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SUBSTANCE USE AND RELATED DISORDERS (F LEVIN AND E DAKWAR, SECTION EDITORS)

HIV, Drug Injection, and Harm Reduction Trends in Eastern Europe and Central Asia: Implications for International and Domestic Policy

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Abstract

Purpose of Review Scaling up evidence-based HIV prevention strategies like opioid agonist therapies (OAT), syringe services programs (SSPs), and antiretroviral therapy (ART) to mitigate the harms of drug injection is crucial within Eastern Europe and Central Asia (EECA), the only region globally where HIV incidence and mortality are increasing.

Recent Findings Though the proportion of new HIV cases directly attributable to drug injection has recently declined, it remains a critical driver of HIV, especially to sexual partners. Concurrently, scale-up of OAT, SSPs, and ART has remained low, contributing to a volatile HIV epidemic among people who inject drugs (PWID).

Summary Despite evidence that drug injection contributes to an evolving HIV epidemic in EECA, coverage of evidence-based harm reduction programs remains substantially below needed targets. Due to a combination of punitive drug laws, ideological resistance to OAT among clinicians and policymakers, and inadequate domestic and international funding, limited progress has been observed in increasing the availability of these programs.

Keywords HIV prevention · Drug injection · Harm reduction · Opioid agonist therapy · Eastern Europe · Central Asia

Introduction

The WHO-defined Eastern European and Central Asian (EECA) region is the only region globally where HIV incidence and mortality continue to rise [1]. While global HIV incidence and mortality have continued to decline, they have increased by 58% and 25%, respectively, in EECA from 2010 to 2015, in the presence of low HIV treatment and prevention coverage [2, 3]. Unlike the global epidemic, HIV in EECA is concentrated in people who inject drugs (PWID), with evidence of generalizing through transmission to their sexual partners due in part to sexual risk behaviors associated with drug injection [3]. Injection drug use in EECA is among the highest in the world, with a prevalence of 1.3% in Eastern Europe and 0.63% in Central Asia [4••].

Strategies to control HIV in this context must include primary and secondary prevention using harm reduction strategies, including adequate coverage with syringe service programs (SSPs) and opioid agonist therapies (OAT) like methadone and buprenorphine maintenance therapy. These programs should be linked to an effective HIV response that increases access to HIV testing and prescription of antiretroviral therapy (ART) as a treatment as prevention strategy. The Joint United Nations Program on HIV/AIDS 90-90-90 strategy in EECA falls far below recommended targets and coverage levels achieved globally, with only 63% of people living with HIV (PLWH) being aware of their status, 45% of those being prescribed ART, and 22% of PLWH on treatment with viral suppression—these levels are markedly insufficient to prevent continued HIV transmission [1, 5].

Strategies to scale up OAT, SSPs, and ART are related and even synergistic. For example, provision of OAT improves the HIV treatment cascade by stabilizing patients so they can

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access and utilize HIV services and achieve viral suppression [6]. Pharmacological drug interactions between ART and OAT can decrease OAT levels and prompt opioid relapse, and for those on OAT who continue to inject opioids or other substances, SSPs can reduce transmission [7].

In the EECA region, scale-ups of ART, OAT and SSPs are crucial for both primary and secondary HIV prevention [8, 9, 10••]. Modeling for Ukraine suggests that the combination of high scale-up of OAT and ART is the most effective prevention strategy, but high coverage of OAT is the most cost-effective approach. This finding is especially noteworthy given that only one country in EECA is a high-income setting [11]. SSPs are also effective in reducing transmission of HIV/AIDS and other blood-borne diseases, though they are less effective than OAT for secondary prevention strategies, such as linking PWID with antiretroviral therapy [12].

Until HIV emerged as a public health emergency in countries of the Former Soviet Union (FSU), OAT was banned for the treatment of opioid use disorder, with standard treatment practices emphasizing instead abstinence strategies without pharmacotherapies [13]. The evolving HIV epidemic, however, helped usher OAT and SSPs into the region for HIV prevention with support from international donors like the Global Fund and PEPFAR over the past 15 years. Unlike SSPs, OAT is a medical treatment that requires addiction treatment specialists to prescribe it. Consequently, addiction treatment specialists (known as narcologists) have been reluctant to prescribe OAT for addiction and instead perceive it as HIV prevention—and not an effective treatment for addiction itself. Thus, scale-up of OAT within EECA has been remarkably slow, and in cases like Russia and Turkmenistan, it remains banned.

