

Contents lists available at ScienceDirect

International Journal of Drug Policy



journal homepage: www.elsevier.com/locate/drugpo

Commentary

Comparing methadone policy and practice in France and the US: Implications for US policy reform



Honora Englander^{a,b,*}, Mathieu Chappuy^{b,c,d}, Noa Krawczyck^e, Jef Bratberg^f, Ruth Potee^g, Marie Jauffret-Roustide^{h,i,j,1}, Benjamin Rolland^{b,c,1}

^a Section of Addiction Medicine in General Internal Medicine and the Division of Hospital Medicine, Department of Medicine, Oregon Health & Science University, Portland, OR, USA

^b Service Universitaire d'Addictologie de Lyon, Centre Hospitalier Le Vinatier, Bron, France

^c Centre de Soins d'Accompagnement et de Prévention en Addictologie, Hospices Civils de Lyon, Lyon, France

^d Service Pharmaceutique, Hospices Civils de Lyon, Lyon, France

^e Center for Opioid Epidemiology and Policy, NYU Grossman School of Medicine, New York NY, USA

f University of Rhode Island College of Pharmacy, Kingston, RI, USA

^g Behavioral Health Network, Springfield, MA, USA

^h Centre d'étude des Mouvements Sociaux (Inserm U1276/CNRS UMR8044/EHESS), Paris, France

ⁱ British Columbia Center on Substance Use (BCCSU), Vancouver, Canada

^j Baldy Center on Law and Social Policy, Buffalo University, New York City, NY, USA

ARTICLE INFO

Keywords: Methadone Opioid-related disorders Policy Pharmacies France

ABSTRACT

Despite being among the most effective treatments for opioid use disorder, methadone is largely unavailable in the United States, due primarily to federal and other policies that limit its availability and regulate clinical decisions about doses, visit frequency, and drug testing. There is unprecedented momentum to change decadesold US methadone policies. Yet uncertainty remains as to whether reforms will be adopted and how policies will be implemented. France has among the best methadone access and lowest overdose death rates worldwide. 87 % of French people with opioid use disorder receive methadone or buprenorphine, versus an estimated 13-20 % in the US. France's opioid-related overdose rates are far lower than the US. This article compares French and US systems, including current and proposed US policies, and underscores potential implications for US policymakers.

In France, methadone can be initiated in specialty addiction settings and hospitals, with subsequent handoff to primary care. Methadone can be dispensed in community pharmacies and filled like other opioids, without requirements for supervised dosing. Decisions about visit frequency, medication doses, and drug testing are governed by clinical best practices and patient-clinician shared decision-making. In the US, methadone for opioid use disorder is regulated unlike any other medication (including methadone for pain) and is governed by strict federal controls, including from law enforcement and healthcare. With few exceptions, methadone for opioid use disorder is only available in Opioid Treatment Programs. US clinicians cannot prescribe methadone for opioid use disorder. Federal rules determine minimum visit frequency, initial dose limits, and other conditions of treatment, which states may further limit.

Policies assert strong influence on patient experience, treatment access, and health outcomes. Despite being less restrictive than the US, the French model includes limits designed to avoid or minimize potential harms. French policies have important implications for potential US reforms.

Background

The US faces an unrelenting epidemic of drug related deaths, with

over 80,000 Americans dying from opioid-related overdoses annually, and many more from other drug-related causes (Centers for Disease Control and Prevention; King et al., 2022). Medications for opioid use

* Corresponding author.

https://doi.org/10.1016/j.drugpo.2024.104487

0955-3959/© 2024 Elsevier B.V. All rights are reserved, including those for text and data mining, AI training, and similar technologies.

E-mail address: englandh@ohsu.edu (H. Englander).

¹ Co-last authors.

disorder, methadone and buprenorphine, are the most effective tools to treat opioid use disorder and are first-line treatment in national and international guidelines (ASAM, 2020; Bertin, 2022; WHO, 2009). Decades of evidence show that methadone reduces opioid cravings and use, reduces HIV and hepatitis C transmission, improves quality of life, and reduces overdoses and deaths. Yet it remains largely inaccessible in the US, where fewer than 1 in 5 Americans who might benefit receive methadone or buprenorphine, with even greater gaps among racial minorities and in rural areas (Barnett et al., 2023; Jones et al., 2023; Joudrey et al., 2023; Krawczyk et al., 2022). These gaps exist despite the fact that methadone was first developed in the US in the 1960s as a novel treatment for opioid use disorder (Dole & Nyswander, 1965).

The substantial gap between opioid use disorder prevalence and treatment access in the US is due largely to policies and practices that control methadone (Englander et al., 2023; Jaffe & O'Keeffe, 2003; Pew, 2022; SAMHSA, 2024; Simon et al., 2022). US methadone policies are mostly unchanged since the 1970s and have been sharply criticized for being outdated and overly restrictive (Adams et al., 2022; Jaffe & O'Keeffe, 2003; Simon et al., 2022). Today there is unprecedented momentum for change. The US Congress is currently considering the Modernizing Opioid Treatment Access Act which, if passed, could permit methadone prescribing by addiction medicine specialists to be filled in community pharmacies (S.644 - Modernizing Opioid Treatment Access Act (M-OTAA), 2023-2024). Moreover, some clinician and patient-groups advocate for more expansive policies (Suen et al., 2024). However, there remains intense debate regarding safety, feasibility and optimal best practices for US methadone delivery. The details of such policies will have profound effects on implementation feasibility, methadone access, patient experience, and health outcomes.

France has among the best treatment access, health outcomes and overdose rates in Europe and worldwide. Compared to the US, where estimates show 13-22 % of Americans with opioid use disorder receive appropriate medications (Jones et al., 2023; Krawczyk et al., 2022), in France, 87 % of people receive methadone or buprenorphine (OFDT, March 2023). In 2021, methadone comprised 44 % of prescribed opioid use disorder medications in France. France has among the lowest rates of opioid-involved overdose deaths across Europe, and 32 times lower rates than the US. In 2019, France estimated 450 opioid overdose-related deaths (0.67 per 100,000 people); when, by comparison, US estimated the 70,980 (21.6 per 100,000) (Nguemeni Tiako et al., 2022).

