Impact of the COVID-19 epidemic on drug markets, substance use patterns, and delivery of harm reduction and treatment services in Ukraine

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List of abbreviations

OAT	Opioid Agonist Treatment
OST	Opioid Substitution Treatment
PWID	People who inject drugs
PWUD	People who use drugs
EMCDDA	European Monitoring Centre for Drugs and Drug Addiction
COVID-19	2019 novel coronavirus disease
IBBS	Integrated bio-behavioral survey
WHO	World Health Organization
HIV	Human immunodeficiency virus
UNODC	United Nations Office on Drugs and Crime
UNAIDS	The Joint United Nations Programme on HIV and AIDS
OR	Odds ratio
aOR	Adjusted odds ratio
CI	Confidence interval

1 EXECUTIVE SUMMARY

The COVID-19 pandemic and public health response continue to have an unprecedented impact on all people across the globe. Lives of people who use drugs may be particularly affected by the loss of income, reduced availability of drugs of choice and limited access to treatment and harm reduction services. This may lead to adverse health outcomes, including the increased risk of drug overdose and blood-borne infections, and progression of untreated co-morbidities common in this population.

This mixed-methods study was conducted to monitor the trends in the drug scene, substance use practices, and availability of prevention and treatment services for people who use drugs in Ukraine in the context of the COVID-19 pandemic.

The findings of the study confirmed that during the initial stage of lockdown implemented by Ukrainian government, many people who use drugs experienced reduced access to their drugs of choice from usual sources. The use of illicit methadone[1], the most common drug prior to the COVID-19 epidemic emergence in Ukraine, decreased significantly, and many users began replacing it with medical methadone[2], purchased in pharmacies using prescriptions from private physicians. Over time, as COVID-19 control measures became less severe, the access to all types of drugs was largely restored. However, the decline of illicit methadone and compensatory increase of medical methadone observed in the initial stages of COVID-19 pandemic did not return to the previous levels when the control measures were lessened. This may indicate a sustained change in the drug scene. There were no major changes in the ways and frequency of any drug use after the COVID-19 control measures were introduced or later in the observation period. Also, no significant change was apparent in terms of proportion of participants reporting unsafe injection practices, such as syringe sharing and use of front-loaded or pre-filled syringes.

Availability of harm reduction services decreased in the initial phase of lockdown in March 2020, but the programs managed to adapt quickly and resumed services. Use of harm reduction programs to obtain syringes or other services did not decrease over the study period. Access to opioid substitution treatment (OST) for patients who received it in public clinics was affected by restrictions for public transportation, contributing to a decrease in coverage of OST in our cohort. On the other hand, the Ministry of Health directive to transfer all patients to take-home dosing of OST helped to minimize dropout. Transportation restrictions, combined with the COVID-19 testing requirements and growing availability of

[1] The term "illicit methadone" in this report refers to methadone substance produced by clandestine laboratories. It is distributed through illegal sources in powder or crystalline form.

[2] The term "medical methadone" in this report refers to medication in tablet form manufactured by pharmaceutical companies in Ukraine and distributed through pharmacies. Pharmacies can legally sell the medication by prescription, which can be obtained from licensed governmental clinics or private physicians. The practice of private physicians, however, as described later in this report, is legally framed as detoxification, but does not include any patient supervision or follow-up and thus cannot be considered to be opioid agonist treatment.

paid prescriptions from private providers led to the overall slowing of enrolment of new patients to OST, especially during the strict lockdown period.

The results of the study indicate that the COVID-19 epidemic and lockdown had a substantial effect on the drug scene in Kyiv. After public transportation re-opened, drug availability and substance use patterns gradually returned to the pre-COVID levels. The shift from illicit to medical methadone was a notable exception, creating significant implications for public health programming. Harm reduction and OST programs managed to adapt to the changes and sustain their coverage. Should the lockdown be introduced again, the lessons learned in this phase of the pandemic should be used to ensure uninterrupted service provision for people who use drugs.

2 BACKGROUND

2.1 DRUG SITUATION IN UKRAINE PRIOR TO COVID-19

The beginning of independence in Ukraine in 1990's in a context of a socio-economic decline, an unemployment increase, widened social disparities, and a decrease in social protection[1,2] led to a rapid and dramatic increase in the supply of illicit drugs combined with an increased demand for drugs. Concurrent social, economic, and psychological factors led to the sharp increase in the number of people who use drugs (PWUD)[3], primarily through injection (people who inject drugs - PWID), with the population estimates exceeding 400,000 in early 2000's. The most recent estimates suggest that there are about 350,000 PWID in Ukraine, and about 31,000 in the capital Kyiv City.[4]

Historically, the drug of choice for PWID in Ukraine was acetylated opium ("shirka"), made by dealers and users at home from locally grown poppy. According to the national integrated bio-behavioural surveys (IBBS), acetylated opium was used by over 90% of PWID in Ukraine.[5] In early 2010's, illicit methadone, produced by clandestine laboratories and sold in crystalline form, appeared on the drug market in Ukraine. Prevalence of its use was first assessed in the 2013 IBBS, when 10% of opioid using PWID reported injecting it in the past 30 days. Prevalence of past 30-day injection use of illicit methadone gradually grew to 23% in the 2017 national survey, whereas use of acetylated opium decreased to 66%. However, more recent studies[6,7] indicated that over 70% of PWID have used illicit methadone in the past 30 days, while use of acetylated opium has declined. This shift was confirmed by the radically reduced seizures of poppy straw.[8]