Ensuring access to OAT and other harm reduction services is a critical strategy for controlling HIV transmission and meeting UNAIDS 90-90-90 targets in EECA, especially given the comparatively low levels of ART coverage among PWID [14–16]. Over the past decade, international agencies like UNAIDS and WHO have continued to call attention to the need for scale-up of evidence-based HIV prevention strategies in EECA. Given the importance of OAT and SSPs for HIV prevention in this region, we conducted a comprehensive review to identify recent trends in HIV, injection drug use, and coverage of OAT and SSPs in EECA since the introduction of these programs. We first summarize recent trends in HIV and injection drug use in EECA. We then discuss the history of drug use in this region that has influenced the trajectory of the overlapping epidemics of HIV/AIDS and opioid use disorders, as well as the current state of drug laws and policing. Next, we summarize recent trends in coverage of different harm reduction strategies in EECA countries. Finally, we examine current policies and funding for harm reduction in the region.

Trends in HIV/AIDS and Injection Drug Use

From 2012 to 2016, the number of new HIV diagnoses per year has risen in most EECA countries, with increases over 25% in Armenia, Belarus, Georgia, Lithuania, and Kazakhstan. Most new HIV infections in the region, however, occur in Russia and Ukraine. In 2017, four EECA countries (Russia, Ukraine, Belarus, and Moldova) had the highest rates of newly registered HIV cases in the entire WHO-designated European region [17]. While the regional trend is increasing, due to monitoring differences, trends for some countries vary by source. The UNAIDS 2017 Databook shows slight declines in HIV incidence in Kyrgyzstan and Tajikistan over the past 5 years, while the European Centers for Disease Control (ECDC) reports an increase for all countries except minimal declines in Estonia and Ukraine.

During the same 5-year period between 2012 and 2016, the percentage of new cases attributable to drug injection has declined across all countries, while the percentage of new cases attributable to heterosexual transmission has increased. The reduction in the proportion of new cases attributable to drug injection during this time ranged from 6% in Lithuania to 52% in Estonia, and most countries saw decreases of at least 25%. Despite this trend, drug injection remains a common mode of HIV transmission, accounting for 25% to 51% of new cases [3, 18]. These estimates vary widely by source, and stigma among PWID has resulted in markedly reduced accuracy in reporting of risk. One Ukrainian study assessing HIV cases attributable to heterosexual transmission found that through triangulation of data, most new cases remained in key populations like PWID [19]. For example, in 2017, over 50% of new HIV cases were among PWID, without real evidence of a decline [20].

Throughout EECA, most people living with HIV (PLWH) inject drugs [21]. Russia and Ukraine have the highest number of PWID, with an estimated 1.5 million PWID in Russia alone. The total number of PWID across EECA is estimated to be 3.2 million [22]. Despite varying estimates, most data demonstrate an upward trend in drug injection in recent years [23]. In Ukraine, which ranks second in the number of new HIV infections in EECA, the number of PWID has increased nearly 12% in the last 5 years, to 346,900 in 2016 [1, 24].

Among PWID, national reports of HIV prevalence among PWID in EECA ranges from 0.5% in Armenia to 48.3% in Estonia. In Russia and Ukraine, as well as Belarus, Latvia, Moldova, and Tajikistan, HIV prevalence among PWID exceeds 20%, well above prevalence estimates in the general population [1, 4••]. Despite small reductions in HIV transmission among PWID, there is marked subnational variation with several cities experiencing high rates of HIV incidence and prevalence among PWID. In Russia, HIV prevalence among PWID was approximately 33% in five major cities in 2015 [3]. In Ukraine, where prevalence among PWID is estimated

to be 21.9% nationally, a 2013 study found HIV prevalence among recruited PWID that ranged from 36.0% to 44.2% among three cities, and HIV incidence exceeded 24.8 infections per 100 person-years [25, 26]. Due to harsh criminalization of drug use, this region experiences some of the highest rates of incarceration globally, with disproportionately high HIV prevalence relative to the community [27••]. Table 1 provides further details on the population of PWID in EECA.

