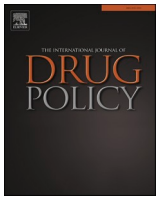
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Policy Analysis



Buprenorphine deregulation as an opioid crisis policy response - A comparative analysis between France and the United States

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ABSTRACT

Background: In passing the *Maintstreaming Addiction Treatment Act*, the United States has abolished its federal X waiver, considered a major barrier to the wider buprenorphine prescribing needed to respond to opioid-related harms. Advocates for this policy have drawn on the French response of deregulating buprenorphine prescribing to address increasing overdose mortality around the turn of the millennium. So far, such policy advocacy has incompletely accounted for contextual and health system differences between the two countries.
Methods: Using the health system dynamics framework, this analysis compares France from 1995 to 2003 (the relevant period of buprenorphine reform) to the US from 2018 until today (the comparison period to explore potential impacts of reform). We used it to guide examination of a) contextual issues relating to opioid use epidemiology and b) health system factors including prescriber supply, sector organization, and insurance coverage for primary care to draw relevant policy learning for the contemporary US.
Results: We identified that the US had a 22.5-fold higher mortality rate and a 2.3-fold higher opioid use disorder (OUD) rate compared to France, despite having rates of prescribed buprenorphine per-capita higher than, and per-person with OUD comparable to, than that of France. These wide gulfs between the scales and nature of the problems between France and the US suggest that relaxing restrictions on buprenorphine prescribing through abolishing the X waiver will be insufficient for achieving hoped-for reductions in overdose mortality.
Conclusion: Health system strengthening with a focus on improvements in primary care prescriber supply, coverage, and coordination are likely higher yield policy complements to relaxing buprenorphine regulation. Such an approach would better prepare the US to adapt to ongoing dynamics and uncertainties in the opioid crisis and to optimize the already relatively high levels of buprenorphine prescribing.

Background

Opioid overdose mortality is a major public health and health system concern in the United States (US). Since 1999, more than one million people have died from drug overdose in the US, the majority of these due to opioids (Ahmad et al., 2022). Likewise, opioid overdose mortality has been a major contributor to declines in national life expectancy (Harper et al., 2021). These alarming trends have only accelerated during the COVID-19 pandemic (Imtiaz et al., 2021). Other high-income countries such as Canada, Australia, the UK, and Sweden, have also seen recent rises in opioid overdose mortality (Degenhardt et al., 2018).

Buprenorphine is a partial opioid agonist which is considered first line therapy for the management of opioid use disorder (OUD) and is thus considered a key intervention for reducing opioid-related mortality (American Society of Addiction Medicine, 2020). It is considered safer, and holding comparable effectiveness, to the full opioid agonist methadone which has been the long-standing global standard for care (Eibl et al., 2017). Buprenorphine also carries a lower risk of overdose compared to heroin, full opioid agonist analgesics (such as hydromorphone and oxycodone), as well as opioids now commonly found in the contemporary North American street drug supply, such as fentanyl and its analogues.

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Despite this relative lower risk, buprenorphine is itself an opioid and carries its own concerns regarding overdose and extramedical use (Degenhardt et al., 2008; Seldén et al., 2012; Sud et al., 2022; Yokell et al., 2011). As such, in most jurisdictions, buprenorphine is scheduled as a controlled substance subject to varying levels of regulation. In the US, buprenorphine use is regulated primarily by the federal *Drug Abuse and Treatment Act* of 2000. This *Act* requires prescribers to apply for a federal waiver to prescribe buprenorphine, for which the completion of federally designated training and registration is required (Priest et al., 2019). Notably, buprenorphine is subject to a looser regulatory regime compared to methadone. Methadone can only be prescribed and dispensed in federally regulated "opioid treatment programs", while buprenorphine has been approved for "office-based" (i.e. non-regulated, normal medical practice) prescribing. Some countries with tighter drug regulatory cultures, such as Russia, have not authorized buprenorphine even for medical use while others such as Singapore have substantially changed regulation in response to harms from buprenorphine use (Degenhardt et al., 2008; Larney et al., 2017). In countries where buprenorphine is available for medical use, policy advocates, clinicians, and people who use substances have raised concerns about poor accessibility (Sud et al., 2022). For example, serial US national drug use surveys demonstrate low receipt of medication assisted therapies for people living with OUD while another study identified that more than half of all rural US counties do not have a prescriber with a federal waiver to prescribe buprenorphine (Andrilla et al., 2019; Krawczyk et al., 2022; Substance Abuse & Mental Health Services Administration, 2019a, 2021). Other agents such as injectable extended-release naltrexone have been introduced as additional therapeutic options in the United States, but uptake has so far been limited and marked by high and rapid rates of discontinuation (Morgan et al., 2018).

Accordingly, major policy initiatives have been proposed and undertaken internationally with a focus on increasing buprenorphine accessibility. These have included health human resource initiatives such as education programs for health providers (Egan et al., 2010), financing initiatives to expand coverage (Chen, 2020), as well as medicines and technologies initiatives such as increasing the availability of alternative delivery formulations (e.g. long-acting injectable and implantable formulations) (Arunogiri & Lintzeris, 2021).