Injection use of amphetamine-type stimulants in Ukraine is less common compared to opioids, with about 40% of PWID reporting it use in the past 30 days.[9] There is a lack of data on non-injecting drug use in Ukraine among the general population, however data are available from the European School Survey Project on Alcohol and Other Drugs (ESPAD) surveys implemented among school-aged children. The most recent data indicate an increase in lifetime use of any type of drug from 14.1% in 2011 to 17.6% in 2019 among 15-16 years old teenagers. The most common drugs in 2019 were cannabis (8.3% lifetime use), inhalants (6.3%) and amphetamine (2.2%).[10]

Acetylated opium mostly was prepared by users from poppy straw at home for own consumption, or purchased from dealers in liquid form. Illicit methadone and amphetamine-type stimulants, in contrast, were mainly distributed through dead drops without meeting the dealer in person. The dead drop-based approach of drug dealing is a recent innovation on the Ukrainian drug scene. It involves contacting a dealer by phone using a trusted number or through an encrypted messenger (usually Telegram), transferring money, and receiving information about where to pick up the dead drop.[6]

Wide-spread syringe sharing, and other risk practices led to the HIV outbreak among PWID.[11] By 2007, Ukraine had the second largest HIV epidemic in Europe, primarily driven by injecting drug use.[12] In response to the high HIV rate, international donor funding increased stimulating research on epidemiology and health outcomes among PWID. Results from these studies described various risk practices such as procurement of drugs in pre-cooked liquid form, drawing prepared drugs from a container shared with other PWID, delivering a drug by backloading or frontloading the solution into users' syringes, or purchasing drugs in pre-loaded syringes.[1,13-16]

Starting in 2007, these behaviors were monitored using biannual IBBS.[17-19] The surveys documented a gradual decrease in key HIV risk behaviors and a corresponding decrease in HIV prevalence. Nevertheless, the most recent IBBS round demonstrated that risk behaviors remain prevalent and lead to continued HIV transmission among PWID. In 2017, 42% of PWID reported using a non-sterile syringe for injection in the past 30 days, and 31% reported sharing containers and other paraphernalia.[9] HIV prevalence among PWID <25 years old increased from 4.3% in 2015 to 5% in 2017, indicating an increase in incidence.[9,19]

The harm reduction program, supported by international donors, expanded rapidly to reach 226,469 individual PWID with the minimum prevention package in 2017.[20] The package is based on WHO recommendations [21], and includes provision of syringes (typically limited to 10 per day), condoms (3 per day), and peer or social worker counselling. The quality of the Ukrainian prevention program has earned positive reviews and was named a best practice in Europe by WHO.[22]

Opioid Substitution Treatment (OST) was introduced in Ukraine in 2004[23] yet scale-up has been slow, constrained by patient, clinic and policy factors.[24-27] In the beginning of 2020, the national program provided OST free of charge to about 13,000 patients through the network of about 250 public health care institutions. This translated to about 4.6% of opioid dependent persons being covered with OST, which is well below the optimal coverage levels recommended by WHO, UNODC and UNAIDS.[28] About 90% of patients receive oral methadone tablets, 10% sublingual buprenorphine tablets, and less than one percent (at two pilot sites and in the penitentiary system) receive liquid methadone. Before 2016, only on-site supervised dispensing of OST medications was allowed. In 2016, the regulations were changed to allow medication dispensing for take-home or by prescription for up to 10 days for patients who have clean urinalysis for 6 consecutive months. In February 2020, about 50% of patients were on take-home dispensing. Private health care providers were not allowed to provide OST, however, they could prescribe methadone or buprenorphine for detoxification purpose. With these prescriptions, medications may be purchased by patients at pharmacies.

2.2 THE COVID-19 EPIDEMIC IN UKRAINE

The first COVID-19 case was reported in Ukraine on March 3 in Western Ukraine, and on March 24 the total number of confirmed cases exceeded 100. The first death was reported on March 11. The government undertook a number of actions to contain the epidemic. National lockdown was declared on March 11, all educational institutions were closed and places of mass gathering were closed, borders closed and travel abroad banned, mass events banned. The state of emergency was declared on March 25. The measures have consisted of travel restrictions (limiting the number of passengers allowed on public transport to 10, closing all metro systems, and banning inter-city travel), recreational activities and social gathering restrictions (limiting the businesses that are allowed to operate to only those considered essential, limiting public social gatherings to 2 people, and suspending operations of all educational institutions), and a re-distribution of responsibilities and resources within its medical systems to accommodate for the higher demand of resources by the multiplying cases of COVID-19. These measures remained in place until May, when the "reopening" began gradually by allowing for some freedom of movement and the reopening of public transportation systems. The reopening process consisted of 3 phases and continued throughout the summer until July, when all activities were resumed, with individual protection recommendations still in place. Since June 18, Ukraine has allowed passenger flights to other countries.

In August, a differential lockdown approach was introduced. All administrative units of Ukraine are marked as green, yellow, orange and red levels, representing the severity of restrictions, with the red being essentially equal to the complete lockdown that was in place in spring. Kyiv City was in the yellow zone until mid-September, and in the orange zone afterwards.