US policymakers are considering major historical reforms that will determine the future of US methadone. France offers a sharp contrast and critical insights. Here, we compare French and US systems, including current and proposed US policies. We organize this paper by outlining policies and regulatory framework governing methadone; describing the settings wherein patients can access methadone; and comparing key features of care delivery, including requirements for visit frequency; methadone dosing; and conditions of treatment (e.g. urine drug screens, counseling requirements). Throughout, we first describe France's approach and then the US's. Table 1 summarizes key comparisons. We conclude by underscoring potential implications for US policymakers.

History and Regulatory Framework

France implemented methadone in 1995, later than many European countries and the US, where methadone was introduced in the 1960s. Propelled by the AIDS epidemic in the late 1980s when HIV prevalence among people who used drugs approached 40 %, France took concrete efforts to advance methadone and buprenorphine as part of a comprehensive national harm reduction strategy (Emmanuelli & Desenclos, 2005). After legalizing pharmacy syringe distribution in 1987, starting in 1995 France promoted buprenorphine and methadone access by assuring widespread treatment services and low-barrier care (described below) (Emmanuelli & Desenclos, 2005; Nguemeni Tiako et al., 2022). Paradoxically, France's strong public health approach co-exists with

laws wherein the possession, use, and distribution of illicit drugs are strictly prohibited and can have serious legal consequences, including fines and imprisonment (Nguemeni Tiako et al., 2022).

In France, methadone is governed by the same agencies and regulating bodies as other medications. Methadone is classified like most other opioids (e.g. buprenorphine, oxycodone) and is subject to specific prescribing requirements (detailed below). As with all medications, France's National Health Authority recommends clinical best practices (Bertin, 2022), and national payers and compliance bodies routinely monitor methadone prescribing, as they do with all controlled substances.

In contrast to France's public health-oriented approach, the US policy landscape governing methadone has been dominated by the war on drugs and tight controls restricting methadone access (Adams et al., 2022; Conway et al., 2023; Simon et al., 2022). US methadone can only be dispensed from federally licensed, highly regulated opioid treatment programs (OTPs) which are subject to strong federal oversight from the Drug Enforcement Agency (DEA) - a law enforcement agency tasked with combatting illicit drug trafficking - and the Substance Abuse and Mental Health Services Association (SAMHSA)(Jaffe & O'Keeffe, 2003). Additionally, methadone treatment is governed by multiple, varying state and local regulatory requirements (Jackson et al., 2020; Jaffe & O'Keeffe, 2003). Methadone - when prescribed for opioid use disorder is subject to a different regulatory framework than all other medical treatments (SAMHSA, 2024). In practice, this means that when indicated for chronic pain, methadone can be prescribed by any physician, in any setting, without federal dosing limits, and dispensed in a bottle or tablet in a community pharmacy. However, when indicated for opioid use disorder, methadone cannot be prescribed, it is subject to strict federal and state rules including dosing limits, and it is illegal to dispense in community pharmacies (SAMHSA, 2024).

Setting: where can patients access methadone?

France has a national network of addiction prevention and treatment centers called CSAPAs ("Centre de Soin, d'Accompagnement et de Prévention en Addictologie"), which provide longitudinal multidisciplinary addiction care, including methadone prescribing and dispensation ("Décret no 2005-1606 du 19 décembre 2005,"). CSAPA addiction centers are distributed across each of France's 101 Departments, and are part of broad public health-oriented efforts to reduce harms of drug use and prevent infections such as HIV and hepatitis C. Any person in France can utilize CSAPA services, which are publicly funded, anonymous, and free. While most centers exist in physical buildings, some exist in nontraditional settings such as methadone buses, jails, or harm reduction centers. Beyond CSAPAs, hospitals, primary care clinicians, and community pharmacies play an important role in France's methadone care continuum. The French ministry of health provides funding to all French hospitals to implement interprofessional hospital-based addiction liaison and care teams. Teams include at least one physician or nurse, and often include psychologists, social workers, and other healthcare professionals (ELSA, 2000).

Patients can initiate methadone in CSAPA addiction centers and hospitals (ANSM, 2024). Once stable, CSAPA/hospital clinicians can handoff prescribing to any primary care clinician, who requires no additional training. Unlike the US, where methadone stability is determined by strict criteria, French prescribers use clinical judgment to determine stability (Bertin). Hence, they can incorporate individualized considerations to optimize patient outcomes. For example, if a rural patient cannot travel routinely to a CSAPA addiction center, they might transfer prescribing sooner to primary care. Methadone can be prescribed and/or dispensed at any CSAPA or community pharmacy. Pharmacies are distributed across urban and rural France, with most areas having at least 1 pharmacy per 2000 inhabitants (TerraVisu, 2024). In practice, about 60 % of French people receive methadone in primary care (and fill prescriptions in pharmacies) and 40 % get

Table 1

Summary of key comparisons between France and the US.