One major policy focus in the US has been to reform the regulatory requirements for prescribing buprenorphine for OUD. Requirements for getting a federal waiver have been characterized as a barrier to care, marginalizing OUD care from mainstream medicine and disincentivizing health professionals from learning about and engaging in buprenorphine prescribing (Fiscella et al., 2019). Policy advocates have noted the dissonance of requiring such regulation for buprenorphine when no such requirements are in place for the equally, or potentially more, risky full opioid agonists that are widely prescribed for the treatment of pain Wakeman and Barnett, (2018). This culminated at the end of 2022 in the passage of the federal *Mainstreaming Addiction Treatment Act*, which officially abolished the federal waiver. This policy intervention has been described by federal drug administrators, bipartisan lawmakers, and physicians as "life-saving" and "historic" in closing the addiction treatment gap (The White House, 2023).

In France, federal regulatory changes to buprenorphine were the focus of a previous policy initiative responding to increasing rates of opioid overdose mortality and related harms, especially the HIV epidemic, around the turn of the millennium (Fatseas & Auriacombe, 2007). The major regulatory changes were to allow buprenorphine prescribing in any healthcare context without requiring any special registration, special training of prescribers, or limits on prescribing. This resulted in large increases in buprenorphine prescribing, particularly by primary care physicians, and coincided with a large reduction in opioid overdose mortality (Auriacombe et al., 2001; Dupouy et al., 2017). This so-called French Model has been explicitly called upon by multiple US policy advocates of buprenorphine deregulation to achieve similar mortality reductions (Fiscella et al., 2019). As one example, it has been claimed that following the French Model in the US would have saved nearly 37,000 lives in the US in 2018 alone (Weimer et al., 2021). The authors acknowledged that this 37,000 figure was calculated by simply multiplying the total number of opioid overdose deaths in the US in 2018 by the opioid overdose mortality reduction in France of 79% achieved between 1995 - 1999. Such a calculation and policy advocacy seems to fall into the 'landless theories' trap identified by Marmor where "the country specific policy context that enables reforms or creates barriers to change" are largely ignored (Marmor, 2017). This is despite the French authors having emphasized this context in their reports on the model (Fatseas & Auriacombe, 2007) and others having identified these differences as potentially insurmountable barriers to policy learning (Bergeron & Colson, 2022).

To better address these barriers and understand what the expected impacts of abolishing the X waiver and attempting to move towards French-style buprenorphine deregulation in the US might be, we have undertaken a national-level comparative analysis of France and the US, two high income countries with substantial and mature health systems infrastructure.

Methods

With respect to comparing health systems, dimensions relating to leadership and governance, human resources, service delivery, medicines and technology, and financing are particularly salient (Papanicolas & Smith, 2013). Coverage and accessibility to care as well as the role of primary care within the larger health system are of particular concern in this analysis. Expansion in access to buprenorphine in France was largely driven by increased prescribing in primary care and proposals for expanding access in the US often depend on primary care prescribing (Fatseas & Auriacombe, 2007; Wakeman & Barnett, 2018).

In addition to health system differences, there may be important differences in context between when France deployed this policy and the contemporary landscape of the US. These include the nature and magnitude of opioid use in the two countries - including rates of opioid use and the substances involved in opioid use and opioid-related harms (Baumgartner et al., 2022). To address both contextual and health system factors when comparing buprenorphine deregulation, we used the health system dynamics framework (Fig. 1) to guide this analysis (Van Olmen et al., 2012).

Specifically, this framework was used to identify relevant points of comparison between France and the US. Our analysis will focus first on the Context of opioid use epidemiology and the drug supply. We will then comparatively analyse Health System factors of health human resources (Resources), the role of primary care (Service Delivery), and financing of clinical services and medications (Resources).

We did not focus on how buprenorphine deregulation was achieved in France, nor specifically on the comparative historical arcs of buprenorphine regulation in each country. Rather, we aimed to understand: 1) whether, and with what adaptations, policy learning might take place in the US and, 2) what the expected health outcomes, primarily in terms of opioid overdose mortality, might be from following a comparable policy trajectory within the contemporary US health system.

We compared France during the period in which buprenorphine deregulation took effect and stabilized (approximately 1995–2003) to the contemporary US (approximately 2018 onwards). These time periods were selected for several reasons. First, 1995 represents the period of the highest rates of opioid-related harms and subsequently prompted reforms related to buprenorphine. Likewise, 1995 was the earliest point from which reliable national-level data are available in public reports in France. We used 2018 onwards as the period of interest for the US as this was consistent with the aforementioned argument that 37,000 deaths could have been avoided in that year, and represented a comparable period of growing opioid-related harms. Likewise, our previous scholarship has also identified that there has been there has been a notable increase in references to the French Model by US scholars in that time