Date	Timeline of key events
3-Mar	First case reported
11-Mar	National quarantine restrictions declared
13-Mar	First death reported
16-Mar	Border closed for entry of foreign citizens
25-Mar	State of emergency declared, lockdown introduced, transportation closed
2-Apr	Additional restrictions for recreational activities, mandatory face masks
11-May	First stage of lockdown release: opening of stores, parks, recreational places with restrictions
20-May	Partial border opening
22-May	Second stage of lockdown release: public transportation opening, small gatherings allowed
1-Jun	Third stage of lockdown release: intercity transportation, educational and sport facilities opening
10-Jun	Forth stage of lockdown release: recreational activities allowed with restrictions
18-Jun	Air transportation allowed
1-Aug	Adaptive lockdown implemented
26-Aug	Recreational activities limited again
9-Nov	New epidemic severity grading introduced
13-Nov	"Weekend lockdown" introduced
2-Dec	"Weekend lockdown" cancelled
19-Dec	New restrictions for recreational activities and public gatherings

The early COVID-19 control measures apparently have had an effect and helped Ukraine to avoid a large wave of the epidemic in spring seen in other European countries. The daily average remained below 1000 cases until late July (Figure 1). The cessation of restrictions and opening of schools in fall rapidly accelerated the epidemic, similarly to other countries. Nevertheless, the full lockdown has not been re-introduced, which led to nearly exponential spread of the coronavirus until December. The number of deaths (Figure 2) followed the growth of new cases, as expected.

Figure 1. Floating 7-day average of daily new COVID-19 cases in Ukraine

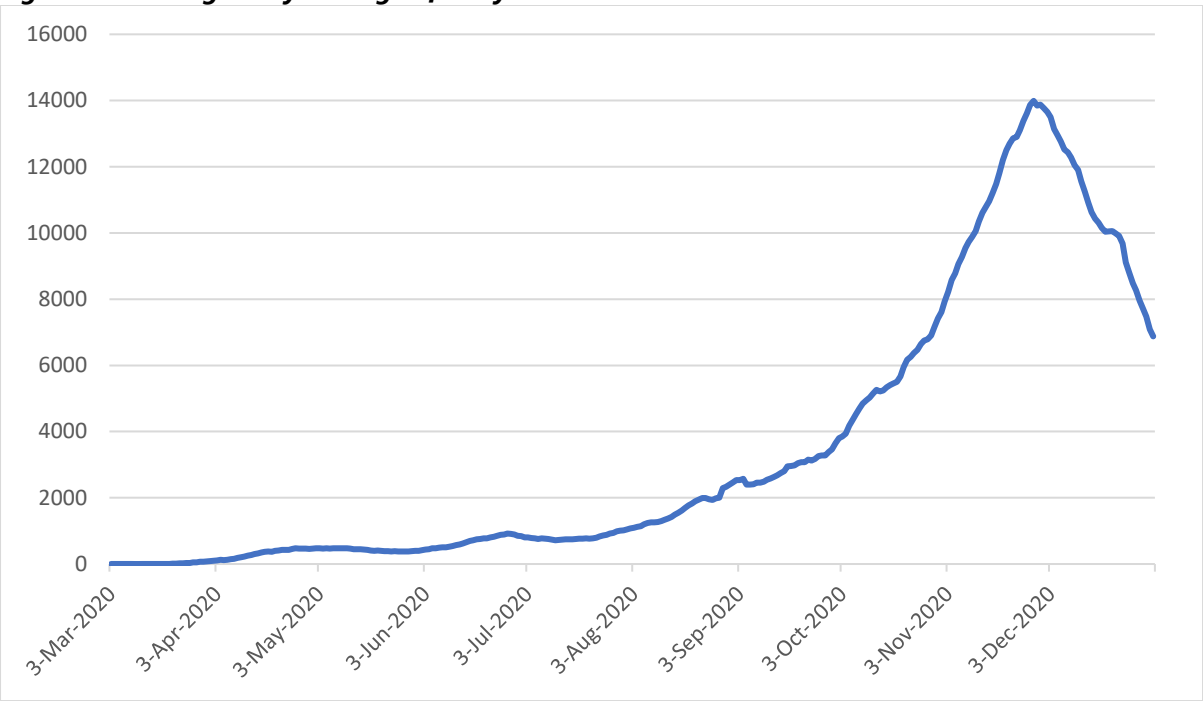
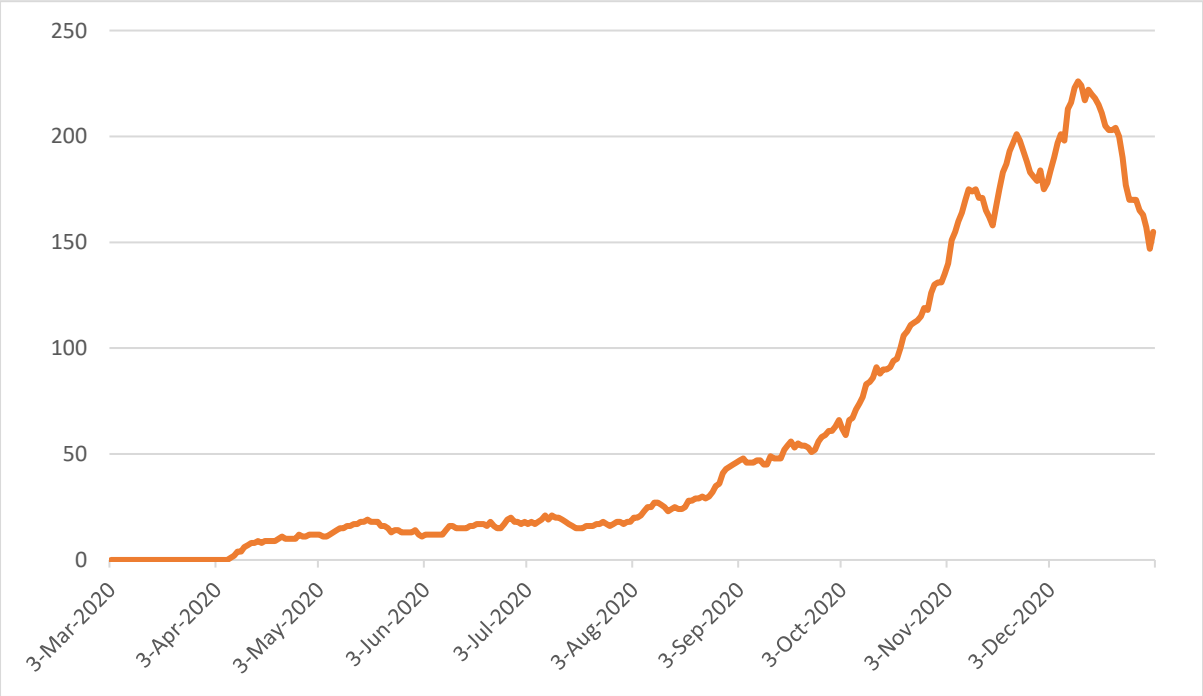


