

registries to track outcomes, adverse events, patient complaints, and feedback. Funds should also be earmarked for investigator-initiated pragmatic trials in off-label or alternative clinics.

With high public enthusiasm, extremely bullish investors, and hundreds of newly established brain wellness clinics, all the pieces are now in place for expansive off-label promotion and use of

psychedelics to quickly mushroom beyond what is safe. While off-label use may be a useful way to provide access to promising treatments, it must be done responsibly and with an eye toward future evidence-based advancements in medical science; regulators, policy makers, and health authorities must carefully examine and create guardrails for the promotion and off-label use of psychedelics.

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VIEWPOINT

Preaddiction—A Missing Concept for Treating Substance Use Disorders

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Despite decades of federal funding to develop and deliver treatments for individuals with serious addictions, treatment penetration rates are less than 20%.¹ Facing a similar situation, the diabetes field increased treatment penetration and impact by identifying and intervening with early-stage diabetes, termed *prediabetes*. We use this example to illustrate the essential elements of this strategic clinical approach and discuss the changes that will be required within the substance use disorder (SUD) field to implement an analogous strategy. We suggest the *DSM-5* diagnostic categories mild to moderate SUD as a starting operational definition for the term *preaddiction*, a commonly understood, motivating term that could engender broader clinical efforts to effect that strategy.

Background

The centuries-old term *addiction* remains widely used in both professional and popular media because it communicates commonly held imagery of those whose once-promising lives were ruined by their uncontrolled use of substances, such as alcohol, opioids, or stimulants. In the scientific literature, addiction was once considered a personality disorder and later, the manifestation of tolerance and withdrawal from hard drug use. However, scientific findings now

suggest impaired control as the core defining diagnostic construct, hypothesized to be the result of gradual use-related damage to brain circuits controlling reward sensitivity, motivation, self-regulation, negative emotional states, and stress tolerance.²

Among those who initiate alcohol or other drug use, progression to serious SUD is not common. When it does occur, the progression is rarely linear or rapid,³ usually following years of harmful misuse that by itself is a serious personal and public health threat.¹ Adolescence is a particularly risky period for transition from use to disorder, likely owing to heightened sensitivity of still-developing brain circuits. Those adolescents at highest risk of transition have earlier onset of use, history of traumatic events, family history of substance use, and/or mental health problems.³ Two points here are important. First, the long latency from use to disorder offers a significant window of opportunity for clinical interventions to stop progression. Second, early-stage harmful substance misuse is a pervasive, costly, and serious public health risk in itself.¹

Recognizing that transition to serious SUD can be progressive but variably manifested, the *DSM-5*⁴ uses 11 equally weighted symptoms of impaired control to define SUDs along a 3-stage severity continuum. The common name *addiction* is reserved for severe SUD, defined

by 6 or more symptoms and found in approximately 4% to 5% of adults. Those with mild to moderate SUD (ie, 2-5 symptoms) comprise a much larger proportion of the adult population (13%) and thus account for far more substance use-related harms to society than those with severe SUD (ie, addiction).^{1,4}

However, treatment efforts and public health policies have focused almost exclusively on those with serious, usually chronic addictions, virtually ignoring the much larger population with early-stage SUDs. Although harmful substance misuse and early-stage SUDs can be identified and severity progression monitored, very little has been done, especially where it is most common, in mainstream health care settings. Indeed, neither clinicians nor the public even have a commonly understood name for early-stage SUD.

Lessons Learned From Type 2 Diabetes: the Role of Prediabetes

Historically, the type 2 diabetes field also focused on the most severely affected, also experiencing treatment resistance, poor adherence, and guarded prognoses.⁵ However, in 2001, the American Diabetes Association strategically suggested the term *prediabetes*, operationally defined by elevated scores on 2 laboratory tests: impaired glucose tolerance and impaired fasting glucose. The term was purposely chosen to capitalize on public motivation to avoid serious diabetes.⁵ Advertising campaigns followed to raise public awareness and advocate for policy change. Partnerships with health care organizations and insurers led to creation and testing of new medications and interventions more appropriate to early-stage cases. Although type 2 diabetes continues to be a serious, pervasive health problem, the strategy has shown increased risk detection rates, shortened delays between symptom onset and treatment entry, and success in halting progression to diabetes.⁶

Could This Strategy Work With SUDs?