History of Drug Use and Injection Practices in Eastern Europe and Central Asia

In the transitional years following the collapse of the Soviet Union, EECA countries experienced social disruption, slowed economies, and unresponsive public health and healthcare systems. During this time, heroin trade routes moved through the region with increasing opium production in Afghanistan, ushering in drug injection, a volatile HIV epidemic, and the growth of informal economies [33, 34]. In the context of social and economic instability and increasing injection drug use, mostly opioids and amphetamines, the injecting practices of PWID in EECA played a crucial role in the dramatic rise of HIV incidence [35–38].

Heroin continues to be the most commonly injected drug throughout EECA [39]. Due to cultural and political differences, Ukraine is an exception, where homemade liquid extract of poppy straw is used instead of heroin, sometimes mixed with diphenhydramine (an antihistamine medicine with sedative and anticholinergic effects), as well as a stimulant prepared from pharmaceutical pseudoephedrine [38, 40]. After opioids, the second most commonly injected drug type in EECA is amphetamine-type stimulants (ATS) [23]. As police have reduced opioid distribution in some regions, many PWID shifted from opioids to stimulants, which are possible to prepare at home and help ameliorate symptoms of opioid withdrawal syndrome. Since opioids remained the preferred substance when available, this shift has led to a rise in polysubstance use.

The lack of heroin and availability of pharmaceutical compounds, combined with barriers to effective addiction treatment, have led to a rise in injection of other types of drugs, including pharmaceuticals, homemade opioids, other types of stimulants, and lab-made methadone [41]. In Georgia, low heroin availability resulted in widespread injection of buprenorphine [42]. Krokodil, a homemade opioid, is a derivative of codeine called desomorphine. It is a short-acting opioid, so withdrawal occurs quickly and multiple injections are required [43–45]. Its use may produce severe tissue damage, followed by necrosis, gangrene, and organ failure [45]. Krokodil injection in EECA has increased since 2011, with use observed in Russia, Ukraine, Georgia, and Kazakhstan [46]. In Georgia, an estimated 17% to 36% of PWID use krokodil [47].

Unsafe injection practices that increase the risk of transmission of blood-borne viruses remain common. Rises in stimulant use, polysubstance use, and homemade opioid use have been linked to an increase in risk factors for HIV transmission. For example, in Ukraine, liquid poppy straw was most often purchased in pre-loaded syringes by PWID, who began to sell drugs to other consumers. In these instances, the drug solution was commonly extracted from a shared container with the user's needle/syringe, or with the dealer's needle/syringe, and front- or back-loaded into the user's syringe [48]. The use of high-dead-space syringes, where larger volumes of contaminated blood remain after injection, has also been associated with higher HIV transmission in PWID [49].

The high frequency of injection by stimulant users has resulted in increased HIV transmission. One study from Russia suggested that frequent (three or more times per week) stimulant injectors were most likely to become HIV-infected in PWID [50]. Other studies have shown links between polysubstance use and increased risk for HIV transmission. In Russia and Estonia, polysubstance injection is associated with higher levels in risky injection practices [51].

In Ukraine, HIV infection was associated with differing types of drugs injected, with HIV prevalence being 17%, 19%, and 39% among stimulant, opioid, and combined opiate/sedative injectors, respectively. The lower prevalence of HIV among stimulant injectors was unexpected considering the higher number of injections and injection partners, as well as riskier sex- and drug-related risk behaviors reported. PWID with HIV in this study were generally older than those who are negative, with a longer duration of drug injection. These factors contributed more to likelihood of HIV infection than the type of drug injected. Compared with stimulant users, opioid and combination opioid/sedative injectors had injected longer (7.1, 11.9, and 12.3 years, respectively) and were more likely to front- or back-load with a dealer (55% of opioid users and 75% of opioid/sedative users did so versus 20% of stimulant users). Stimulants users more often prepared drugs by themselves while the other two groups bought them from dealers [52].