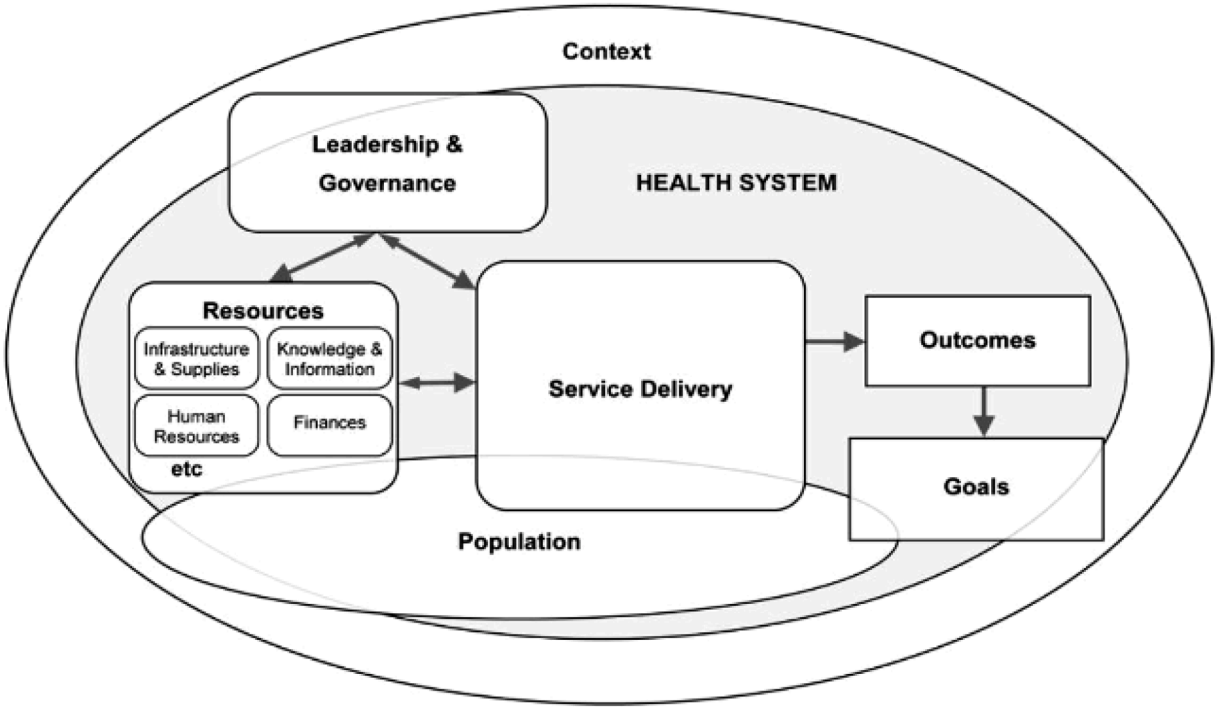


Fig. 1. The health system dynamics framework.
The health system dynamic framework by van Olmen and colleagues, is licensed under CC BY-NC—ND 3.0. No changes were made to the original image.

period (Kankanam Gamage et al., 2023).

Using our analytical framework, we identified the data that we needed to collect, and iteratively identified documents that would provide this information. These documents were from established sources that collate health systems and epidemiological data in a standardised format (e.g. European Observatory on Health Systems, the Commonwealth Fund, the European Monitoring Centre for Drugs and Drug Addiction). Further documents were identified through purposive snowball sampling. For data on health systems, we used reports on country health systems. These included reports, white papers, and websites prepared by their government and health departments; Health Systems in Transition reports (Health Systems in Transition Series (HiTs), n.d.); and profiles prepared through the Commonwealth Fund. For data on drug policy and OUD treatment, we collected national drug strategies and policies; and data on drug use epidemiology and treatment, which included reports prepared through the European Monitoring Centre for Drugs and Drug Addiction. When relevant data were not available from these official sources, we drew data from the peer-reviewed scientific literature.

Results

Contextual factors

Opioid use epidemiology

The first analytic point of comparison we consider pertains to the epidemiology of opioid use in each country, an important contextual factor. This comparison suggests that there are stark differences in the scale and nature of the problems in France 20 years ago and the contemporary US that will make a *simple* transposition of buprenorphine deregulation unlikely to render the desired effects.

Overdose deaths are the most visible part of a crisis of harms. To better compare the scale of the opioid crises, it is helpful to examine overdose mortality together with other measures including rates of OUD as well as estimates of opioid use (Table 1). These data are collected from France's contribution to the European Monitoring Centre for Drugs & Drug Addiction's 1997 annual report (which includes data collected from 1995), according to standards set by the European Information Network on Drugs and Drug Addiction (European Monitoring Centre for Drugs & Drug Addiction, 1997). For the US, we used the 2018 US National Survey on Drug Use and Health (Substance Abuse & Mental Health Services Administration, 2019b) for rates of OUD and opioid use and Centres for Disease Control and Prevention National Vitals Statistics System data for opioid overdose mortality (Data Access - Vital Statistics Online, 2023). For the calculation of rates, we used World Bank data for an estimated population of France in 1995 of 59,541,904 and of the US in 2018 of 326,838,199 (The World Bank).

Table 1
Rates of opioid overdose mortality, opioid use disorder, and opioid use US (2018) versus France (1995).

Outcome	US (2018)	France (1995)	US rate : France rate
Opioid overdose mortality (rate per 100,000)	47,718 (14.6)	386 (0.65)	22.5: 1
Opioid use disorder (rate per 100,000)	2,028,000 (620.5)	160,000 (268.7)	2.3: 1
Opioid use (rate per 100,000)	10,250,000 (3136.1)[a]	238,167 (400.0)[b]	7.8: 1

[a] Represents past year opioid use. Lifetime opioid use data not reported in the National Survey on Drug Use and Health.
[b] Represents lifetime heroin use, with heroin being the only opioid collected. Past month heroin use was estimated at 0% and so could not be used to make a comparison.