France	US Historical ³⁰ (pre-April 2024)	US Changes with SAMHSA rules effective April 2, 2024 ⁸
History and Policy Framework	Delini landeene gevening wethedene is	
national harm reduction public health strategy.	dominated by the war on drugs and tight controls.	
Methadone is governed by same agencies and regulating	Methadone for opioid use disorder is governed	
agencies as other medications.	differently than other medications (including	
	law enforcement (DEA) and healthcare (SAMHSA).	
	State laws add additional restrictions, vary widely.	
Clinician judgment, national guidelines, and shared decision-	Strict federal controls determine medication	Some lessening of specific federal controls
making inform medical decisions.	dosage, visit frequency, and other conditions of	(specified below), no impact on more stringent
	treatment. Many states impose more stringent	state rules.
Detions over and save	Tules.	
Patient experience and care		
Setting: where can people access methadone?		
Methadone initiation		
Any CSAPA or hospital clinician can initiate methadone.	Methadone must be started at OTP or hospital, with	
Mathedaus and he discoursed forms (CADA as been ited as be	very few exceptions using "/2-hour rule."	
prescribed (and filled in a community pharmacy).	prescriptions not permitted.	license to dispense methadone to patients without
·······		becoming an OTP.
Addiction consultation services available in every French	Any hospital clinician can initiate methadone, a	
hospital.	practice that is increasing but rare. Continuation	
	requires OTP linkage after discharge.	
CSAPAs exist across all 101 departments	OTP only; no OTPs in 80% of US counties	
Most are in physical buildings	Most are in physical buildings	Allows for admitting patients for methadone
methadone buses (2 nationwide operating at present) Telehealth permitted rarely used	Telehealth prohibited	conditions (no audio-only)
Methadone maintenance		
Any physician, including primary care, can continue	Dispensed from OTP clinician only: not prescribed	
methadone.	a spended non off childen only, not prescribed	
Methadone can be dispensed from CSAPAs or filled via	No primary care, specialty addiction care, or	
secure prescription at any pharmacy	pharmacy-based care	
Permitted in all residential addiction settings	Not permitted or feasible in many residential	
	addiction settings	
Dosing		
Medication dosing		
No legal restrictions.	First dose 20-30 mg; permitted to give additional 10	ocentions permitted (for example, if nation)
	ing for max dose up to 40 mg of day 1.	transferring from another OTP and dose
		documented)
Take home dosing: In-person visit requirements		
Not regulated. Typically patients present daily (M-F) for the	Patients required to present in-person 6 days/ week	New patients can receive up to max 7 days of take-
first 1-2 weeks of treatment, after which visit frequency	for the first 90 days of treatment, 5 days/ week for	home doses during the first 14 days of treatment,
decreases (figure). Maximum prescription duration if filled	the second 90 days, 4 days for the third 90 days,	up to max 14 take home doses from 15 days of treatment and up to max 28 take-home doses from
at community pharmacy is 20 days.	vear.	31 days in treatment. Allows greater flexibility for
	,	split dosing and take-home dosing.
Available methadone formulations		
Liquid available in 5, 10, 20, 40 and 60 mg aliquot bottles (in	DEA has strong preference for liquid methadone	
color-coded, single-dose vials); capsules are available in 1, 5,	dispensed through a computerized pump, can be	
10, 20, and 40 mg amounts.	dispensed to the nearest milligram. Pill or troche	
French law requires that patients start with liquid for the	strongly discouraged and not available in many	
first year of treatment, after which they can transition to		
capsules, with the goal of reducing risk for diversion.		
However, clinicians can request exceptions to this rule to		
Conditions of Treatment what is required to be al	alo to bo oligiblo for mothadono?	<u> </u>
OUD history		
Clinician judgment determines eligibility. Patients must be	Must have history of OUD for at least 1 year. For	Any moderate/severe OUD, OUD in remission, or
at least 15 years old to receive methadone.	people under 18, must have two documented	risk of recurrence/overdose. No requirement of
	unsuccessful attempts at detoxification or drug-free	other treatment attempts for minors <18
	treatment within a 12-month period. Some	
	exceptions (incarceration, pregnancy) permitted.	
Physician visit		
Required before initiating methadone.	In person visit within 14 days of initiating treatment (though often required on day 1) Law parmits using	Allows for audio-visual telehealth (no audio-only).
	hospital or PCP evaluation for initial dosing (though	
	many state authorities or clinics do not allow).	
Urino Drug Tosting (UDT)	,	· · · · · · · · · · · · · · · · · · ·
UDT required before initiating mothodono: othonwise access	Minimum eight random drug totte per vear	Still 8 LIDT/ year. Take home doring door set
required by regulations and utilized as clinically indicated	Twenty-three states require more than 8	require negative toxicology though patients cannot
, ,	random urine drug tests in the first year of	have "active substance use disorder" to take home
	treatment.	methadone.
Mandatory Counseling		
No mandatory counseling, though all CSAPAs offer	OTPs must provide adequate SUD counseling as	
interdisciplinary services including medical, social, and	clinically necessary. 23 of 50 states require	
psychological care.	counseling as a condition of treatment.	
Health System Requirements		
Methadone storage and security		
Methadone must be stored in lockable cabinets or rooms	DEA mandates OTPs adhere to strict storage and	
equipped with a reinforced alert or security system (same as	security regulations. For example: methadone	
with other opioids).	should be stored in a vault "constructed of at least	
	8 incres of reinforced concrete or other substantial	
	1/2-inch steel rods tied 6 inches on center " If the	
	vault weighs less than 750 pounds (340.2 kg) it	
	must be "bolted or cemented to the floor or wall in	
	such a way that it cannot be readily removed."	
	Vaults must be equipped with an alarm system	
	(sometimes required to transmit a signal directly to police) and may require a specific electronic	
	medical record for computerized dispensation of	
	methadone	

Abbreviations: **SAMHSA**: Substance Abuse and Mental Health Services Association; **OUD**: Opioid Use Disorder; **DEA**: Drug Enforcement Agency; **CSAPA**: Centre de Soin, d'Accompagnement et de Prévention en Addictologie [Center for Health, Accompaniment and Prevention in Addiction]; **OTP**: Opioid Treatment Program; **UDT**: urine drug test.

methadone from CSAPAs addiction centers. Of those receiving methadone care in CSAPAs, about half receive methadone dispensed from the CSAPA and half fill a prescription in a pharmacy (OFDT, March 2023).

In the US, ambulatory patients must receive methadone at federally licensed Opioid Treatment Programs (OTPs). OTPs offer methadone, buprenorphine, and some forms of behavioral therapy. As of 2019, 80 % of US counties had no OTP, leaving many areas with no methadone access, particularly in rural areas. Opioid Treatment Programs can create mobile treatment units; however, such units remain nearly nonexistent due to high costs and strict regulations. Vehicles cost \$250,000 or more, have high maintenance costs, must return to the home Opioid Treatment Program nightly per DEA rules, even if that is hundreds of miles away (Gibbons et al., 2022). Ambulatory methadone access outside of Opioid Treatment Programs is extremely rare and difficult to implement (Skogrand et al., 2024; Taylor et al., 2022). And though hospital-based services which can initiate methadone are expanding, they remain rare across the US (Englander et al., 2022).

In the US, there are no federal restrictions on the use of methadone for opioid withdrawal management among patients hospitalized with a medical or surgical condition other than addiction. However, to continue methadone after discharge patients must enroll in an Opioid Treatment Program and most hospitals do not provide methadone (Calcaterra et al., 2024; Priest et al., 2020). Methadone is unavailable in the most US jails, outpatient, and residential addiction treatment settings (Beetham et al., 2020).

