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Stalled Scale-Up of Opioid Agonist Therapies for HIV Prevention in Kazakhstan: History, Policy, and Recommendations for Change

POLICY COMMENTARY

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ABSTRACT

HIV incidence and mortality are increasing in Eastern Europe and Central Asia and are concentrated in people who inject drugs. Maintenance with opioid agonist therapies (OAT) like methadone or buprenorphine is the best treatment for opioid use disorder and a key HIV-prevention strategy in the region. In Kazakhstan, the scale-up of methadone has been minimal since methadone's introduction in 2008 and has been supported through international charitable organizations. As the Republic of Kazakhstan is designated to assume financial and administrative oversight of OAT, legislative gains can ensure treatment continuity and scale-up. Here, we review legislative barriers to OAT scale-up in Kazakhstan using an implementation science lens. We review legislative, political, and cultural barriers that undermine the efficient distribution and allocation of medications and impose burdensome clinical and administrative demands on patients and clinicians. Legislative reform is required to support further OAT expansion. We therefore provide policy recommendations to overcome these barriers to increase access to this life-saving, life-prolonging, evidence-based medical treatment. Minimally, these include increased numbers of clinical sites and patients at these sites; re-engineering OAT delivery across the country and directly to patients; introducing newer formulations of OAT; and creating an open bidding process to procure treatment medications.

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BACKGROUND

While HIV incidence and mortality have declined in other global regions over the past decade, in Eastern Europe and Central Asia (EECA), both HIV-related incidence and mortality are increasing (UNAIDS 2022a). This epidemic is driven by drug injection, primarily of opioids, for which opioid agonist therapies (OAT) are among the best and most cost-effective strategies (Tan et al. 2019; Ward et al. 2022). In the Republic of Kazakhstan (RK), only 0.4% of ~95,000 people who inject drugs (PWID) receive OAT at 16 sites (El-Bassel et al. 2022); effective OAT coverage requires 20% PWID to reduce HIV incidence. Figure 1 depicts all OAT sites in Kazakhstan and their starting years.

Since 2008, ~1400 patients have cumulatively received OAT in Kazakhstan. Though the government repeatedly announces plans for expanding coverage (Government of the RK 2022), scale-up has been slow. This lack of progress has caused concrete harm. Since 2010, new HIV infections in the country have risen by 88%, and PWID account for almost one-quarter of new HIV infections, despite representing less than 1% of the adult population of Kazakhstan (UNAIDS 2022b).

METHODOLOGY

We reviewed all legislation relevant to OAT in Kazakhstan using an implementation science lens. To conduct the analysis, two authors (AL and RI) reviewed and annotated all Kazakhstani legislation related to drug policy in general and to OAT specifically (RSPCMH 2023). All laws referenced by the original legislation were also included in the analysis. AL and RI also identified current legislative barriers to methadone scale-up and potential opportunities for change. They met with local Kazakhstani methadone policy experts, OI and ZS, to discuss how these laws have been implemented in practice. Finally, implementation policy experts, FA and LM, provided guidance on scale-up interventions that have worked in other EECA countries.

BARRIERS TO OAT

POLITICAL AND CULTURAL BELIEFS

The national methadone program has repeatedly faced potential closure (Table 1), with ongoing political and legal opposition. Supporters of closure often have close economic and political ties to the Russian Federation, which bans methadone entirely, as opioid use disorder (OUD) is perceived to be a moral failing rather than a medical condition (Chingin & Fedorova 2014; Ibragimova 2019; EHRA 2018).

Table 1 provides insight into the cultural and political barriers to scaling up OAT in Kazakhstan. Broadly looking at formal submissions to lawmakers, detractors of methadone have inaccurately described it as a synthetic drug discovered during the Third Reich (linking it to the Nazis), 'unnatural' like illicit synthetic narcotics, and 'worse than heroin' (Anon 2014; Anon 2011; Weber 2021). Challengers emphasize that OAT is simply moving 'from one addiction to another' (Silantje 2023), which does not align with current understandings that OUD is a chronic, relapsing condition. Finally, methadone (or withdrawal from methadone) is misstated as causing aggression. Major political figures, like parliamentary member Meruert Kazybekova, state publicly that methadone caused the 2004 Orange Revolution in Ukraine (Subbotina 2017), and this misbelief persists, including in a current petition to President Tokayev to end methadone therapy (Abdinova 2023).