Figure 2. Floating 7-day average of daily COVID-19 death cases in Ukraine



3 STUDY METHODOLOGY AND ANALYTICAL APPROACH

Goal of the study

When the COVID-19 pandemic reached Ukraine in March 2020 and the government introduced a range of response measures, fragmented information started coming from the harm reduction programs and community representatives that the pandemic started to affect drug supply, consumption practices, and availability of treatment and prevention services. In response, we proposed this study to systematically document the COVID-19 impact on illicit drug markets (in terms of changing availability, purity, pricing), changes in drug use patterns (amounts, combinations, route of administration), and ways of obtaining those substances, and changes in key service provision.

Aim 1: To describe and evaluate changes in drug-related behavior and service use among regular users of illicit psychoactive drugs.

For this aim, a cohort of 51 PWUD was recruited in Kyiv, and was followed for six months. An existing database of participants from other studies was used to contact initial seeds and offer participation in this study and to recruit other participants through snowball sampling. To be eligible, the participants had to report any drug use in the past 30 days, to be 18 years old or older, and to have a mobile device with internet connection. Those who were interested were assigned a unique identification number and provided with a link to the survey platform. For data collection, a free web-based platform Kobotoolbox© (https://www.kobotoolbox.org/) was used. The first assessment form began with the informed consent, describing the purpose of the study, the anonymous participation procedures and confidentiality protection. In the beginning of each survey, participants entered their participant identification number. The follow-up assessments were conducted every 2 weeks (with ±3 days windows) for 6 months (13 assessments total). A Timeline Followback Method customized for the purpose of the current study was used for data collection.[29] The baseline survey collected data on socio-demography (age, sex, education, employment), drug use history (drugs used lifetime, last year, last 2 weeks - frequency, amount, routes of administration), drug supply (how drugs are obtained, in what amounts, prices), and treatment history. At each assessment, we asked about past 2 weeks drug use, supply methods, overdose experience, risk behaviors (questions from Ukrainian IBBS), perception of trends in drug availability, harm reduction and treatment service use. Data on injection risk behaviour from the assessment rounds 1, 4, and 7 were not collected due an error in the online data collection system.

Analytic approach. The sociodemographic and behavioral profile of the study participants was described using frequencies and proportions (for categorical variables) and median and interquartile range (IQR) for continuous variables, as appropriate. Frequencies in the main outcome variables were plotted on the time axis to visualize the trend. Mixed-effects generalized linear models, accounting for within-subject correlation across time points, were used to test the hypothesis of a linear trend for key outcome variables in each domain. The assessment number, ranging from 1 to 13, was used as a continuous variable representing time. Odds Ratios (ORs) for the assessment number represent an incremental increase or

decrease in the estimated odds of achieving the outcome (see Annex) at the subsequent assessment. The models were adjusted for the duration of drug use, sex, and baseline lifetime exposure to OST. Analysis was done using SPSS v.23 and R v.4.0.3.

Aim 2: To explore changes in the drug scene and service provision using key informant in-depth interviews.

For this purpose, four key informants (1 addiction treatment (detox + rehabilitation) physician, male; an OST physician, male; a harm reduction (HR) service provider, female; and a PWUD community representative, male) were recruited and monthly in-depth interviews were conducted with each key informant at the same assessment time points with the main cohort. Qualitative interview guides were developed to monitor the trends in drug scene and service provision from additional perspective. The data collection process consisted of an in-depth, semi-structured interview conducted via phone. Experienced interviewers were specifically trained in conducting qualitative data collection through in-depth interviews and in human subjects protection.

Aim 3: To triangulate the trends in drug use patterns and service availability using in-depth interviews with the cohort participants.

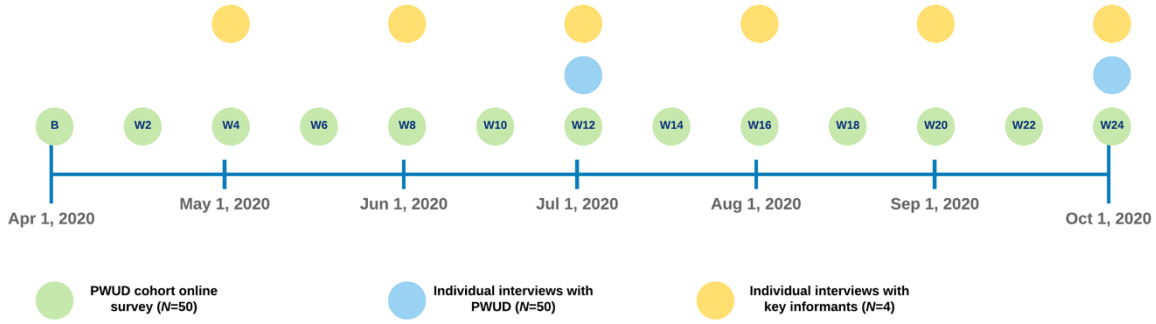
A sub-sample (N=25) of the cohort participants were invited for in-depth interviews half way through the six month study period (3-month interviews in July) and at the end of follow-up (6-month interviews in October, 2020) to verify the findings from the structured interviews. The interviews were conducted by phone by the same interviewers as for the Aim 2.