Medication formulations, storage requirements, and the role of the community pharmacy

In France, patients may take-home methadone dispensed from the CSAPA addiction center, fill a methadone prescription at any pharmacy, or take methadone under direct supervision at a hospital or CSAPA. Patients fill methadone in pharmacies as they would for any medication, and there is no dedicated counter or requirement for supervised dosing as in Australia, United Kingdom, and Canada (Pew, 2023; Priest et al., 2019). Like other opioids, methadone is prescribed using "secured prescriptions" which are specially designed to prevent falsification or alteration. Prescriptions can include up to 14 days of syrup (i.e. liquid) methadone and 28 days of methadone capsules at a time. Refills are not permitted (Code de la santé publique, 04 février 2022). There are a range of syrup and capsule amounts (table). Generally, patients take syrup for 1 year before transitioning to capsules, which patients often prefer and which promotes broad methadone adoption (Boucherie et al., 2015). Rules specify that French CSAPA addiction centers and pharmacies must store methadone in lockable cabinets or rooms equipped with a reinforced alert or security system, just as with other opioids. And, as with other opioids, CSAPAs and pharmacies must maintain medication logs including date, quantity, and dispensing amounts. Logs are subject to inspection by national supervising authorities.

US pharmacies cannot dispense methadone for opioid use disorder (though notably, they can dispense methadone – the same compound for pain). In the US, methadone is available primarily in liquid form with limited tablet/capsule formulations, and US pharmaceutical manufacturers, wholesalers and distributors have signaled reluctance to expand formulations. Opioid Treatment Program methadone storage and security requirements are extensive (e.g. vaults weighing 750 pounds, alarm systems) (table).

Visit frequency

In France, there are no regulatory limits on methadone in-person visit frequency or allowable take-home doses beyond a rule limiting methadone prescriptions to 14 days for syrup and 28 days for pills (table) (Code de la santé publique, 04 février 2022). Typically, during initiation, patients present daily (Monday through Friday) for the first two weeks wherein CSAPA clinicians adjust medication doses and assess for ongoing cravings, withdrawal, or over-sedation (Bertin, Version du 10 mars 2022). Typically, thereafter, patients visit the CSAPA addiction center less frequently. Once patients are stable, clinicians usually prescribe up to 14-28 days of methadone at a time (Fig. 1).

In the US, federal regulations determine minimum Opioid Treatment Program visit frequency. Historically, new patients were required to present in-person 6 days/ week for the first 90 days, after which they were eligible to reduce visits to 5 days/week for the next 90 days, and accordingly thereafter (SAMHSA, 2015). During the COVID-19 pandemic, US federal regulations were loosened to permit greater use of take-home methadone doses (Levander et al., 2022). These flexibilities were associated with increased patient-satisfaction and no worse outcomes related to overdose deaths, urine drug positivity, medication diversion, or treatment retention (Amram et al., 2021; Figgatt et al., 2021; Jones et al., 2022; Williams et al., 2023). Despite this, many OTPs did not continue offering allowable flexibilities (Figgatt et al., 2021; Levander et al., 2022). Effective April 2024, the US Substance Abuse and Mental Health Services Association, SAMHSA, updated its guidance to extend far greater flexibilities (SAMHSA, 2024) (Fig. 1), however if and how this guidance will be adopted at state and Opioid Treatment Program-levels remains uncertain.

Methadone Dosing

In France there are no regulatory limits on methadone dose amounts. Clinicians can tailor doses to individual patient needs, including dividing doses multiple times per day such as in cases of pregnancy or acute pain.

US federal guidelines govern first day dosing (table) (Substance Abuse and Mental Health Services Administration, 2021). Thereafter, there are no rules governing dosing, however many Opioid Treatment Programs rely on protocols that were developed before fentanyl dominated the drug supply (Buresh et al., 2022), which in many cases takes months to reach therapeutic doses. Divided doses are frequently not permitted, even in pregnancy and other clinically necessary scenarios.

Other conditions of treatment

In France, a physician must complete a history and physical and obtain a urine drug test before initiating methadone. There are no requirements for periodic urine drug tests and no mandatory counseling (table). Care at CSAPA addiction centers is anonymous and free, and methadone care in pharmacies, primary care, and hospital is paid for by single payer public insurance.

In the US, federal rules mandate that patients complete a history and physical within 14 days of initiating treatment, though many states require it on day 1. Federal rules dictate that patients must have at least 8 random urine drug tests per year, and counseling is mandated in 23 of 50 states (Russoniello et al., 2023). Some insurers do not cover methadone, and not all clinics accept all insurance types (e.g. Medicare, Medicaid). US patient out-of-pocket methadone expenses vary widely, commonly costing people without insurance as much as \$550/month (Lopez, 2020; NIDA, 2021). Additional costs (e.g. daily transportation, in-person dosing interfering with employment) further increase financial burden on patients (Englander et al., 2023).



Fig. 1. Comparison of methadone visit frequency in France and US in first 90 days of treatment.

*In France, clinicians rely on best practice, clinical judgement, and shared decision-making to determine visit frequency.

**In US, federal laws dictate minimum visit frequency, shown here. State laws, individual OTP policies, and individual clinicians impose more stringent limits and may not adopt afforded flexibilities. The Substance Abuse and Mental Health Services Association (SAMHSA) changes went into effect April 2, 2024, though most OTPs have not adopted flexibilities.

Harm reduction integration

In France, methadone is part of a national harm reduction strategy wherein abstinence is neither a prerequisite nor a condition of care (Janssen et al., 2024; Nguemeni Tiako et al., 2022). Patients can access naloxone, syringes, and other harm reduction supplies where they receive methadone. CSAPA addiction centers exist adjacent to broader networks including harm reduction centers ("Décret no 2005-1606 du 19 décembre 2005,"), drug-user unions, and nationally coordinated drug checking systems. French patients generally report high satisfaction with methadone, citing trust with healthcare clinicians and shared decision-making - versus methadone as a form of social control - as paramount to their experience (Jauffret-Roustide, 2004).

In the US, treatment is siloed from harm reduction (Krawczyk et al., 2022). The US treatment paradigm focuses overwhelmingly on abstinence from opioids and other drugs as both the purpose and condition of methadone treatment (Frank et al., 2021; Simon et al., 2022). Variable state laws, clinic and pharmacy policies often further restrict access to harm reduction supplies and practices (Davis & Carr, 2022).