ROLE OF LOCAL ADVOCACY

Methadone was introduced after international funders collaborated with local advocacy organizations to introduce and sustain Kazakhstan's OAT program. In 2017, the Prime Minister's Office created a Working Group of local experts, including advocates, to counter demands by the Ministry of Internal Affairs that OAT be closed. Despite uniform reports of the beneficial impact of OAT, some members dissented and pushed for the program's closure. Local advocacy groups continued to defend the program via public rallies, writing to politicians, and filing an official complaint with the UN, citing a human rights violation (EHRA 2018). This advocacy continues; one website operated by local activists, pereboi.kz, tracks treatment disruptions in

YEAR	POLICY CHANGE	ACTIVITIES	OAT CENSUS (SITES) (CHERCHENKO 2023)	SOURCE
1998	Order 10	Establishes regulation of narcotics. List of narcotics is updated regularly and continues to include methadone (Order 470 2019).	0	(Law of the RK 1998; Government of the RK 2019)
2005	Order 609	Allows Kazakhstan to start OAT using methadone	0	(MOH of the RK 2005)
2008		Kazakhstan's first OAT sites open: Pavlodar and Temirtau. Only people with HIV are allowed	50 (2)	
2009		People without HIV are allowed	44 (2)	(Zeng 2012)
2010	Order 333	Allows a third OAT site (Oskemen)	95 (3)	(Smaqov 2017)
2011	Order 2	Regulations on OAT staffing, services, and organization. Revised in 2020 (Order KR DSM-205/2020)	114 (3)	(Acting Minister of Health of the RK 2011; Minister of Health of the RK 2020a)
2012	Order 691	Allows seven new OAT sites (Oral, Aktobe, Kostanay, Ekibastuz, Karaganda, Semey, Taraz)	176 (10)	(Minister of Health of the RK 2012)
2013			212 (10)	
2014	Order 188	Establishes structure of Kazakhstani addiction treatment, including OAT sites. Lists staffing requirements, performance assessment metrics. Updated several times, most recently in 2020 (Order KR DSM-224/2020)	230 (10)	(Minister of Health of the RK 2014, 2020c)
2014	Order 943	Establishes stringent requirements (i.e., presence of paramilitary security staff) for transportation of narcotics.	230 (10)	(Minister of Internal Affairs of the RK 2014)
2014–2017	Formal requests to prime minister to ban methadone	Ak Zhol Democratic Party unsuccessfully campaigns to close the OAT program		(Smaqov 2017)
2015	First clinical guidelines for methadone	Highly restrictive, no take-home dosages, maintenance for as little as six months	293 (10)	(RCHD 2015)
2016			323 (10)	
2017	Ministry of Internal Affairs creates methadone working group.	OAT program effectiveness demonstrated by working group; small subgroup of the working group issues dissenting opinion requesting ban on OAT; four new sites opened (Almaty, Kyzylorda, Lisakovsk, Atyrau)	354 (14)	(EHRA 2018)
2018	Concerns about sustainability appear	Patient enrollment halted. Activists and international organizations appeal. Government supports continuation	251 (14)	(EHRA 2018)
2019	Order 196	New Rudny site opens, with Petropavl soon to follow in 2020. Another four sites (Astana, Shymkent, Turkestan, Almaty region) permitted but not opened as of February 2023	297 (15)	(Minister of Health of the RK 2019)
2020	Order KR DSM-203/2020	Establishes examination procedure for detection of OUD and/or acute opioid intoxication; lists mandatory inpatient treatment criteria	314 (16)	(Minister of Health of the RK 2020b)
2021	Supply chain challenges	National distributor Chempharm (Хмфарм) refuses to continue supplying methadone, halting new enrollment	272 (16)	(Ibragimova et al. 2022)
2022	International donors announce that OAT funding will end in 2023	Kazakhstan plans to revise legal landscape for OAT	342 (16)	

Table 1 Timeline for Key Legislative and Policy Changes.

Figure 1 Map of OAT sites in Kazakhstan and their start years.

the country and advocates for consistent methadone distribution (UNHCHR 2022). Additionally, advocates communicate with local newspapers and organizations to help dispel methadone-related myths, like the ones described above (Smagulov 2023).

FUNDING AND PROCUREMENT CHALLENGES

Since the OAT program's inception, it has been fully funded by the Global Fund to Fight HIV, Tuberculosis, and Malaria (Global Fund), despite Kazakhstan's promise to be state-funded by 2017 (Asipova 2017; Global Fund). Funding from Global Fund is scheduled to end in 2023, as Global Fund transitions its support for HIV prevention and treatment to the Kazakhstani government (Global Fund). Concerns persist about the state's ability to sustain funding (HRI 2021; Weber 2021). While the government has been working to establish effective methadone supply and procurement systems (Vice Minister of Health of the RK 2021), to date, they have yet to be implemented.

As of February 2023, methadone is purchased from a single Italian vendor, Molteni, and is distributed by КРС Medservice Plus, LLC (Acting Minister of Health of the RK 2022; Cherchenko 2023). Frequent interruptions to procurement and distribution mean that many patients temporarily receive dosage reductions or have their treatment discontinued, which can be dangerous — potentially triggering drug injection, overdose, and suicide (Carroll 2019).

CLINICAL PROTOCOL

In 2015, Kazakhstan established highly restrictive national OAT treatment guidelines. Before treatment, patients must be formally diagnosed through detailed observation, a physical and neurological exam, extensive laboratory testing, and confirmatory urinalysis. Eligibility requires official registration at a government clinic located within the region of the OAT program. Patients must also be at least 18 years old and have confirmed infection with HIV or viral hepatitis, confirmed drug injection for at least three years, at least two hospitalizations for OUD, or be pregnant. These criteria are stricter than accepted within the international practice (WHO 2009) and exclude some patients with polysubstance use disorder ([Country Coordinating Committee] 2021). While methadone itself is free, for laboratory testing, patients must have private insurance or pay out-of-pocket. Any laboratory abnormalities (e.g., a positive HIV test) require evaluation by specialists, including transportation costs to multiple providers in the case of comorbidities.