Analytic approach for the Aims 2 and 3. The qualitative data were analysed with MAXQDA software using thematic analysis approach. Following the multiple rereading of the transcripts, the list of initial codes was developed. A set of codes and subcodes was agreed and applied to the transcripts; however, if new ideas emerged and were identified in the text, they were included in the list of hierarchical codes. This approach helped to identify commonalities and differences in data and to draw descriptive and explanatory conclusions clustered around the key themes.

Human subjects protection. The survey was anonymous and did not collect any personally identifiable information. All data were collected and stored through secure protocols. The study protocol and informed consent forms were approved by the Ukrainian Institute on Public Health Policy IRB#1.

Limitations. The sample size for the quantitative part of the study was small and was be limited to the established regular drug users who had access to internet. The sample was further limited to the residents of the capital city of Kyiv, who were recruited using snowball sampling. Therefore, the results may be not generalizable to the entire drug using population in Ukraine.

Figure 3. Study timeline



4 RESULTS

4.1 CHARACTERISTICS OF THE COHORT AND RETENTION

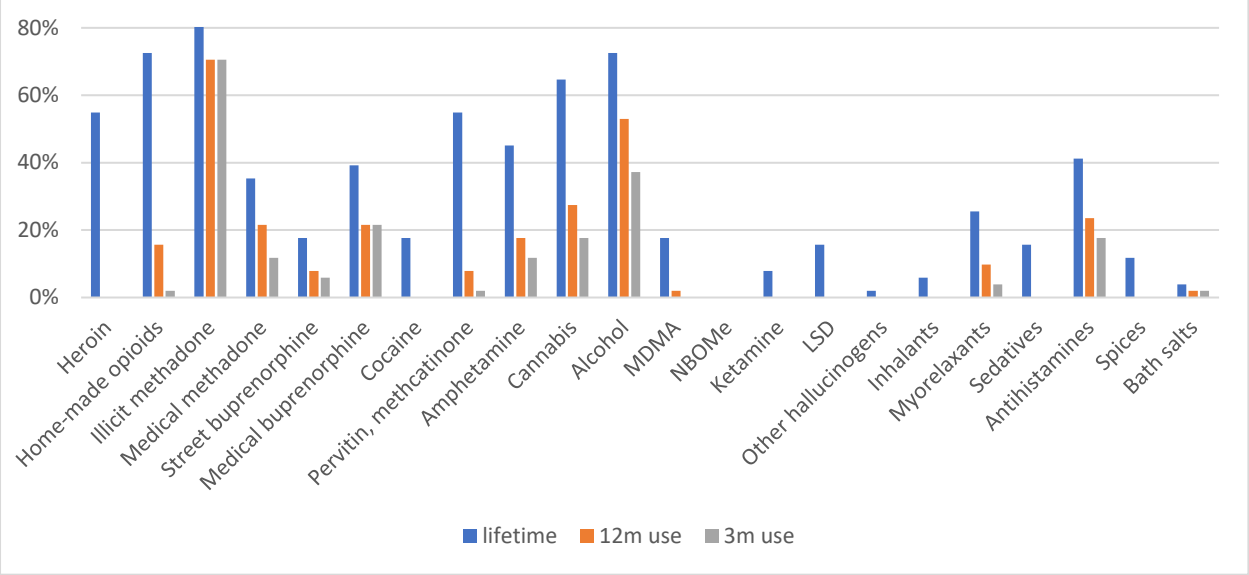
We recruited a cohort of 51 individuals who use drugs regularly between 7-13 April. Main socio-demographic characteristics of participants at baseline are presented below (Table 1).

Table 1. Socio-demographic characteristics of the cohort participants

Variables		Mean (Range), N (%)
Age, years		38 (18-54)
Injection drug use duration, years		19 (1-34)
Gender	male	37 (72.5%)
	female	14 (27.5%)
Education	Secondary school	2 (3.9%)
	High school	7 (13.7%)
	College	22 (43.1%)
	Incomplete higher education	10 (19.6%)
	Complete higher education	10 (19.6%)
Employment	Unemployed	23 (45.1%)
	Employed fully or partially	21 (41.2%)
	Work and study	1 (2.0%)
	On social assistance	6 (11.8%)

All participants in the cohort had a history of drug injection (Figure 4). Majority injected opioids, primarily illicit methadone. Over a half used ATS (injecting or intranasally) and over 40% used antihistamines (primarily as an adjuvant to injected opioids). Median duration of problematic drug use was 19 years. Majority of participants (34/52, 65%) had a history of at least one treatment episode. About a third was ever treated with OST, which was the most common type of treatment in the lifetime.

Figure 4. History of drug use among cohort participants.



We managed to retain 90% (46/51) of participants by the end of follow-up.