Limitations of the French methadone comparison

Despite its success, the French model is not perfect. Common concerns include long wait-times to initiate care in CSAPA addiction centers; lower access among some populations, including in rural areas or among immigrant populations who may benefit from culturally specific services (Benyamina, 2014); and the possibility of methadone misuse or diversion. However, while rates of diversion and misuse are difficult to measure, reported rates in France are low. In a study of people who utilize CSAPA addiction centers and harm reduction centers, 90 % of people report obtaining methadone and buprenorphine from medical prescribers (Jauffret-Roustide et al., 2013), and 95 % of people prescribed methadone report taking it orally (OFDT, March 2023). Importantly, France's constitution prohibits the collection of racial demographics, so racial disparities are largely unknown (Nguemeni Tiako et al., 2022). Further, while all primary care clinicians in France may continue prescribing methadone, many feel under-prepared or hold stigmatizing attitudes towards patients with opioid use disorder, (Gimenez et al., 2024) and some patients report being refused methadone by primary care or in pharmacies. Finally, France has not yet been tested by the challenges of fentanyl and other high potency synthetic opioids which dominate the US unregulated drug supply, which would test methadone and other harm reduction systems. While considerable, these differences underscore the need to understand models like France that have achieved broad methadone access.

Discussion

France has integrated and adopted methadone across the healthcare continuum, including specialty addictions care, hospitals, primary care, and pharmacies. Unlike US policies which prioritize abstinence, France's policies and systems promote engagement in care. The French model serves as a population-health strategy with widespread methadone access and few if any negative consequences. Compared with the US, methadone in France imposes fewer regulatory controls, yet experiences fewer methadone and opioid-related deaths. Between 2011 and 2021, methadone prescriptions in France increased from 32 % to 44 % of the total prescribed medications for opioid use disorder (OFDT, March 2023), with a reduction in methadone-related deaths during this same time (Revol et al., 2023). There have been numerous calls to transform US methadone systems to be more accessible, equitable, coordinated, and patient centered. France's provides a potential roadmap with key implications for US policymakers.

First, pharmacy-based methadone is a critical component of France's approach and may be the only practical way for the US to expand beyond the very limited Opioid Treatment Program footprint. Only 20 % of US counties have an OTP, with hours-long drive times in many parts of the US (Krawczyk et al., 2023). By contrast, 89 % of the US population lives within 5 miles of a pharmacy, and pharmacies are set up to store and dispense controlled medications (Berenbrok et al., 2022). The Modernizing Opioid Treatment Access Act (M-OTAA), currently being considered by the US Congress, would take the critical step to allow pharmacies to dispense methadone. However, the degree of policy-controls and requirements of pharmacies remain uncertain. The US Drug Enforcement Agency (DEA) requirement that Opioid Treatment Programs store methadone in a 750-pound or bolted vault contrasts with France's requirement for safe, secure methadone storage - like all other opioids - and underscores the need for practical approaches to pharmacy-based methadone. Further, the US experience with buprenorphine offers a cautionary tale: over 40 % of US retail pharmacies do not stock buprenorphine (Weiner et al., 2023) due to multiple factors, including federal policies which increase liability and restrict access

H. Englander et al.

across medication distributors, pharmacies, and pharmacists (Qato et al., 2022). US pharmacy-based methadone adoption will likely require incentives, and at minimum cannot introduce disincentives to stocking and dispensing methadone. France shows that this is feasible and safe.

By contrast, France's pharmacy-based methadone model is not burdensome to patients, clinicians, or pharmacists, and does not impose administrative or financial disincentives on pharmacies or pharmacists offering care. Patients fill methadone at any community pharmacy, and there are no requirements for supervised doses or drug testing. If adopted, similar policies in the US would reduce the treatment burden on patients, for example, by reducing travel hardships and work conflicts. Such changes would be a critical step to humanizing care and improving treatment retention (Englander et al., 2023; Frank et al., 2021).

France's model of methadone initiation by specialists and hospital clinicians with handoff to primary care warrants consideration in the US. US addiction physicians alone are unlikely to be able to meet the widespread need for methadone care (Joudrey et al., 2023). In 2022, methadone was available in only 49 % of census tracts, which are geographic entities within counties. A recent study found that expanding prescribing to include addiction specialists and primary care would increase this to 63 % and 86 % of US census tracts respectively, with the most gains in rural and suburban areas (Joudrey et al., 2023). France's approach of specialists or in hospital clinicians initiating methadone with handoff to primary care after stabilization - offers a practical approach to how the US might achieve widespread methadone access. Further, implementing widespread community methadone systems with less regulatory controls has potential to increase hospital-based methadone access. Currently, hospital clinicians often avoid starting methadone because they have nowhere to refer patients after discharge or because post-hospital care coordination is overly complicated (Calcaterra et al., 2024). If patients could fill a discharge prescription and follow up in primary care this would be a radical improvement on current access challenges. France's success with primary care and pharmacy-based methadone is consistent with experiences in other countries that have demonstrated that integrating methadone as part of routine clinical practice leads to improvements in patient satisfaction, treatment retention, and mortality (Facher, 2024; Gauthier et al., 2018; Jin et al., 2020; McCarty et al., 2021; Mullen et al., 2012; Nolan et al., 2015).

The US is at a critical juncture: current policies are failing to curb opioid-related deaths and highly effective treatments remain inaccessible, despite years of a national public health state of emergency. It is time to change 50 years of an intractable status quo policy on US methadone. France offers critical lessons for how to expand methadone access and address the unrelenting US crisis of opioid-overdoses and drug-related harms.

CRediT authorship contribution statement

Honora Englander: Writing – review & editing, Writing – original draft, Funding acquisition, Conceptualization. Mathieu Chappuy: Writing – review & editing, Resources, Conceptualization. Noa Krawczyck: Writing – review & editing, Conceptualization. Jef Bratberg: Writing – review & editing. Ruth Potee: Writing – review & editing, Conceptualization. Marie Jauffret-Roustide: Writing – review & editing, Conceptualization. Benjamin Rolland: Writing – review & editing, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Dr. Krawczyk was supported by the National Institute on Drug Abuse of the National Institutes of Health under Award Number K01DA055758. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. Dr. Krawczyk receives consulting fees for expert witness testimony in ongoing opioid litigation. Jef Bratberg is a consultant on a grant from Pew Trusts and Brandeis University grant studying pharmacy and Opioid Treatment Program (OTP) business models.

Acknowledgments

Authors would like to thank Dr. Christope Icard for supporting this work.

Ethics approval

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

Funding sources

This research received funding from the following sources

Dr Englander received a grant for this work from the US Fulbright program, the Franco-American Fulbright Commission, the Fondation Neurodis, and the Centre Le Hospitalier Vinatier.

Sponsor had no role in study design; data collection, analysis or interpretation; writing of the report; or decision to submit the article for publication.