It is evident from these data that there are substantial and consistent differences in the magnitude of opioid use and opioid-related harms between the two jurisdictions. Most strikingly, there is a 22.5-fold difference in rates of overdose mortality. Actual differences in opioid use are likely much higher than the 7.8-fold difference reported here since the French rates capture any self-reported lifetime use which, because of the longer timeline, will relatively overestimate use compared to the US rates which capture self-reported past year use. If we take the important

comparative parameter to be OUD rates, the US has a 2.3-fold larger problem than France did. This appears to be a more tractable problem than opioid overdose mortality; however, in order to claim any effects on mortality in the US from French-style widening of buprenorphine prescribing, we would need to establish a relationship between OUD rates and opioid overdose mortality.

Either way, these differences introduce an important *uncertainty of scale*. In the simplest scenario, buprenorphine prescribing in the US would have to be 22.5-fold higher than seen in France to see a comparable effect on overdose mortality. Such a scenario, however, involves a questionable assumption of linearity across scales. One of the important injunctions of characterizing health systems, and large-scale health problems, as complex, is that the scales of problems matter (Khan et al., 2018). In complex systems, problems at one scale are typically not just linear magnifications of the same problem at a smaller scale (Bar-Yam, 2006; Sturmberg & Martin, 2013). We will return to this point when we move to discussing matters relating to the health system proper.

Characteristics of the drug supply

Another major challenge to the comparison, and what is likely driving these differences of scale, is the nature of the drugs involved. While both countries have been confronting harms related to "opioids", there is massive variability in the potency and physiological effects of different opioids. Buprenorphine itself is an opioid that carries unique properties of high affinity to, but only partial agonism of, mu-opioid receptors. These properties support its use as a treatment for OUD. On review of the French Observatory for Drugs and Drug Addiction's reports during the period in question, the only opioid of concern with respect to use, problematic use, and overdose mortality was heroin. Heroin is a mid-potency opioid with moderation duration of action derived from processing the extract of the opium poppy (Goldstein, 1991). Different cultivation, extraction, and processing approaches yield heroin products with different physiological, psychoactive, and health effects (Ciccarone, 2005). However, the vast majority of heroin traded and used in France during the period in question would have been supplied from Afghanistan as well as countries in southeast Asia and would have been of relatively consistent potency (European Monitoring Centre for Drugs & Drug Addiction, 2001; Gibson et al., 2005).

The contemporary US drug supply is drastically different. Over the last several years, the US drug supply has become contaminated with fentanyl and its derivatives (O'Donnell et al., 2017), which have been major drivers of mortality (Gladden et al., 2019). Fentanyl is a very high potency, relatively short-acting, full mu-opioid agonist. It is also synthetically produced — it does not require access to the opium poppy for manufacture. In 2018, illicitly manufactured fentanyl was involved in 67.9% of opioid overdose deaths in the US, representing an 11.1% increase from the previous year alone. The US drug supply also includes heroin, which was involved in 39.4% of deaths – a 1.5% reduction from the previous year – and prescription opioids such as morphine and oxycodone, which were involved in 28.7% of deaths – a 6.6% reduction from the previous year (proportions across drug types are non-cumulative as multiple opioids are often identified in post-mortem toxicology). In addition, there is known adulteration of the purported opioid drug supply by non-opioid synthetic substances. One prominent example is xylazine — a tranquillizer usually used for animals which may extend the short-duration of fentanyl and increase psychoactive effects (Friedman et al., 2022), but also increases the risks of sedation, overdose, and death (Bowles et al., 2021; Johnson et al., 2021).

The vast majority of the evidence for the safety and effectiveness of buprenorphine as treatment for OUD has come in the context of injection heroin use — i.e., in the kind of context seen in France at the turn of the millennium (Mattick et al., 2014). Early reports and studies suggest that important outcomes such as treatment retention may be non-different for people who use fentanyl as compared to heroin Wakeman et al. (2019). However, buprenorphine's partial agonism and high affinity for mu-opioid receptors — typically seen as an advantage in reducing opioid use and opioid overdose mortality — may be an important limitation of its effectiveness and desirability in the face of high potency synthetics such as fentanyl (Silverstein et al., 2019). There are also important concerns around precipitated withdrawal and underdosing which limit the utility of buprenorphine for people using fentanyl (Varshneya et al., 2021). This has been recognized with, for example, practice guidance calling for increasing use of full opioid agonists such as methadone as appropriate agonist therapy for people who use fentanyl (Bromley et al., 2021).

This is not to conclude that expansion of buprenorphine use may not be protective for people who use drugs in the US. In high fentanyl environments, like British Columbia (Canada), both buprenorphine and methadone show comparable protective effects against opioid overdose mortality (Pearce et al., 2020). In fact, in this environment mortality rates for people ceasing buprenorphine were lower than those ceasing methadone. Other studies have further suggested such a protective effect with intermittent buprenorphine use. For example, one US study demonstrated that people who had exposure to extramedical buprenorphine (i.e. buprenorphine that has been shared, traded, or sold rather than prescribed to them) were at lower risk of opioid overdose, including people who used fentanyl (Carlson et al., 2020).

Taken together, however, it is clear from this contextual comparison that in such complex and distinct drug supply environments between France and the US, we cannot predict a simple linear transposition of the effects of buprenorphine deregulation.