Homemade opioid use is also linked to risky injection practices. Recent research in Ukraine has shown that people who inject krokodil have higher injection-related risk [25]. In a study of 550 PWID in three Ukrainian cities (Odessa, Mykolaiv, and Donetsk), 25% of the sample injected desomorphine. Krokodil use is substantially higher in eastern Ukraine—Donetsk (45.9%)—than in the south—Odessa and Mykolaiv (7.5 and 16.7%, respectively). In this sample, krokodil users injected more frequently daily and with others than non-krokodil users. Younger injectors were more likely to prefer krokodil and inject more frequently relative to their peers, with authors concluding that krokodil use is a marker of HIV risk-taking behavior among PWID.

Table 1 Overview of population of people who inject drugs in Eastern Europe and Central Asia in 2016

	Armenia	Azerbaijan	Belarus	Estonia	Georgia	Kazakhstan	Kyrgyzstan	Latvia	Lithuania	Moldova	Russia	Tajikistan	Turkmenistan	Ukraine	Uzbekistan
Estimated number of people who inject drugs	9400	71,283	66,500	9000	49,700 [28] (2014)	120,500	25,500 [29] (2014)	6151 [30]	–	30,200 [31]	–	23,500 [4••] (2006)	–	346,900	48,000
HIV/AIDS															
Prevalence among PWID	0.5%	8.5%	25.1%	48.3%	2.2%	8.5%	12.4% [4••]	18.5%	2.2%	–	–	27.0% [18]	–	21.9%	5.6%
Incidence in general population (per 1000 population)	0.09	0.10	0.20	0.21 [18]	0.28	0.16	0.13	0.23	0.09	0.38	–	0.15	–	0.38	-
% new cases attributable to PWID [18]	11.6%	27.2%	25.1%	13.1%	28.5%	30.5%	26.0%	17.0%	38.8%	4.9%	–	17.9%	–	26.0%	–
Hepatitis C prevalence among PWID [32]	52.1%	62.8%	70–95%	–	57–74%	–	45.2%	–	–	35.3–65.4%	69%	22.7–49.3%	–	55%	36%

Data are reported from the Joint United Nations Report on HIV/AIDS (UNAIDS) 2017 Databook unless otherwise indicated

Drug Policies and Criminalization

Most EECA countries have harsh drug laws and policies that have resulted in the stigmatization and marginalization of PWID. Though these types of regulations have been shown to be ineffective in reducing the availability of drugs or prevalence of drug use, antidrug ideology has continued to drive severe policies and sentencing [47]. In 2015, for example, Belarus introduced a new law that fines non-medical drug use and sentences people with two offenses in 1 year to a minimum 2-year prison term [3]. Across the five countries of Central Asia, Ukraine, and other Eastern European countries, possession of small amounts of illegal substances results in various criminal and administrative charges, though there has been some decriminalization of certain minor charges in Kazakhstan, Kyrgyzstan, and Tajikistan [34, 53]. Estonia has recently introduced legislation to decriminalize possession of small amounts of drugs for personal use and offer the possibility of drug treatment as an alternative to incarceration, although incarceration remains common for any amount of drug possession as an administrative offense [54, 55].

In many EECA countries, police often engage in punitive practices towards PWID and have been found to conduct "extrajudicial arrests," or arrests without a legal cause, sometimes arresting people at legal SSP sites who possess empty needles or those at methadone clinics. This type of police harassment results in decreased willingness to engage in effective HIV prevention programs [56–58]. Combined with harsh drug laws and sentencing, these practices also lead to increased HIV/AIDS risk factors among PWID [59]. One recent study in Russia found that extrajudicial arrests were common among PWID and were associated with riskier injecting practices such as needle sharing as well as increased likelihood for overdose [60]. In Odessa, Ukraine, most PWID reported experiencing various types of police intimidation, including police planting drugs, bribery, and threats to report on other PWID [61]. In Kyrgyzstan, researchers found that even when new policies were introduced to prohibit police from interfering with harm reduction programs, only half of 319 surveyed police understood syringe possession laws and less than half viewed syringe exchange programs positively [62].

Drug criminalization has also resulted in high rates of incarceration for PWID, with over one-third of prisoners having injected drugs before arrest throughout EECA [27••]. Given the high prevalence of HIV among PWID throughout EECA, high incarceration rates for PWID have led to a concentration of the HIV epidemic in prisons [27••, 63].