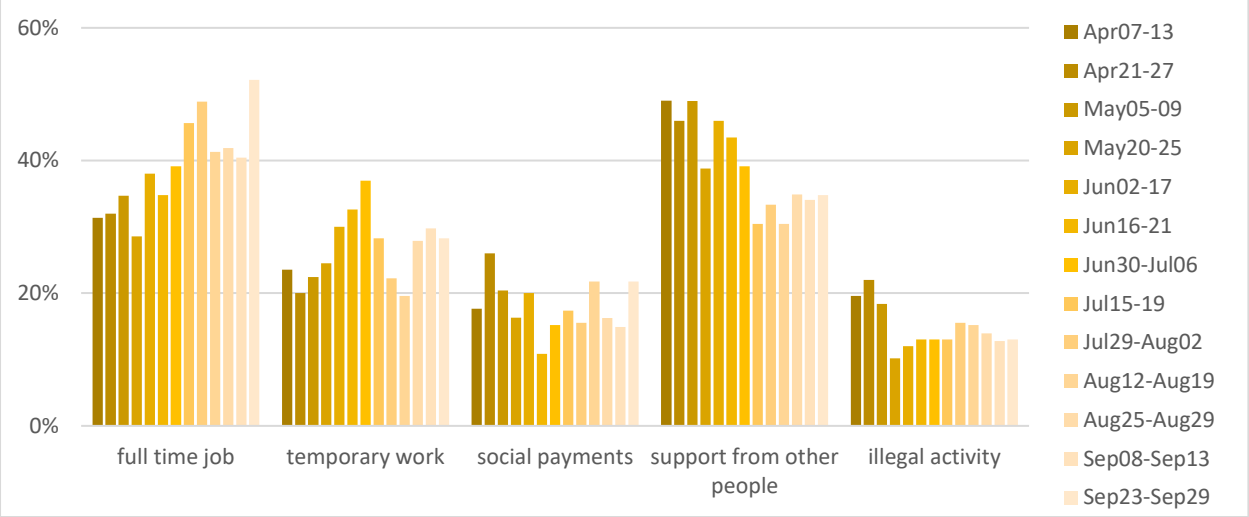
4.2 Trends in source of income

Full- or part-time job as the main source of income was reported by 55% of participants at baseline, increasing to 76% in late July and to 80% by late September (Figure 5).

Qualitative results:

The same trend was reported in qualitative interviews with PWUD and with the PWUD community representative: many PWUD who did not work before the pandemic got a job after the end of the strict lockdown. Similar to the surveys, many PWUD reported that before the pandemic they were supported by their family members, did not work or were involved in the illegal activities (mostly stealing). During pandemic *"there was less support from the family, the expenses increased, so we had to think about increasing the income. Many guys went to work at the construction, I found a temporary job for the summer"* (Male, 37). "*With this lockdown, it became more difficult to engage in illegal affairs, transport did not go, there were fewer people in the stores, so the income from illegal activities decreased*" (Male, 27). Many male PWUD reported they started working in the auto service, cleaning or delivery companies, females worked as assistants to the disabled persons or in the stores. By the end of the summer, illegal sources of income reportedly returned, however not to the pre-COVID levels.

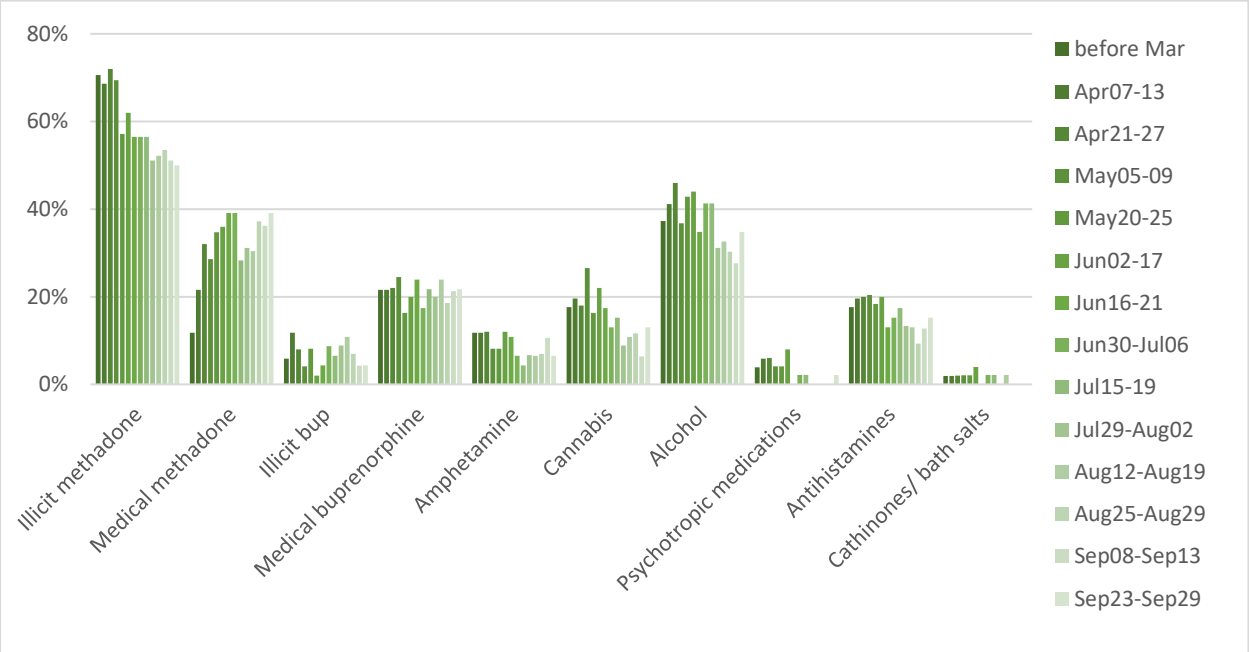
Figure 5. Main source of income



4.3 TRENDS IN SUBSTANCE USE

Illicit methadone remained as the most prevalent drug used in the cohort. There was a sustained decrease in the proportion reporting its use in the past 14 days, from over 70% at baseline to 51% in September (Figure 6).