References

- Adams, Z., Krawczyk, N., Simon, R., Sue, K., Suen, L., & Joudrey, P. (2022). To save lives from opioid overdose deaths, bring methadone into mainstream medicine. *Health Affairs Forefront*. https://doi.org/10.1377/forefront.20220524.911965
- Amram, O., Amiri, S., Panwala, V., Lutz, R., Joudrey, P. J., & Socias, E. (2021). The impact of relaxation of methadone take-home protocols on treatment outcomes in the COVID-19 era. *The American Journal of Drug and Alcohol Abuse*, 47(6), 722–729. https://doi.org/10.1080/00952990.2021.1979991
- ANSM. Bases de données publiques des médicaments: résumé des caractéristiques du produit, Methadone. Retrieved March 20, 2024, from https://base-donnees-publique.medica ments.gouv.fr/affichageDoc.php?specid=63009443&typedoc=R.
- ASAM. (2020). The ASAM national practice guideline for the treatment of opioid use disorder: 2020 focused update. *Journal of Addiction Medicine*, 14(2S Suppl 1), 1–91. https://doi.org/10.1097/adm.00000000000633
- Barnett, M. L., Meara, E., Lewinson, T., Hardy, B., Chyn, D., Onsando, M., Huskamp, H. A., Mehrotra, A., & Morden, N. E. (2023). Racial inequality in receipt of medications for opioid use disorder. *The New England Journal of Medicine*, 388(19), 1779–1789. https://doi.org/10.1056/NEJMsa2212412
- Beetham, T., Saloner, B., Gaye, M., Wakeman, S. E., Frank, R. G., & Barnett, M. L. (2020). Therapies Offered at Residential Addiction Treatment Programs in the United States. JAMA, 324(8), 804–806. https://doi.org/10.1001/jama.2020.8969
- Benyamina, A. (2014). The current status of opioid maintenance treatment in France: a survey of physicians, patients, and out-of-treatment opioid users. *International Journal of General Medicine*, 7, 449–457. https://doi.org/10.2147/ijgm.S61014
- Berenbrok, L. A., Tang, S., Gabriel, N., Guo, J., Sharareh, N., Patel, N., ... Hernandez, I. (2022). Access to community pharmacies: A nationwide geographic information systems cross-sectional analysis. J Am Pharm Assoc (2003), 62(6), 1816–1822. https://doi.org/10.1016/j.japh.2022.07.003
- Bertin, C.e.a. (2022). Haute Autorité de santé (HAS): Bon usage des médicaments opioïdes : Antalgie, prévention et prise en charge du trouble de l'usage et des surdoses.
- Boucherie, Q., Frauger, E., Thirion, X., Mallaret, M., & Micallef, J. (2015). New methadone formulation in France: Results from 5 years of utilization. *Therapie*, 70 (2), 223–234. https://doi.org/10.2515/therapie/2015016
- Buresh, M., Nahvi, S., Steiger, S., & Weinstein, Z. M. (2022). Adapting methadone inductions to the fentanyl era. Journal of Substance Abuse Treatment, 141, 108832. https://doi.org/10.1016/j.jsat.2022.108832
- Calcaterra, S. L., Dafoe, A., Tietbohl, C., Thurman, L., & Bredenberg, E. (2024). Unintended consequences of methadone regulation for opioid use disorder treatment among hospitalized patients. *Journal of Hospital Medicine*. https://doi.org/10.1002/ jhm.13329
- Centers for Disease Control and Prevention, N. C. f. I. P. a. C. (2023). https://www.cdc. gov/drugoverdose/deaths/index.html#:~:text=Opioids%20were%20involved% 20in%2080%2C411.and%20without%20synthetic%20opioid%20involvement.
- Code de la santé publique: Partie réglementaire (Articles R1110-1 à R6431-76), (2022). https://www.legifrance.gouv.fr/codes/article_lc/LEGIARTI000045117827/2022-0 2-04/.
- Conway, A., Krawczyk, N., McGaffey, F., Doyle, S., Baaklini, V., Marshall, A. D., ... Cerdá, M. (2023). Typology of laws restricting access to methadone treatment in the

International Journal of Drug Policy 129 (2024) 104487

United States: A latent class analysis. International Journal of Drug Policy, 119, 104141. https://doi.org/10.1016/j.drugpo.2023.104141

