VIEWPOINT

Buprenorphine Deregulation and Mainstreaming Treatment for Opioid Use Disorder
X the X Waiver

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Buprenorphine, a partial opioid agonist medication for opioid use disorder (OUD), reduces overdose mortality rates.[1] Yet, amidst a national epidemic of opioid-related deaths, 40% of the 2.4 million persons with OUD receive pharmacologic treatment, much less continue treatment.[1] Federal policies surrounding buprenorphine constrain its wider use through separate US Drug Enforcement Agency (DEA)–amended licenses ("waivers") after approved training.[1] Removing buprenorphine prescribing regulations in France yielded increases in its use by persons with OUD.[2] Notably, deaths from opioid overdoses in France declined 79% over the subsequent 3 years.[2] If extrapolated to the United States, this translates to more than 30 000 fewer annual deaths from opioid overdoses. We propose deregulating the prescription of buprenorphine for treating OUD. We discuss the rationale for the current regulations, the evidence for deregulation, and a framework based on rational policies to ensure that deregulation achieves its intended purpose while minimizing consequences.

Rationale for Regulations

The rationale for US policies governing opioid agonist therapy for OUD treatment originates in the 1914 Harrison Narcotics Tax Act and subsequent Supreme Court jurisprudence. The regulatory framework is derived from the 1970 Controlled Substances Act, which restricts treatments of OUD using opioid agonists, such as methadone, to opioid treatment programs.[3] The original rationale for this legislation was preventing opioid agonist misuse, overdose, and deaths.[3] The US Congress changed this policy under the Drug Addiction Treatment Act of 2000, which was intended to expand the treatment of OUD beyond opioid treatment programs to primary care.[1] The Drug Addiction Treatment Act of 2000 (DATA 2000) established requirements for US Food and Drug Administration (FDA)–approved schedule III-V medications for OUD-related treatment.[1] Buprenorphine, coformulated with naloxone, became the first and only FDA-approved scheduled medication under this legislation. Prescribing buprenorphine for OUD treatment (but not pain) requires prescribers to complete an approved training), attest to their referral capacity, and submit an application. Following Substance Abuse and Mental Health Services Administration (SAMHSA) approval, the DEA issues a waiver license number that begins with an "X." X-waivered prescribers face heightened scrutiny by federal and state law enforcement officials, including periodic audits that are intended to minimize diversion and misuse.

Rationale for Deregulation

The rationale for deregulating buprenorphine for OUD is based on safety, access, the nature of misuse, and the need to mainstream treatment. First, buprenorphine's comparative safety undermines a critical rationale for regulation. Buprenorphine, regardless of prescribing intent, is safer than commonly prescribed full-opioid agonists. Buprenorphine's ceiling associations with respiratory depression reduce its lethality from overdose.[4] Between 2002 and 2013, 464 deaths were reported to the FDA that involved buprenorphine sublingual products, which are typically prescribed to treat OUD.[4] These US numbers do not address whether buprenorphine caused the fatality. International data document that buprenorphine-related deaths mostly occur with concomitant alcohol and/or sedative use.[4] By contrast, nearly half a million Americans died of drug overdoses between 2000 and 2014, mostly from full-agonist opioids.[4] This paradoxical overregulation of a safer medication stems from the flawed logic of "prescribing intent." Buprenorphine's X-waiver only applies when it is prescribed to treat OUD, but not for pain. Ironically, a comparatively safer medication that is critical to reducing deaths from the opioid epidemic is regulated more tightly than medications largely responsible for creating the epidemic.

Second, deregulation would improve access to buprenorphine during the opioid national emergency. Despite promotion and training initiatives by SAMHSA and legislation that has expanded patient limits and waivers to nurse practitioners and physician assistants, access to buprenorphine has not kept pace with the current epidemic, particularly in rural communities.[1] Buprenorphine training requirements, X-waiver applications, and DEA audits discourage prescribing buprenorphine.[1] Even when clinicians are motivated to seek an X-waiver, they often need to convince their cross-covering or supervising colleagues to obtain waivers. Regulations also disrupt the continuity of buprenorphine treatment during transitions of care. They discourage hospitalists from prescribing buprenorphine on hospital discharge (prescribing buprenorphine during in-hospital care is typically exempt). Regulations discourage correctional clinicians from continuing buprenorphine treatment following an arrest or initiating treatment prerelease and emergency medicine clinicians from initiating a potentially life-sustaining treatment following near-fatal opioid overdose despite evidence demonstrating the benefits.