Intervening early is not a new concept, nor is it easy to implement. The diabetes field likely succeeded owing to a broad, well-organized, and sustained strategy applied concurrently at the clinical, public, and policy levels. If an analogous approach is to be effective in the SUD field, it will require similarly integrated efforts in 3 important areas.

Measures to Define and Detect Preaddiction | The diabetes field already had easy-to-use, insurance-reimbursed laboratory tests to define and detect prediabetes. No such objective tests are yet available in the SUD field, but efforts are underway to better characterize the neurofunctional domains indicating predisposition to addiction and its clinical course.⁷ Meanwhile, *DSM-5* diagnoses are reliable and could be implemented in many clinical settings. The criteria defining mild to moderate SUD are one reasonable starting point for operationally defining preaddiction until more objective measures are developed.

There may be concern that our suggested term *preaddiction* is ill advised because it is pejorative and will simply intensify stigma. We contend that preaddiction is exactly the right term for 2 reasons. First, the terms *addict*, *schizophrenic*, and *diabetic* are certainly pejorative because they describe a person by their disease state. In contrast, addiction, schizophrenia, and diabetes are simply descriptions of diseases. Second, the term *addiction* is well

understood by clinicians and patients as a serious condition to be avoided. Thus, preaddiction has inherent motivational properties that convey the need for clinical action and patient change—just as prediabetes and precancerous currently do.^{1,4}

Engaging, Effective Interventions for Preaddiction | Importantly, the diabetes field did not simply prescribe insulin for those with prediabetes. Instead, they developed specially designed prediabetes medications and behavioral interventions.

In the SUD field, screening, brief intervention, and referral to treatment¹ and a computerized version of cognitive behavioral therapy for SUD⁸ both have potential as preaddiction interventions.⁸ However, a much broader range of medications and social support interventions are needed for those with early-stage SUD to arrest impaired control and/or to reduce the motivational properties of substances. Beyond clinical interventions, many commercial products such as Twitter, TikTok, and YouTube have used influencers and virtual coaches to motivate and sustain a range of healthy behaviors and might be adapted to address preaddiction.

Public and Clinical Advocacy | There is broad clinical and public awareness that genetic and behavioral factors create vulnerability and progression to type 2 diabetes, but that progression can be halted with detection and early intervention. However, few in the public or in general medical practice know how to recognize—or what to do—when substance use begins to transition to SUD. There are procedures for screening and tracking early-stage SUDs, but these are infrequently taught in US medical or nursing schools, rarely reimbursed by insurers, and thus, rarely applied in mainstream health care organizations.

Conclusions

Addiction is the most severe and chronic of the SUDs. It has been the almost exclusive focus of US clinical and policy efforts. However, serious addiction only results after years of unhealthy substance misuse that could be identified and managed much earlier. Because few of those who use substances transition to severe SUD,³ there is understandable concern regarding false positive identification and unnecessary treatments. Importantly, even low-level substance misuse is a major cause of motor vehicle crashes, interpersonal assaults, and overdose deaths among young adults.¹ Thus, failure to intervene is a greater clinical and public health concern than risk of unnecessary treatment. Finally, although there are not yet enough engaging, effective, therapeutic interventions for early-stage SUD, this was also true in the diabetes field. The introduction and promotion of the term *prediabetes* essentially created the market conditions necessary to stimulate those clinical services.

The diabetes example illustrates why a similar strategy has not yet happened in the SUD field: poor integration into the rest of mainstream health care, lack of a prominent advocacy group demanding clinical and policy changes, and little reimbursement for interventions with less severe SUDs. Nonetheless, the diabetes example shows that an early intervention approach can work given a comprehensive, sustained effort. That example also suggests the potential impact from a parallel strategy to reduce addiction problems by more aggressive efforts to identify and reverse preaddiction.

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