Health system factors

Besides contextual factors relating to the drug supply, the epidemiology of opioid use, and pharmacological properties of buprenorphine, we must also consider comparisons of the health system through which buprenorphine is delivered. One of the key components of the scalability and accessibility of buprenorphine in France was its delivery through primary care settings. It has been estimated that across all French health system regions, greater than 90% of buprenorphine prescribing was by general practitioners (Cadet-Taïrou & Chollet, 2004; Fatseas & Auriacombe, 2007). Likewise, in the US, it has been suggested that treatment discontinuation is less likely when medications for OUD are prescribed by the primary care provider (Munger & Back, 2022). We compared primary care across the US and French health systems in terms of intersecting factors of: 1) health human resources and supply, 2) the overall position of primary care within each health system, and 3) insurance coverage for health services and medications. Key differences between France and the US further complicate the transposition of policy, but also identify potential opportunities to address opioid-related harms in the US through health system improvement.

Health human resources

Primary care is often considered a sector of the health system through which medical technologies can be scaled because of this sector's reach to a large and diverse population, sometimes whose only point of contact with the health system is primary care. Indeed, primary care physicians were major targets for another initiative to expand opioid prescribing in the US — pharmaceutical manufacturers such as Purdue Pharma Ltd successfully marketed their opioid analgesic products to primary care and achieved unprecedented levels of mass, high dose prescribing (Van Zee, 2009).

Besides accessibility, primary care can offer a suitable setting for OAT delivery due to its ability to foster collaboration between different professionals needed to optimize OUD care. Greater commitments to primary care and primary care coordination reflect values that acknowledge the complexity of disease management and the need for a multifaceted, multidisciplinary, comprehensive and holistic approach to health care. So far, delivery of medications for OUD in the US has been dominated by specialized opioid treatment programs with poor integration with primary care (Community Health Centers &

Medication-Assisted Treatment for Opioid Use Disorder - Issue Brief, 2020).

Most primary care physicians in France and the US are in private practice and are reimbursed for their services by a mix of employment- and government-based insurance programs (Rice et al., 2020; Sandier et al., 2004). Both countries also share a specialist dominated medical system, as reflected in a hospital-centric system and specialist dominance in the development of reimbursement and care structure policy (Ricketts et al., 2012).

Despite these similarities, France has generally had a consistently higher physician supply rate than the US, with 27% more physicians per 1000 inhabitants (Table 2). While absolute physician supply rate does not sufficiently account for physician availability and is an imperfect proxy for access to health services (Islam et al., 2023), recent comparisons between the US and other OECD countries, including France, have identified that lower physician supply patterns with less physician visits per capita (Tikkanen & Abrams, 2020). This lower physician visit rate holds for the US despite having a higher burden of chronic disease (Tikkanen & Abrams, 2020). In order to compare with France once it had already achieved the purported effects of buprenorphine deregulation, we used rates from 2003 for France and 2018 for the US, using Organization for Economic Cooperation and Development, World Health Organization, and American Medical Association data (OECD, 2016, 2022; Petterson et al., 2018).

This difference in physician supply becomes more pronounced when we consider the distribution of physicians across speciality versus primary care medicine. In France in 1995, approximately 50% of physicians practiced in primary care (OECD, 2016; Sorum, 1998). In the US, the mix is tilted much more heavily in favour of specialist practice, with primary care physicians (including family physicians, pediatricians, general internists, general practitioners, and geriatricians) representing 31.9% of the physician workforce (Petterson et al., 2018). Thus, the overall supply of primary care providers in the US, and thus access to primary care, is approximately half of that of France (Table 2), reducing the comparative ability to reach people living with OUD through this health sector.

An important note, however, is that primary care reform is an active focus of US health policy (Rice et al., 2020). One health human resources avenue through which the primary care workforce is being expanded is through the training, engagement, and reimbursement of non-physician primary care providers such as nurse practitioners and physician assistants. Besides bringing different skill sets than physicians, nurse practitioners and physician assistants are typically reimbursed at significantly lower rates than their physician colleagues. Physician compensation rates in the US are much higher than in France (Kringos et al., 2015), and thus it is sensible that reforms and attempts at expansion of primary care be achieved through lower paid non-physician health professionals.

A recent important buprenorphine prescribing reform was the passage in the US Congress of the *Comprehensive Addiction and Recovery Act* which expanded prescribing privileges to nurse practitioners and physician assistants (Andrilla et al., 2020; Comprehensive Addiction & Recovery Act of 2016, 2016). If the US is to truly draw on the French experience that buprenorphine prescribing in primary care is a key intervention for reducing opioid overdose deaths, then this expansion of privileges, as well as increased involvement of nurse practitioners and physician assistants in primary care overall, may align well with this policy direction. However, it should be noted that, given differences in approaches to primary care, expanding prescribing rights to non-physicians has not been a part of the French Model. Accounting for this larger, non-physician primary care workforce that is eligible to prescribe buprenorphine improves the relative numbers between France and the US (Table 2). But the gap does not fully close, with France still holding a 36% larger prescribing primary care workforce.