Trends in Coverage of Harm Reduction Services

Table 2 summarizes the availability and coverage of opioid agonist therapies (OAT) with methadone and buprenorphine and syringe service programs (SSPs) in EECA. Though harm reduction programs are generally available in most EECA countries, coverage has remained low and few countries meet the thresholds that are necessary to slow HIV transmission. Figure 1 shows the 2016 coverage levels of three effective evidence-based HIV prevention strategies: (1) OAT, (2) SSPs, and (3) ART for PLWH.

Opioid agonist therapies are available in all but three EECA countries. Methadone is the sole form of OAT available in seven EECA countries, including Armenia, Azerbaijan, Belarus, Moldova, Kazakhstan, Kyrgyzstan, and Tajikistan [10••]. All forms of OAT are banned in Russia, the country with the largest number of PLWH who inject drugs in the region, as well as in Turkmenistan and Uzbekistan. A pilot OAT program was begun in Uzbekistan in 2004 and subsequently revoked in 2009, though plans now exist to reopen a new pilot methadone program [34, 66]. Kazakhstan's OAT programs are also at risk of closure due to political pressure from Russia [67]. Since the introduction of OAT programs in the early to mid-2000s, coverage has consistently remained low in countries where OAT is offered [68] (Fig. 1). Only two countries (Georgia and Lithuania), out of the 11 countries for which data are available, meet the minimum WHO recommendation of at least 20% coverage of OAT among PWID [69]. In the past 2 years, only two countries have increased the number of OAT sites, while the number of sites has remained essentially unchanged in all other EECA countries that provide OAT [70]. In prisons, where PWID are often concentrated and within-prison drug injection is common, coverage of OAT is even lower, with availability of OAT in prisons documented in only five of 15 EECA countries (Armenia, Estonia, Kyrgyzstan, Latvia, and Moldova) [27••, 71, 72].

Nearly all countries in EECA currently provide SSPs, except Turkmenistan. Between 2016 and 2018, availability of SSPs has generally either increased or remained the same. Four of 14 countries saw an increase in the number of SSP sites and eight had no change, while two experienced slight decreases [65, 70]. In 2016, only two countries (Tajikistan and Estonia), however, met the UNAIDS recommended target of providing at least 200 needles per PWID per year, the threshold demonstrated to be effective in reducing HIV transmission [73] (Fig. 1). Despite widespread evidence of increased injection risk among incarcerated PWID, SSPs are not available in prisons in most EECA countries, with only four (Armenia, Kyrgyzstan, Moldova, and Tajikistan) providing such programs to varying degrees [70, 74].

HIV Treatment as Prevention

In addition to OAT and SSPs, identifying and treating PLWH with ART is a highly effective strategy to reduce HIV transmission [75]. Consequently, UNAIDS set forth a 90-90-90

Table 2 Overview of harm reduction programs in Eastern Europe and Central Asia for 2016

	Armenia	Azerbaijan	Belarus	Estonia	Georgia	Kazakhstan	Kyrgyzstan	Latvia	Lithuania	Moldova	Russia	Tajikistan	Turkmenistan	Ukraine	Uzbekistan
Opioid agonist therapy	Yes	Yes	Yes	Yes	Yes	Yes*	Yes	Yes [64]	Yes	Yes	No	Yes	No [27••]	Yes	No [27••]
Number of sites [65]	4	2	19	8	18	10	30	10	19	19	0	6	0	169	0
% PWID on OAT	5.3%	0.5%	4.7%	11.4%	21.5%	0.5%	4.8%	–	34.2%	3.3%	–	2.4%	–	3.2%	–
Coverage	Low	Low	Low	Low	Medium	Low	Low	–	Medium	Low	–	Low	–	Low	–
Availability in prisons (year) [27••]	Yes (2011)	No	–	Yes (2009) [64]	No	No	Yes (2008)	Yes (2012)	No	Yes (2005)	No	No	No	No	No
Syringe service programs	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Number of sites [10••]	12	17	34	37	14	155–168	48	19	11	28	20	51	0	1667	235
Number of needles and syringes distributed per PWID per year	72	34	41	230	91	120	153	84	102	88	2 [27••]	345	0	71	–
Coverage	Low	Low	Low	High	Low	Medium	Medium	Low	Medium	Low	Low	High	–	Low	–
Naloxone															
Available	No	No	No	–	Yes	No	Yes	No	No	Yes	–	Yes	–	No	–