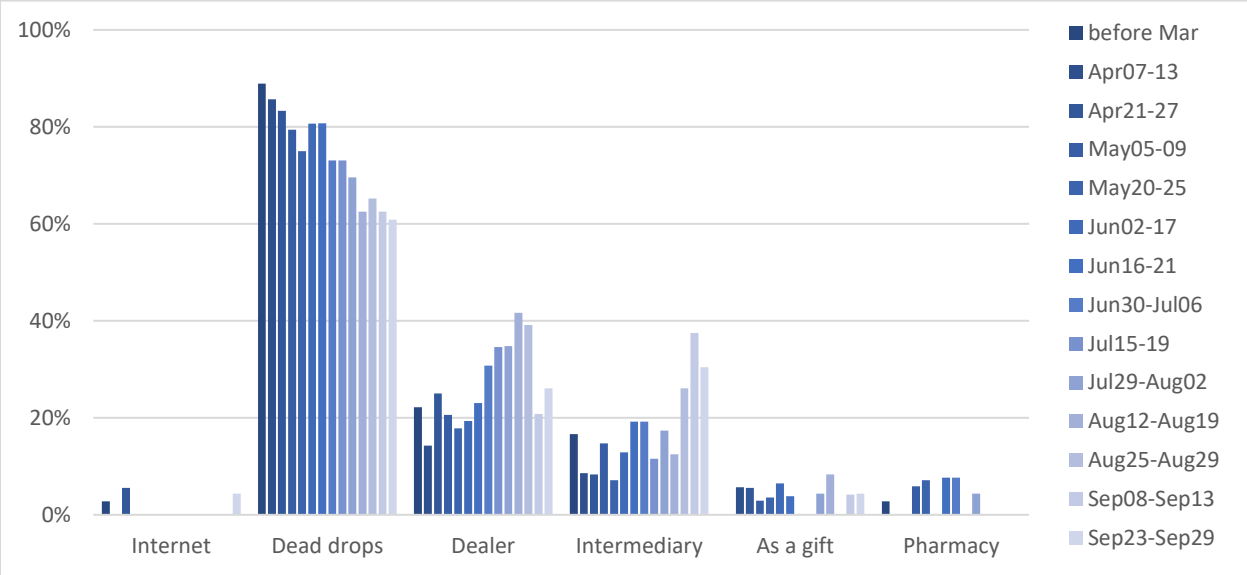
Figure 6. Proportion of respondents reporting the use of specific drugs in the past 14 days (note: the first column shows the drugs used in the past 3 months prior to March 2020)



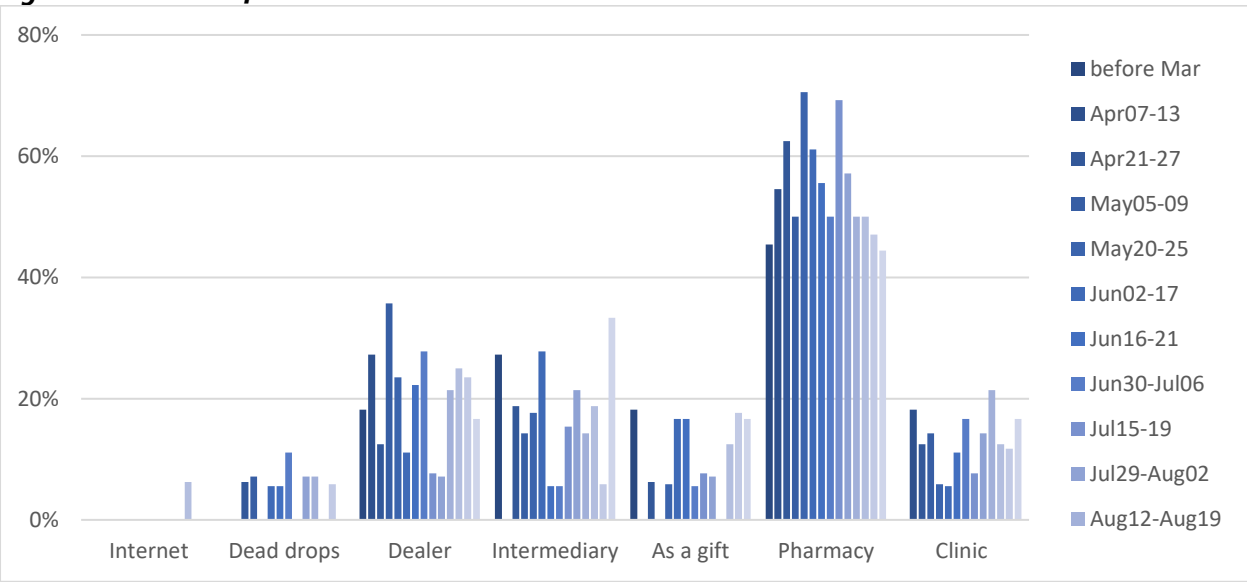
This decline was strongly statistically significant, after accounting for within-subject correlation and controlling for the effect of sex and duration of drug use (assessment number aOR=0.8 [95% CI 0.7-0.9]) (Annex 1), and was confirmed by the qualitative interview data. The main reason for the decline in illicit methadone use was the limitations in public transportation, which complicated the usual way of purchase through dead drops (aOR=0.7 [0.6-0.8]). The decrease in use of dead drops continued throughout the study, including after the transportation was re-opened. There was an increase of purchase of illicit methadone via

more traditional interaction with dealers in July-August, and obtaining through friends in August-September (Figure 7).