From the mid 1990s, France went from nearly no buprenorphine prescribing to almost 83,000 patients in treatment by 2003, representing about half of all people living with OUD in France. Buprenorphine prescribing is not new to the US, with the first formulations receiving regulatory approval in 2002, and there have been waves of buprenorphine prescribing expansion over the last two decades. By 2018, there were an estimated 1,037,787 people treated with buprenorphine (Olfson et al., 2020). Thus, when we look at comparative rates of buprenorphine prescribing in France and the US, we see that the US has *already* surpassed the per capita rate seen at the height of prescribing in France by more than 2.5-fold and has approximately the same rate when normalized to the rate of OUD (Table 2). When we consider buprenorphine prescribing against the relative supply of primary care providers, the comparative rate is already more than 3.5-fold in favour of the US.

The structure of primary care

Another important dynamic of French primary care that has been identified as contributing to the model's success for opioid-related harms is the good integration between primary care prescribers with other professionals, most notably pharmacists who see OUD care as within their scope of practice, and the integration of primary care with social services (Dupouy et al., 2020; Fatseas & Auriacombe, 2007). Although the majority of this reform occurred after the period of interest, France also substantially changed reimbursement for services to promote more longitudinal care with primary care serving a more "soft" gatekeeping type function within the health system (Rodwin, 2018; Sandier et al., 2004). While this policy change has to some extent been successfully contested by French specialists, it has resulted in greater continuity of care and access to care (Ricketts et al., 2012). In contrast, the US has faced challenges with respect to multiple fundamental parameters that are characteristic of high-performing primary care systems (Forrest et al., 2007; Starfield, 1995; Starfield et al., 2005; Valderas et al., 2009). As one example, due to poor coordination between medical and psychosocial services, the requirement for a buprenorphine prescriber to have access to behavioural health services has been consistently identified as a key barrier to OUD care (Fiscella et al., 2019). In 2021, in an important policy move towards buprenorphine deregulation that was explicitly in response to policy advocacy, the US Department of Health and Human Services ultimately removed requirements for training and for the provision of psychosocial services alongside buprenorphine prescribing (Health and Human Services Department, 2021). However, this exemption is allowed only for those prescribers who prescribe to a maximum of thirty patients. No such restrictions on the maximum number of patients treated were ever in place in France.

Outside of buprenorphine prescribing specifically, there have been

Table 2
Physician supply and buprenorphine prescribing, US (2017–2018) versus France (2003).

Outcome	US (2017–2018)	France (2003)	US: France
Physicians per 1000 inhabitants	2.6	3.3	0.79: 1
Primary care *physicians* per 1000 inhabitants	0.83	1.67	0.49: 1
Primary care *professionals* eligible for buprenorphine prescribing per 1000 inhabitants[a]	1.22	1.67	0.73: 1
Buprenorphine prescribing (total)	1,037,787	78,150[b]	13.28: 1
Buprenorphine prescribing per 1000 inhabitants	3.18[c]	1.24[d]	2.56: 1
Buprenorphine prescribing per 1000 people living with OUD	511.73	488.44	1.05: 1
Buprenorphine prescriptions per primary care prescriber	2.61	0.74	3.52: 1

[a] Including US nurse practitioners and physician assistants.
[b] The OFDT estimated between 71,800 and 84,500 for 2003 (National report 2004 - OFDT, 2022), we have used the mean.
[c] Using OECD data for 2018 population of 326,838,000.
[d] Using OECD data for a 2003 population of 63,038,000.

incremental reforms towards higher quality, coordinated primary care in the US (Rice et al., 2020). Most relevant to this discussion of opioid-related harms, these have included initiatives to develop patient centred medical homes and community health centers (CHCs). Recent increases in funding for CHCs in particular have aimed to expand comprehensive primary care services to Medicaid-insured persons. The populations that these primary care developments target are currently demonstrating the highest rates of growth of opioid-related harms. In the last few years, rates of opioid overdoses have increased the most amongst poorer, lower educated, un- or under-insured, racialized individuals who use primarily fentanyl and its derivatives (Davenport & Matthews, 2018; Friedman & Hansen, 2022; Han et al., 2017; Miller et al., 2021; Wu et al., 2016).

There have been previous substantial expansions of buprenorphine prescribing in the US (Krawczyk et al., 2022). Between 2009 and 2018, there was a doubling in the annual rate of buprenorphine prescribing per 1000 population from 1.97 to 4.43 (Olfson et al., 2020). However, a decade of research has demonstrated that this expansion has primarily privileged a different population — higher income, employed, insured, white people who primarily use prescription opioid analgesics (Goedel et al., 2020; Hansen et al., 2016; Lagisetty et al., 2019; Stein et al., 2018). Recent data from the Department of Health and Human Services, which has been the primary agency coordinating federal opioid initiatives, shows a 142% increase in buprenorphine prescribing through CHCs (Digital Communications Division, 2018). Though this may be taken as an encouraging sign that contemporary policy may be better aligning with current needs, the impacts of the overdose crisis are rapidly shifting across racial lines and there is as of yet little evidence that any changes in buprenorphine prescribing are closing disparities across racial groups (J. R. Friedman & Hansen, 2022; Goedel et al., 2020).