Data are reported from the Joint United Nations Report on HIV/AIDS (UNAIDS) 2017 Databook unless otherwise indicated

*Currently enrolling no new patients

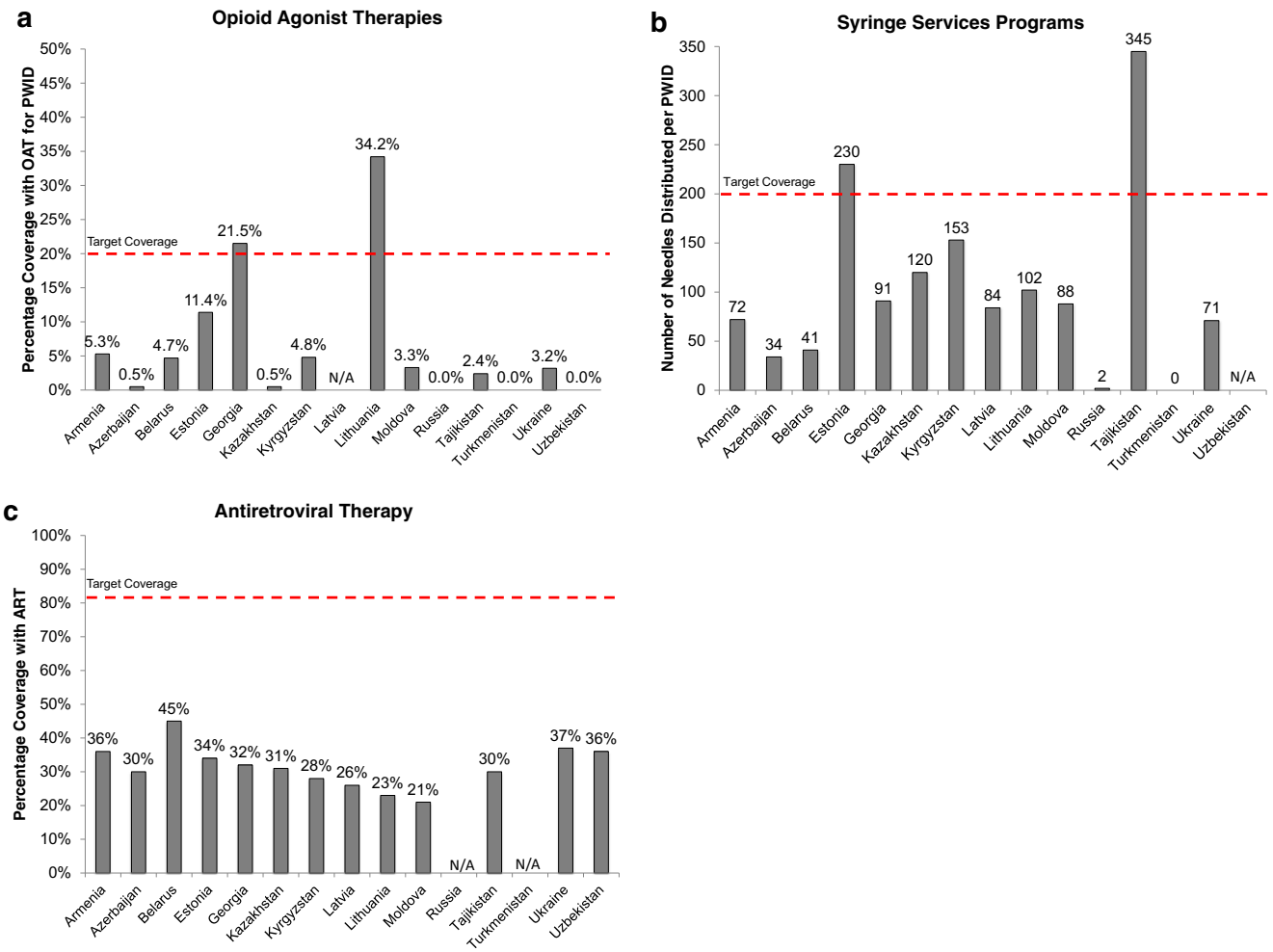

Fig. 1 Coverage levels of effective HIV prevention strategies in people who inject drugs by country in 2016: **a** opioid agonist therapies, **b** syringe services programs, and **c** antiretroviral therapy

