test results, communicating them to patients in a sensitive and informative manner, and incorporating them into personalized treatment plans alongside other relevant factors. Without clear and consistent approaches, the risks of confusion, misinterpretation, and ineffective interventions rise significantly.

- **Ethical and Legal Considerations:** The potential for genetic discrimination against individuals with or at risk for SUDs is significant, and measures to mitigate risk must be prioritized.[41] 42 CFR part 2 recognizes the sensitivity of SUD patient information and protects those in certain treatment settings from discrimination, particularly from law enforcement or the courts.

  Robust genetic counseling practices and informed consent procedures are also essential to ensure patients understand the potential benefits and limitations of a test without feeling pressured or stigmatized. Furthermore, a test's accessibility and affordability need careful consideration to avoid exacerbating existing health disparities.

Conclusion

By prioritizing ongoing research, responsible use, and ethical practices, healthcare practitioners might ensure that genetic tests become tools for empowering individuals and safeguarding their well-being in the face of SUD vulnerability. With careful navigation and a commitment to patient-centered care, these tests have the potential to be a useful piece of data in comprehensive and multidimensional risk assessments.

Resources for Providing Comprehensive, Patient-Centered Care

Patients across settings, those with SUDs or a vulnerability to use disorders require compassionate, whole person care that is evidence-based and equitable. Practitioners play a vital role in ensuring these principles through the provision of care that considers the entirety of an individual's medical and personal history. This is of particular importance for those who may be vulnerable to SUDs. Practitioners should consider the following issues when caring for individuals.

- **Screening for substance use disorders.** Screening for SUDs should be a part of each patient visit. Screening does not take long, and it should be delivered in a compassionate and evidence-based manner. SAMHSA provides resources on screening for SUDs, as well as how to be reimbursed for certain screening activities on its SBIRT Webpages.

- **Screening may reveal the presence of an SUD**. If a patient is found to have an undiagnosed SUD it is important to discuss this with them and to offer help in a person-centered manner. By ensuring effective informed consent and tailoring treatment plans to align with patients' unique needs and preferences, healthcare providers can foster therapeutic rapport, optimize treatment efficacy, and ultimately contribute to more successful and sustainable recovery trajectories. For more information on treating opioid use disorders, see SAMHSA's TIP 63 - Medications for Opioid Use Disorder. Information on treating stimulant use disorders can be found in TIP 33 - Treatment for Stimulant Use Disorders. Information on treating alcohol use disorder is available in SAMHSA's Advisory on Prescribing Pharmacotherapies for Patients With Alcohol Use Disorder. Information on treating co-occurring disorders can be found in TIP 42 - Substance Use Treatment for Persons With Co-Occurring Disorders.

- **Pain management is more than a prescription.** Individuals might require pain management for acute pain or for co-existing chronic pain conditions. In some instances, people with a history of SUDs require controlled medications for pain, and this can be accomplished as part of evidence-based, compassionate, and personalized care. In all cases, management of pain should include a patient-centered and multidisciplinary approach that includes allied health team members and support and interventions that address the experience of the individual's pain. SAMHSA's TIP 54: Managing Chronic Pain in Adults With or in Recovery From Substance Use Disorders provides helpful advice on pain management among those with a history of SUDs. The CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022 is another comprehensive resource.

- **Harm reduction can save lives.** Harm reduction is an evidence-based approach that is critical to engaging with people who use drugs and equipping them with life-saving tools and information to create positive change in their lives and potentially save their lives. This approach meets people where they are and provides access to services and supports such as opioid overdose reversal medications, including naloxone and nalmefene, overdose prevention education, and substance testing kits, as well as education to reduce risk of infectious disease transmission through injection drug use. Harm reduction also emphasizes patient education and navigation to services that prevent or limit infectious disease transmission. Further information can be found on SAMHSA's Harm Reduction Webpages.

- **Biological specimen testing is not punitive**. The use of biological specimen test results, obtained after appropriate patient education and informed consent, holds

significant value for informing clinical decision-making with respect to patient safety, as opposed to punitive applications. By providing objective data on a patient's vulnerability to a disorder or substance use patterns, these tests can guide healthcare providers in adjusting treatment strategies, ensuring appropriate interventions and monitoring patient progress, all while considering the individual's unique needs and risk factors. Using test results to engage in a conversation with the patient and prioritize patient safety helps to establish trust, promote transparency, and facilitate a more effective rapport, ultimately enhancing treatment outcomes and mitigating potential adverse consequences. Further information about biological specimen testing can be found in TAP 32 – Clinical Drug Testing in Primary Care.

- **People seeking care may also have other health issues**. Practitioners should work with patients to ensure access to additional health services as needed. Indeed, those with SUDs may have physical or mental health conditions that they wish to be addressed. Additionally, they may request counseling or might need family therapy. For more information about referral centers in your local area, see FindTreatment.gov and FindAHealthCenter.gov. Additional information on family therapy can be found in SAMHSA's Advisory on The Importance of Family Therapy in Substance Use Disorder.

- **Additional Supports**. Individuals with a vulnerability to SUDs may require referral to additional supports, such as vocational counseling, case management, and recovery supports. For more information on employment and recovery, see Substance Use Disorders Recovery with a Focus on Employment and on SAMHSA's Recovery Webpages.

- **Caring for people with SUDs is empowering for the provider and patient**. Many primary care and behavioral health providers would benefit from expanding their skills and knowledge about evidence-based interventions to prevent and treat SUDs, medications to treat OUD and alcohol use disorder, and additional resources to support patients with SUDs. In December 2022, the requirement to obtain a special waiver to prescribe buprenorphine for OUD was lifted. Now, where state law allows, any practitioner with a valid state license and DEA registration to prescribe Schedule III medications may prescribe buprenorphine for OUD. This expands opportunities to provide care and the ability to provide treatment to those with OUD across different settings. For more information on removal of the Data-Waiver, see SAMHSA's Website.

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SAMHSA CLINICAL ADVISORY

Acknowledgments: This Advisory was developed by U.S. Department of Health and Human Services, Substance Abuse and Mental Health Services Administration (SAMHSA), Center for Substance Abuse Treatment.

Recommended Citation: Substance Abuse and Mental Health Services Administration. *Considerations for Genetic Testing in the Assessment of Substance Use Disorder Risk. Clinical Advisory*. Publication No. PEP24-02-014. Rockville, MD: Substance Abuse and Mental Health Services Administration. 2024.

Publication No. PEP24-02-014
Released 2024