Coverage for health services and medications

It is widely known that private costs of health services and medications are a major challenge for the US health system (Glied & Zhu, 2020; Naci et al., 2014). Cost-related non-adherence is prevalent and persistent in the US Medicare population despite expansion in coverage for medications (De Avila et al., 2021). Lack of coverage, high medication costs, and high out-of-pocket costs can lead to worse health outcomes and greater health system utilization (Blanchard et al., 2013; Mikyas et al., 2014). Furthermore, at least two studies have demonstrated lower health system costs with higher adherence to buprenorphine for people living with OUD in the US (Ruetsch et al., 2017; Tkacz et al., 2014). A recent US study has demonstrated that, despite the lower costs of buprenorphine over time, even small increases in out-of-pocket costs are associated with significant decreases in treatment retention and days of buprenorphine coverage (Dunphy et al., 2021). Overall, despite recent expansions of insurance access through the *Affordable Care Act*, there continue to be major gaps in health service and medication insurance coverage in the US including specifically in the populations with the highest rates of opioid-related harms (Rice et al., 2020).

With the passage of the *Universal Health Coverage Act* (CMU) in 2000, France achieved universal health coverage. This legislation extended government-financed comprehensive insurance coverage — including for primary care services and medications — to the remainder of the population who did not have access through employment and unemployment schemes (Sandier et al., 2004). While the demographic dynamics of people who used opioids in France have not been studied in as much detail as the contemporary US, available reports suggest that this population did have lower coverage through employment-based insurance, with upwards of 8% having no coverage at all (European Monitoring Centre for Drugs & Drug Addiction, 1997). About 60% of people living with OUD were estimated to be unemployed, identifying potential challenges with a primarily employment-based insurance system. Likewise, 70–90% of opioid users were coded as "French" — it is unclear if the remaining 10–30% referred to racialized French citizens, non-citizens residing in France, or both. While coverage for care seems to have been as highly relevant for those most affected by the French opioid crisis as it is for the contemporary US, by 2000 the CMU extended comprehensive coverage to all French residents, regardless of citizenship or employment status. The degree of universality in health insurance coverage is indicative of the value orientations towards health equity, including who deserves access to care.

Besides health insurance coverage, French reimbursement mechanisms for insured services are important comparative issues to consider. Typical employment-based insurance coverage was on a reimbursement model — patients would pay out-of-pocket for services and medications and then be reimbursed at a later date by their insurance schemes at set rates. In some cases, this could mean substantial initial out-of-pocket costs that might act as a barrier to accessing care for those who are of lower income, though it should be noted that physicians could opt to be paid directly through public insurance. However, for chronic disease-related illnesses including opioid addiction, reimbursement was made directly to providers at the full cost, regardless of employer- or public-based insurance (Fatseas & Auriacombe, 2007). This is in addition to long-standing full coverage for OUD care in specialized settings (i.e. using methadone in specialized drug treatment centers) (European Monitoring Centre for Drugs & Drug Addiction, 1997). This helped to minimize financial barriers to access OUD care, even in primary care settings. Thus, there are substantive differences in access and capacity to adhere to buprenorphine therapy between France and the US. Alone, policies at the level of health professionals' eligibility for buprenorphine prescribing are unlikely to have any impact on these important differences.

Discussion

Problems of scale

From our analysis, it is evident that expecting similar results from a simple, 1:1 transposition of the French model to the US is naive and is perhaps even untenable. The first major challenge is that of scale – not only is the scale and nature of the US problem substantially larger than that of France, so too *already* are the rates and absolute amount of buprenorphine prescribing. It is unclear whether it is tenable for the US system to reach the proportional scale of buprenorphine prescribing. Assuming linearity and using opioid mortality as the index for comparison as per the claims of policy advocates, this would mean at least a 22.5-fold increase in current prescribing rates and an 80-fold greater rate of buprenorphine prescribing per primary care prescriber between the contemporary US and France at the height of its buprenorphine prescribing. Given that major previous US policies around buprenorphine prescribing eligibility have resulted in much more modest increases, other policies will be needed to achieve such high levels of prescribing (Barnett et al., 2019; Olfson et al., 2020).

Problems and considerations of scale are one of the major features of complex systems, including health systems (Gunderson & Holling, 2002; Sturmberg & Martin, 2013). The health system dynamics framework's explicit acknowledgement of complex dynamics within and around health systems, including considering the role of non-health system contextual factors, is one of the major strengths of this framework (Khan et al., 2018). An important further development of this framework would be to explicitly grapple with problems of scale. Approaches to complex system dynamics have been successfully applied to understand OAT and thus provide some useful conceptual ground from which to further develop approaches to issues of scale (Salamanca-Buentello et al., 2022).

Differences in values

The values embedded in both drug policies and health systems — particularly regarding the role of primary care and insurance coverage

as discussed above— are especially salient and relevant to consider in an analysis of health system dynamics (Van Olmen et al., 2012). In the US, the increasing acceptance and incorporation of harm reduction into drug policy approaches has been a recent phenomenon (Baumgartner et al., 2022). This may be observed, for example, in recent efforts to make naloxone, an opioid antagonist used as an overdose reversal agent, more accessible in the US (Murphy et al., 2019). Historically, policies to address drug-related harms have been largely prohibitive or punitive in nature, taking a 'war on drugs' stance by relying on criminalization to deter drug use and distribution. In tandem, there has been a broader sociocultural emphasis of abstinence over treatment and harm reduction strategies, and a view of drug use and addiction as a moralistic failure that should be addressed through willpower alone (Saloner et al., 2018). These values likely resulted in fewer resources being allocated to evidence-based treatment compared to other policies. Prior to our period of interest, France had also enacted similar abstinence-orientated drug policy goals. From the mid-1990s, a shift to a more harm reduction orientation occurred, triggered by increasing prevalence of HIV/AIDS related to injection drug use (Bergeron & Colson, 2022; Bergeron & Kopp, 2002; Hedrich et al., 2008).