strategy to identify 90% of all PLWH, of which 90% should be prescribed ART and 90% of these should take ART at sufficient levels to achieve viral suppression. This strategy requires that 81% of all PLWH are on ART, yet no country within EECA is close to achieving this goal. The extraordinarily low levels of ART coverage within EECA are in part related to reluctance to treat PWID with ART, and PWID remain the majority of all PLWH. A systematic review has found that providing PLWH with OAT is effective at initiating PLWH on ART and achieving high levels of viral suppression, and one study of PWID with HIV showed that receipt of OAT resulted in significantly higher levels of HIV diagnosis, ART treatment, and viral suppression [6, 76].

Current Harm Reduction Policies and Funding

In the context of harsh drug laws and ongoing stigma towards drug use and people who use drugs, policies and practices related to harm reduction programs further inhibit program growth and uptake of services. Across the region, OAT has remained particularly controversial among policymakers, administrators, and clinical providers. Though OAT has been superficially accepted as part of international HIV prevention strategies, cultural and ideological views towards PWID have inhibited clinician buy-in and uptake of these programs. In many EECA countries, OAT has been introduced as HIV prevention and supported by international funders, yet those who must provide this treatment are addiction treatment specialists who do not support OAT as an effective treatment for opioid use disorders. Consequently, these programs have remained "pilot" projects to satisfy donors but have failed to gain widespread adoption. Until funders require that adequate coverage levels be a criterion for continued funding, such programs are unlikely to expand.

Though OAT is ostensibly available in most EECA countries, restrictions about eligibility for OAT have resulted in restricted access to treatment [68]. To obtain OAT, PWID in seven EECA countries are required to register in a national

database, which often leads to targeting by police and prohibits people who register from having a driver's license and obtaining certain types of employment [56, 77]. Other EECA countries impose minimum age requirements, limit the number of people who can access OAT, and require evidence of a pre-determined length of opioid dependence or evidence of previous failures in abstinence-focused treatment programs before initiating OAT [78].

Incremental changes to improve patient access to OAT have occurred in some countries. In 2015, for example, a group of Ukrainian OAT administrators and clinicians leveraged research about treatment barriers to successfully advocate for changes in government regulations. The new order eliminated a policy requiring two unsuccessful detox attempts before receiving OAT, allowed providers to transfer OAT patients from specialty treatment settings to pharmacies or non-specialty settings, allowed PWID to receive prescription OAT as self-administered treatment up to 10 days, allowed OAT patients to be treated outside of government clinics if patients can afford to pay for treatment, and allowed OAT to be prescribed in police lock-up, probation, pre-trial detention and prisons [79].

Another consequence of ideological and policy barriers has been insufficient resources allocated for harm reduction services, and funding has remained generally low across the EECA region [80]. Most programs were initially introduced and sustained through foreign aid organizations like the Global Fund. Between 2012 and 2014, international donors were responsible for most or all funding for harm reduction programs [22]. Despite recent increases in domestic spending for HIV prevention overall, only four of 15 countries fully fund OAT programs in domestic programs [5]. Given the Global Fund's recent reduction or withdrawal of projects from many EECA countries, the availability of services may decline as programs become dependent on government funding [65].

Conclusion

Despite evidence of an ever-growing HIV epidemic and heightened levels of drug injection in Eastern Europe and Central Asia, coverage of evidence-based harm reduction programs remains substantially below needed targets. Due to a combination of punitive drug laws, ideological resistance to OAT and associated institutional and policy barriers, and inadequate domestic and international funding, limited progress has been observed in increasing the availability of these programs. Reversing this trend in this volatile region will require funders, policymakers, health providers, and patients to adopt common goals for harm reduction and HIV prevention.

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