Third, buprenorphine regulation is premised on the faulty assumption that buprenorphine diversion is driven by a desire to "get high." Yet, buprenorphine obtained

Table. Buprenorphine Policy Roadmap of Aims, Actions, and Accountable Entities

Aim	Action	Accountable Entity
Substantively and rapidly expand the prescription of buprenorphine for opioid use disorder	Pass legislation removing the waiver requirement for buprenorphine by creating a buprenorphine exemption from the Controlled Substances Act	US Congress
Mainstream prescribing buprenorphine and reduce prescriber fears and patient stigma associated with receiving buprenorphine	Eliminate buprenorphine regulations based on prescribing intent and halt routine DEA audits	DEA
Ensure basic competence in prescribing buprenorphine (and use of full-opioid agonists for pain) for all clinicians holding DEA licenses	Require basic training linked to DEA licenses (initial and renewal)	SAMHSA/DEA
Encourage medical schools and nurse practitioner, physician assistant, and residency training programs to incorporate buprenorphine training into their curricula	Exempt clinicians from previously mentioned training based on evidence of completing certified training during residency	DEA
Encourage clinicians to seek advanced training in diagnosing and treating opioid use disorder	Offer merit-based incentive payment system bonus points for completing of advanced buprenorphine training	CMS/SAMHSA
Integrate substance use disorder counselling into primary care	Develop billing codes for certified substance use counselors working in primary care	CMS
Improve access to addiction medicine specialists	Use add-on payments to billing codes to incentivize licensure	CMS
Improve affordability for uninsured and low-income patients	Offer pharmacy subsidies through 340B programs based on the number of uninsured and low-income patients receiving buprenorphine	HRSA
Evaluate the benefits and unintended consequences of the program to inform changes in policy	Systematically evaluate trends in prescribers, people receiving buprenorphine, time in treatment, and the net effect on overdoses, emergency department visits, hospitalizations, and deaths	CDC

Abbreviations: CDC, Centers for Disease Control and Prevention; CMS, Centers for Medicare and Medicaid Services; DEA, Drug Enforcement Agency; HRSA, Health Resources and Services Administration; SAMHSA, Substance Abuse and Mental Health Services Administration.

buprenorphine obtained illicitly is mostly used for self-medication to relieve withdrawal symptoms rather than for euphoria.[4] People denied treatment for OUD are at higher risk for seeking diverted buprenorphine.[4] This suggests that regulations constraining access to buprenorphine may paradoxically contribute to a market for illicit buprenorphine among those who seek treatment. To date, regulations and laws grounded more in ideology than evidence and data have failed to prevent the escalation in deaths from misuse of prescription and nonprescription full-agonist opioids.

Lastly, deregulation could help integrate opioid disorder treatment into primary care. The DATA 2000 has failed—too few physicians have obtained X-waivers.[1] Regulations reinforce the stigma surrounding buprenorphine prescribers and patients who receive it while constraining access and discouraging patient engagement and retention in treatment.[1] This marginalization created by X-waivers undermines the principle that OUD is a chronic condition that is similar to other chronic medical or mental health conditions that are managed by primary care clinicians. Models for integrating buprenorphine into primary care exist,[5] but the marginalization likely impedes such integration and extends to residency training. Only 10% of recent family residency graduates reported being adequately trained to prescribe buprenorphine and only 7% reported actually prescribing it.[6] Buprenorphine deregulation would mainstream prescribing, reduce stigma, and accelerate integration into primary care, as it did in France.[2]

Rational Policies

Addressing the opioid overdose epidemic calls for rational policies associated with prescribing buprenorphine. We propose deregulating buprenorphine within a policy framework (**Table**) based on clear aims, policies, and accountable entities, including the US Congress and federal agencies. The aims are to: (1) substantively and rapidly expand and mainstream buprenorphine prescribers by eliminating regulations based on prescribing intent, (2) reduce the fear and stigma that are associated with prescribing and receiving buprenorphine, (3) ensure basic prescribing competence for buprenorphine and full opioid agonists among all DEA license holders while encouraging health care training programs to include buprenorphine treatment in their curricula, (4) encourage clinicians to seek advanced training, (5) integrate counseling for OUD into primary care while ensuring access to addiction medicine specialists for consultation and the referral of complex patients, (6) improve buprenorphine treatment affordability for low-income and uninsured patients, and (7) systematically evaluate the benefits and harms of these policies to guide future amendments and/or the sunsetting of specific policies.

The opioid public health emergency demands transformative change in the treatment of OUD. Deregulating buprenorphine with a policy roadmap represents such a change. If such changes prove even half as effective as in France, thousands of lives could be saved.

ARTICLE INFORMATION

Published Online: December 26, 2018. doi:10.1001/jamapsychiatry.2018.3685

Conflict of Interest Disclosures: None reported.

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