Policy lessons for the contemporary US

The drastic differences in the nature and scale of the problems, as well as health systems, does not mean that there are no policy lessons to be considered for the US from France. However, these lessons may not be the ones that the US health system, and the American health *culture*, want to learn. The pharmaceuticalization of health problems, as well as social problems, in high income countries and particularly the US is well documented (Abraham, 2010; Williams et al., 2011). The massive exposure of the US population to opioids since the turn of the millennium has been driven in part by such a pharmaceuticalization of pain Tafreshi et al. (2022), and the development of buprenorphine itself as a therapeutic has been closely tied to a century-long fantasy of developing a non-addictive pain reliever (Campbell & Lovell, 2012).

This analysis suggests that investments in health system reform, and more generally the embedding of buprenorphine and drug therapies into social and health systems (Sud et al., 2021; Whyte et al., 2002), are just as important as abolishing the X waiver and relaxing regulations around buprenorphine prescribing. While the health system dynamics framework recognizes that health system components constantly interact with each other, it does not explicitly address how. Drawing from non-health fields such as ecology and economics, existing complex adaptive system models have been characterized by the properties of resilience, capacity, and connectedness (Salamanca-Buentello et al., 2022). If we apply this to our current analysis, we can observe that the US system of care for OUD has displayed characteristics of low resilience (e.g. regulatory inflexibility with buprenorphine prescribing), low capacity (e.g. fewer resources to address opioid-related harms), and low connectedness (e.g. poorer coordination between providers and services). Therefore, relevant health system reforms may focus around addressing the dynamics and interactivity between the regulatory environment, healthcare providers, treatment settings, and people receiving care. Tangibly, this may involve improving access to high quality primary care, financing of pharmaceutical coverage, and extension of health insurance, in addition to the regulatory changes in buprenorphine regulation and prescribing eligibility that have now been made.

Access to primary care has been lauded internationally as an important general health promotion strategy (World Health Organization, 2018). In one widely cited county-level analysis from the US, access to primary care was associated with improved life expectancy and reduced mortality for cancers, cardiovascular disease, and respiratory tract diseases. However, for substance use and injury, no such beneficial association was found, suggesting important opportunities for improvements in these fields (Basu et al., 2019). Taking an increasing focus towards health system improvement would also increase primary care capacity and effectiveness for the delivery of other medications, such as methadone and slow release oral morphine, that are essential for OUD treatment in the face of a high potency, contaminated street drug supply (Samet et al., 2018). This aligns with policy conundrums and conflicts often discussed in the context of health system reforms in lower income countries (Agyepong, 2018). Strict application of the French model by simply deregulating buprenorphine prescribing is reminiscent of a "disease-focused" approach to a large-scale health problem, and one that, given key differences between France and the US, is unlikely in isolation to achieve the desired results (Gonzalez, 2005; Mills, 2005). On the other hand, an approach that strengthens the health system, with a focus on primary care and health insurance expansion may better optimize the high levels of buprenorphine prescribing that already exist.

Limitations

A limitation of this analysis is that some key components of OUD treatment regimes have not been comparatively analysed. These include: the roles of speciality- and facility-based treatment approaches, including those most focused on methadone treatment; and a detailed examination of the roles, perspectives, and regulation of community-based pharmacists who are linchpins to successful outpatient OUD therapy. A broader analysis that includes these considerations may come to different conclusions around important policy lessons and nuances for the US based on the French experience. Furthermore, a comparison across multiple additional jurisdictions in which primary care-based OUD reforms have been contemplated or implemented may provide additional health system and contextual dimensions to consider when formulating new policy.

Conclusions

While US policy advocates and policy makers should be applauded for loosening the regulatory regime for buprenorphine, a health system strengthening approach is likely to better prepare the US health system to respond to the constantly changing dynamics of the opioid crisis and related health and social challenges (Gonzalez, 2005). This is especially important to consider given that between 2009 and 2015 the number of GPs in France initiating buprenorphine decreased by 43.8% with a corresponding decrease in the number of patients using buprenorphine in favour of methadone, despite ongoing OUD treatment needs (Dupouy et al., 2020). This phenomenon, which some have dubbed as "The End of the French Model" should be taken as a sign that even successful policy transforms in response to changing contexts. When comparing the two countries to consider how to best respond to the contemporary crisis of opioid-related harms, US policy advocates and law makers should examine not just the specific policies relating to buprenorphine deregulation, but the full health system context in which these policies developed.

Disclosures

The authors have no conflicts of interest to declare.

Ethics approval

The authors declare that the work reported herein did not require ethics approval because it did not involve animal or human participation.

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CRediT authorship contribution statement

Abhimanyu Sud: Methodology, Investigation, Funding acquisition, Formal analysis, Conceptualization, Writing – original draft. **Kellia Chiu:** Writing – review & editing, Methodology, Investigation, Formal analysis. **Joseph Friedman:** Writing – review & editing, Investigation, Formal analysis. **Julie Dupouy:** Writing – review & editing, Investigation, Formal analysis.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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