- Davis, C. S., & Carr, D. H. (2022). Repealing State Drug-Paraphernalia Laws The Need for Federal Leadership. *The New England Journal of Medicine*, 387(15), 1344–1346. https://doi.org/10.1056/NEJMp2207866
- Décret no 2005-1606 du 19 décembre 2005. In Relatif aux missions des centres d'accueil et d'accompagnement à la réduction des risques pour usagers de drogues et modifiant le code de la santé publique (Vol. NOR : SANP0524015D).
- Dole, V. P., & Nyswander, M. (1965). A medical treatment for diacetylmorphine (heroin) addiction: A clinical trial with methadone hydrochloride. JAMA, 193(8), 646–650. https://doi.org/10.1001/jama.1965.03090080008002
- Emmanuelli, J., & Desenclos, J. C. (2005). Harm reduction interventions, behaviours and associated health outcomes in France, 1996-2003. Addiction, 100(11), 1690–1700. https://doi.org/10.1111/j.1360-0443.2005.01271.x
- Englander, H., Gregg, J., & Levander, X. A. (2023). Envisioning minimally disruptive opioid use disorder care. *Journal of General Internal Medicine*, 38(3), 799–803. https://doi.org/10.1007/s11606-022-07939-x
- Englander, H., Jones, A., Krawczyk, N., Patten, A., Roberts, T., Korthuis, P. T., & McNeely, J. (2022). A taxonomy of hospital-based addiction care models: A scoping review and key informant interviews. *Journal of General Internal Medicine*. https:// doi.org/10.1007/s11606-022-07618-x
- Evolution des pratiques en ELSA, en intra et en extrahospitalier (2000). Retrieved March 20, 2024, from https://www.calameo.com/books/005544858080078220c4a.
- Facher, L. (2024). Switzerland had a drug overdose crisis. Then it made methadone easy to eet. StatNews.
- Figgatt, M. C., Salazar, Z., Day, E., Vincent, L., & Dasgupta, N. (2021). Take-home dosing experiences among persons receiving methadone maintenance treatment during COVID-19. Journal of Substance Abuse Treatment, 123, Article 108276. https://doi. org/10.1016/j.jsat.2021.108276
- Frank, D., Mateu-Gelabert, P., Perlman, D. C., Walters, S. M., Curran, L., & Guarino, H. (2021). It's like 'liquid handcuffs': The effects of take-home dosing policies on Methadone Maintenance Treatment (MMT) patients' lives. *Harm Reduction Journal*, 18(1), 88. https://doi.org/10.1186/s12954-021-00535-y
- Gauthier, G., Eibl, J. K., & Marsh, D. C. (2018). Improved treatment-retention for patients receiving methadone dosing within the clinic providing physician and other health services (onsite) versus dosing at community (offsite) pharmacies. *Drug and Alcohol Dependence*, 191, 1–5. https://doi.org/10.1016/j.drugalcdep.2018.04.029
- Gibbons, J. B., Stuart, E. A., & Saloner, B. (2022). Methadone on Wheels—A New Option to Expand Access to Care Through Mobile Units. JAMA Psychiatry, 79(3), 187–188. https://doi.org/10.1001/jamapsychiatry.2021.3716
- Gimenez, L., Bonis, D., Morel, M., Palmaro, A., Dassieu, L., & Dupouy, J. (2024). Barriers and facilitators to the involvement of general practitioners in the prescription of buprenorphine. *Journal of Substance Use and Addiction Treatment, 156*, Article 209182. https://doi.org/10.1016/j.josat.2023.209182
- Jackson, J. R., Harle, C. A., Silverman, R. D., Simon, K., & Menachemi, N. (2020). Characterizing variability in state-level regulations governing opioid treatment programs. Journal of Substance Abuse Treatment, 115, 108008. https://doi.org/ 10.1016/j.jsat.2020.108008
- Jaffe, J. H., & O'Keeffe, C. (2003). From morphine clinics to buprenorphine: Regulating opioid agonist treatment of addiction in the United States. *Drug and Alcohol Dependence*, 70(2 Suppl), S3–11. https://doi.org/10.1016/s0376-8716(03)00055-3
- Janssen, E., Vuolo, M., Spilka, S., & Airagnes, G. (2024). Predictors of concurrent heroin use among patients on opioid maintenance treatment in France: A multilevel study over 11 years. *Harm Reduction Journal*, 21(1), 15. https://doi.org/10.1186/s12954-024-00934-x
- Jauffret-Roustide, M. (2004). Du point de vue des usagers, quels sont les effets, les bénéfices et les difficultés suscités par les TSO ? Alcoologie et Addictologie.
- Jauffret-Roustide, M., Pillonel, J., Weill-Barillet, L., Léon, L., Le Strat, Y., Brunet, S., Benoit, T., Chauvin, C., Lebreton, M., & Barin, F. (2013). Estimation de la séroprévalence du VIH et de l'hépatite C chez les usagers de drogues en France-Premiers résultats de l'enquête ANRS-Coquelicot 2011. Bulletin Epidémiologique Hebdomadaire-BEH, (39-40), 504–509.
- Jin, H., Marshall, B. D. L., Degenhardt, L., Strang, J., Hickman, M., Fiellin, D. A., Ali, R., Bruneau, J., & Larney, S. (2020). Global opioid agonist treatment: A review of clinical practices by country. *Addiction (Abingdon, England)*, 115(12), 2243–2254. https://doi.org/10.1111/add.15087
- Jones, C. M., Compton, W. M., Han, B., Baldwin, G., & Volkow, N. D. (2022). Methadoneinvolved overdose deaths in the US before and after federal policy changes expanding take-home methadone doses from opioid treatment programs. JAMA Psychiatry, 79(9), 932–934. https://doi.org/10.1001/jamapsychiatry.2022.1776
- Jones, C. M., Han, B., Baldwin, G. T., Einstein, E. B., & Compton, W. M. (2023). Use of medication for opioid use disorder among adults with past-year opioid use disorder in the US, 2021. JAMA Network Open, 6(8), Article e2327488. https://doi.org/ 10.1001/jamanetworkopen.2023.27488
- Joudrey, P. J., Halpern, D., Lin, Q., Paykin, S., Mair, C., & Kolak, M. (2023). Methadone prescribing by addiction specialists likely to leave communities without available methadone treatment. *Health Affairs Scholar*, 1(5). https://doi.org/10.1093/haschl/ qxad061
- King, C., Cook, R., Korthuis, P. T., Morris, C. D., & Englander, H. (2022). Causes of death in the 12 months after hospital discharge among patients with opioid use disorder. *Journal of Addiction Medicine*, 16(4), 466–469. https://doi.org/10.1097/ adm.00000000000915
- Krawczyk, N., Joudrey, P. J., Simon, R., Russel, D. M., & Frank, D. (2023). Recent modifications to the US methadone treatment system are a Band-Aid—not a solution—to the nation's broken opioid use disorder treatment system. *Health Affairs Scholar*, 1(1). https://doi.org/10.1093/haschl/qxad018

- Krawczyk, N., Rivera, B. D., Jent, V., Keyes, K. M., Jones, C. M., & Cerdá, M. (2022). Has the treatment gap for opioid use disorder narrowed in the U.S.?: A yearly assessment from 2010 to 2019. *The International Journal on Drug Policy*, 103786. https://doi.org/ 10.1016/j.drugpo.2022.103786
- Levander, X. A., Pytell, J. D., Stoller, K. B., Korthuis, P. T., & Chander, G. (2022). COVID-19-related policy changes for methadone take-home dosing: A multistate survey of opioid treatment program leadership. *Substance Abuse*, 43(1), 633–639. https://doi. org/10.1080/08897077.2021.1986768

Lopez, G. (2020). Methadone can help people beat opioid addiction — If they can afford it. Vox News.

McCarty, D., Bougatsos, C., Chan, B., Hoffman, K. A., Priest, K. C., Grusing, S., & Chou, R. (2021). Office-based methadone treatment for opioid use disorder and pharmacy dispensing: A scoping review. *The American Journal of Psychiatry*, 178(9), 804–817. https://doi.org/10.1176/appi.ajp.2021.20101548

Mullen, L., Barry, J., Long, J., Keenan, E., Mulholland, D., Grogan, L., & Delargy, I. (2012). A national study of the retention of Irish opiate users in methadone substitution treatment. *The American Journal of Drug and Alcohol Abuse, 38*(6), 551–558. https://doi.org/10.3109/00952990.2012.694516

Nguemeni Tiako, M. J., Netherland, J., Hansen, H., & Jauffret-Roustide, M. (2022). Drug overdose epidemic colliding with COVID-19: What the United States can learn from France. American Journal of Public Health, 112(S2), S128–s132. https://doi.org/ 10.2105/ajph.2022.306763

NIDA. (2021). Medications to treat opioid use disorder research report: How much does opioid treatment cost?.