OUD diagnosis may result in the suspension of one's driver's license until sobriety is confirmed (Acting Minister of Health of the RK 2020). Additionally, patients are reported by name in the national narcological registry — another deterrent for those seeking treatment — as registration can limit employability, exacerbate police harassment, and heighten stigma (Ibragimova 2023; Minister of Health of the RK 2020b). Irrespective of substance use, removal from the registry is not allowed for those remaining on methadone.

MEDICATION DOSING

The 2015 OAT guidelines do not include buprenorphine and start with methadone dosages of 10–30mg, with daily increases of 5–10mg (and a maximum weekly increase of 30mg) until the patient is stabilized at 60–120mg daily (RCHD 2015). Several clinical studies confirm that doses of 90mg or more and take-home dosing are associated with better health outcomes (Ivasiy et al. 2022; Farnum et al. 2021; Meteliuk et al. 2021). Rather than treating OUD as a chronic disease, as recommended globally (WHO 2009), Kazakhstani policies provide maintenance for six months, followed by treatment that tapers off upon the patient's request. At least two years of therapy have been recommended for the best outcomes (Jaffe & O'Keeffe 2003), and abbreviated treatment duration results in heightened mortality after leaving treatment (Kleber 2008).

Take-home dosing is not allowed, making OAT incompatible with employment, family life, and transportation realities. Daily travel is often long (>1 hour each way) and expensive ([Forum of People who Use Drugs Kazakhstan], 2020). Missing four consecutive days requires starting the induction process anew. Consequently, personal or family emergencies disrupt treatment at vulnerable times. Clinically stable patients have demonstrated improved outcomes with early take-home dosing (Kleinman & Sanches 2023). Health- or criminal justice-related disruptions result in treatment discontinuation, as hospitals and correctional settings are unable to supply methadone due to the highly regulated criteria for transporting the medication (Minister of Internal Affairs of the RK 2014).

CLINICIAN BURDENS

PWID often have multiple comorbid conditions (Bromberg, Mayer & Altice 2020), requiring separate evaluations before initiating OAT. Such practices undermine overall health, as OAT induction and stabilization is often needed before other conditions can be addressed. Experiencing the continuous symptoms of opioid withdrawal while seeking illicit opioids is time-consuming and uncomfortable. Treating OUD first allows patients to address other health concerns.

Moreover, clinicians must see patients daily, leading to work fatigue, as they cannot take days off. One study found that a rapid shift to take-home dosing for clinically stable patients resulted in substantial reductions in clinical encounters and duties, allowing clinicians to focus on expanding telehealth and patient enrollment (Meteliuk et al. 2021).

FUTURE DIRECTIONS AND CONCLUSION

The barriers to OAT legislation are not insurmountable. Ukraine, another post-Soviet country in EECA experiencing challenges with intrusion from Russia, failed to make OAT scale-up gains until they were deeply involved with effective implementation. For example, only 2.9% of the 347,000 PWID were prescribed OAT (Mazhnaya et al. 2018). They doubled OAT coverage by February 2022 by deploying NIATx (McCarty et al. 2007), a bundle of effective implementation tools which, in turn, guided OAT delivery legislation, increased access to take-home dosing, and allowed primary care providers to prescribe OAT (Altice et al. 2022).

Kazakhstan has multiple opportunities to create system efficiencies and scale-up OAT (Table 2). With methadone treatment already free (Minister of Health of the RK 2021), other government initiatives could further reduce treatment barriers and increase access. Given the legislative restrictions and an unfavorable implementation environment, future strategies will require a more complete landscape analysis, followed by an active facilitation process to make rapid, achievable changes that can be sustained.

OBSERVED BARRIER	RECOMMENDATION
Complex OAT procurement and delivery leading to treatment interruptions	1. Change legislation to increase flexibility in medication storage and transportation 2. Introduce process-improvement changes to increase system efficiency
Requirement of daily in-person treatment	1. Add sublingual and/or long-acting injectable buprenorphine to national formulary 2. Introduce take-home dosing
Multiple specialist visits needed before OAT initiation	Initiate OAT at first office visit
Low starting dose and slow increase to optimal dose	Accelerate stabilization protocol
Requirement to obtain multiple specialist visits and lab tests before accessing OAT	Address OUD first, and address non-emergent comorbidities after stabilization
Lack of OAT site accessibility	1. Allow any licensed prescriber to prescribe OAT 2. Expand the types of clinics allowed to dispense OAT
Patient fears of registration consequences	3. Remove registry entirely or remove stable methadone patients from the narcological registry 4. Eliminate or loosen residency permit requirements for program participation
Cost of obtaining lab testing for OAT access	Supply all testing needed for OAT program free of charge

Table 2 Recommendations for Reducing Barriers to OAT.

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COMPETING INTERESTS

The authors have no competing interests to declare.

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