Nolan, S., Hayashi, K., Milloy, M. J., Kerr, T., Dong, H., Lima, V. D., Lappalainen, L., Montaner, J., & Wood, E. (2015). The impact of low-threshold methadone maintenance treatment on mortality in a Canadian setting. *Drug and Alcohol Dependence*, 156, 57–61. https://doi.org/10.1016/j.drugalcdep.2015.08.037

OFDT. (2023). Trainments de substitution aux opioids en France, Bilan 2023. http://www. ofdt.fr/BDD/publications/docs/TabTSO230418.pdf.

- Pew. (2022). Overview of opioid treatment program regulations by state. https://www.pewtr usts.org/en/research-and-analysis/issue-briefs/2022/09/overview-of-opioid-treat ment-program-regulations-by-state.
- Pew. (2023). In Australia, primary care and pharmacies deliver methadone. Pew Charitable Trusts. Retrieved March 20, 2024 from https://www.pewtrusts.org/en/resear ch-and-analysis/fact-sheets/2023/05/in-australia-primary-care-and-pharmacies-de liver-methadone.
- Priest, K. C., Gorfinkel, L., Klimas, J., Jones, A. A., Fairbairn, N., & McCarty, D. (2019). Comparing Canadian and United States opioid agonist therapy policies. *The International Journal on Drug Policy*, 74, 257–265. https://doi.org/10.1016/j. drugpo.2019.01.020
- Priest, K. C., Lovejoy, T. I., Englander, H., Shull, S., & McCarty, D. (2020). Opioid agonist therapy during hospitalization within the veterans health administration: A pragmatic retrospective cohort analysis. *Journal of General Internal Medicine*, 35(8), 2365–2374. https://doi.org/10.1007/s11606-020-05815-0
- Qato, D. M., Watanabe, J. H., & Clark, K. J. (2022). Federal and State Pharmacy Regulations and Dispensing Barriers to Buprenorphine Access at Retail Pharmacies in the US. JAMA Health Forum, 3(8). https://doi.org/10.1001/ jamahealthforum.2022.2839e222839-e222839.
- Revol, B., Willeman, T., Manceau, M., Dumestre-Toulet, V., Gaulier, J. M., Fouilhé Sam-Laï, N., & Eysseric-Guérin, H. (2023). Trends in Fatal Poisoning Among Drug Users in France From 2011 to 2021: An Analysis of the DRAMES Register. JAMA Netw Open, 6 (8), Article e2331398. https://doi.org/10.1001/jamanetworkopen.2023.31398 Russoniello, K., Harrington, C., Beydoun, S., & Borrego, L. (2023). State-Specific Barriers
- Russoniello, K., Harrington, C., Beydoun, S., & Borrego, L. (2023). State-Specific Barriers to Methadone for Opioid Use Disorder Treatment. *Journal of Law, Medicine & Ethics*, 51(2), 403–412. https://doi.org/10.1017/jme.2023.73

SAMHSA. (2015). Federal Guidelines for Opioid Treatment Programs. Substance Abuse and Mental Health Services Administration. HHS Publication No. (SMA) XX-XXXX. SAMHSA. (2024). 42 CFR Part 8 Final Rule, Revised.

- Simon, C., Vincent, L., Coulter, A., Salazar, Z., Voyles, N., Roberts, L., Frank, D., & Brothers, S. (2022). The methadone manifesto: Treatment experiences and policy recommendations from methadone patient activists. *American Journal of Public Health*, 112(S2), S117–s122. https://doi.org/10.2105/ajph.2021.306665
- Skogrand, E., Sharpe, J., & Englander, H. (2024). Dispensing methadone at hospital discharge: One hospital's approach to implementing the "72-hour rule" change. *Journal of Addiction Medicine*, 18(1), 71–74. https://doi.org/10.1097/ adm.00000000001246

Substance Abuse and Mental Health Services Administration, S. (2021). Medications for opioid use disorder. Treatment Improvement Protocol (TIP) Series 63.

- Suen, L. W., Incze, M., Simon, C., Englander, H., Bratberg, J., Groves Scott, G., & Winograd, R. (2024). Methadone's Resurgence in Bridging the Treatment Gap in the Overdose Crisis:Position Statement of AMERSA, Inc (Association for Multidisciplinary Education, Research, Substance Use, and Addiction). Journal of Substance Use and Addiction. https://doi.org/10.1177/29767342241255480
- S.644 Modernizing Opioid Treatment Access Act (M-OTAA). (2023-2024). Retrieved March 20, 2024 from https://www.congress.gov/bill/118th-congress/senatebill/644?q=%7B%22search%22%3A%22S+644%22%7D&s=1&r=14.
- Taylor, J. L., Laks, J., Christine, P. J., Kehoe, J., Evans, J., Kim, T. W., Farrell, N. M., White, C. S., Weinstein, Z. M., & Walley, A. Y. (2022). Bridge clinic implementation of "72-hour rule" methadone for opioid withdrawal management: Impact on opioid treatment program linkage and retention in care. *Drug and Alcohol Dependence*, 236, Article 109497. https://doi.org/10.1016/j.drugalcdep.2022.109497
- TerraVisu. Nombre de pharmacie pour 10 000 habitants par bassin de vie en 2023. Retrieved March 20, 2024 from https://www.data.gouv.fr/fr/reuses/terravisu-nombre-de -pharmacie-pour-10-000-habitants-par-bassin-de-vie-en-2023/.

H. Englander et al.

- Weiner, S. G., Qato, D. M., Faust, J. S., & Clear, B. (2023). Pharmacy Availability of Buprenorphine for Opioid Use Disorder Treatment in the US. JAMA Netw Open, 6(5), Article e2316089. https://doi.org/10.1001/jamanetworkopen.2023.16089
 WHO. (2009). WHO guidelines approved by the guidelines review committee. Guidelines for the psychosocially assisted pharmacological treatment of opioid dependence.
- Williams, A. R., Krawczyk, N., Hu, M.-C., Harpel, L., Aydinoglo, N., Cerda, M., Rotrosen, J., & Nunes, E. V. (2023). Retention and critical outcomes among new methadone maintenance patients following extended take-home reforms: A retrospective observational cohort study. *The Lancet Regional Health - Americas, 28*, Article 100636. https://doi.org/10.1016/j.lana.2023.100636