Figures 7. Sources of illicit methadone.



Figures 8. Sources of medical methadone.



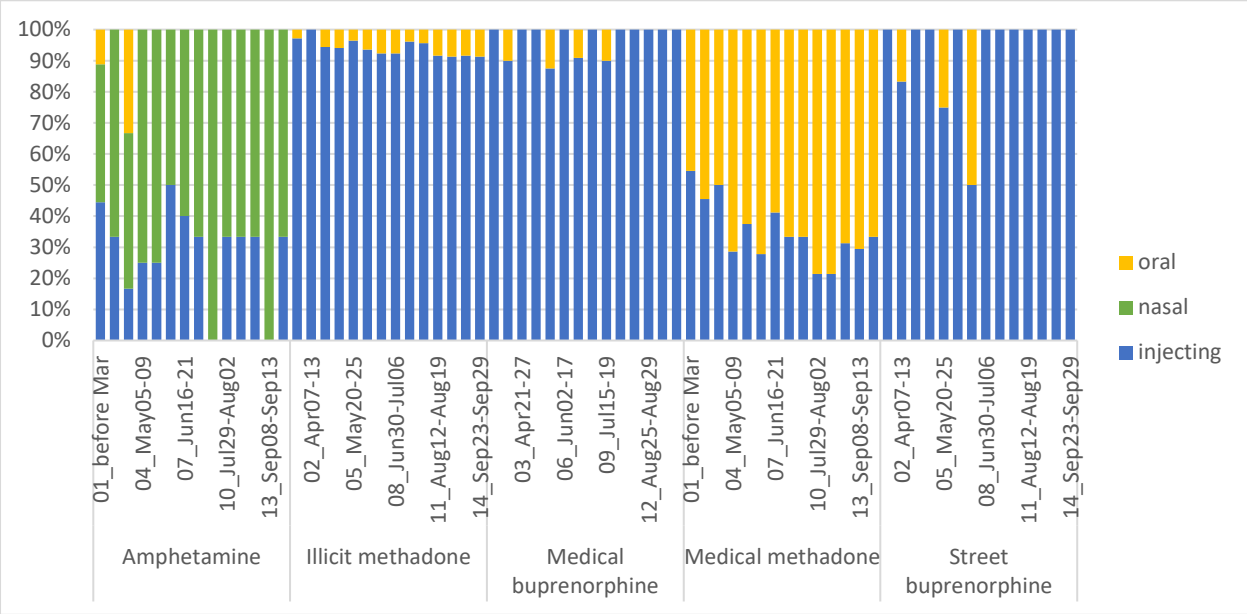
As a result of hindered access to illicit methadone from sources common in pre-COVID period, there was a notable increase, up to 40%, in medical methadone use. As shown above (Figure 8), the main source of medical methadone was pharmacies. This recent trend in the Ukrainian drug scene became possible due to the legislature that allowed private medical providers (licensed private physicians) to prescribe methadone and buprenorphine for detoxification purposes. For a relatively small fee (~10-14 EUR), these physicians provide prescriptions for up to 1g of methadone in tablets or 112mg of buprenorphine in sublingual tablets, which can be used to purchase the medication in pharmacies. In practice, there is no medical supervision nor follow-up after the prescription is issued, suggesting that the intent is not to detoxify nor treat opioid dependence. A substantial proportion (up to 20%) of

medical methadone obtained by prescription is becoming available on the black market, as seen from the proportion of PWUD purchasing it from other sources.

The increase in medical methadone use was close to reaching statistical significance (aOR=1.1 [1.0-1.2]), while controlling for the effect of duration of drug use, sex and lifetime exposure to OST.

However, there is a big difference in how illicit and medical methadone are used. The majority of users of illicit methadone reported injecting, whereas medical methadone was used orally (Figure 9). The apparent decline in injection use of medical methadone was not statistically significant (aOR=0.9 [0.8-1.0]). In contrast, buprenorphine is primarily used through injection, regardless of whether it is obtained from the street sources (this maybe the prescribed buprenorphine sold on the street) or by prescription.

Figure 9. Method of substance use for most common drugs (data on medical methadone and buprenorphine excludes participants who reported receiving OST at governmental programs).



Importantly, the decreasing trend in the use of illicit methadone, and the compensatory increase of the use of medical methadone obtained by prescription did not reverse after the restrictions for public transportation and other epidemic control measures were released. This suggests that this change in the drug scene became sustainable, at least during the study period, due to the convenience and other perceived advantages of the prescription source.

Note: In November 2020, a new Standard for treatment of opioid use disorders was approved by the Ministry of Health,[30] which introduced a requirement of supervised medication administration during detoxification. This should limit the practice of private prescription dispensing.

Qualitative results:

The participants' accounts from the qualitative research confirm the results of the surveys. According to both providers and PWUD, before COVID-19 pandemic, the most popular drug was illicit methadone (synthetic, or "crystal" methadone)

purchased through dead drops or (less often) directly from the dealers. Other most popular types of drugs in the recent years were medical methadone and buprenorphine obtained by prescription from private physicians, as well as "bath salts" (likely synthetic cathinones) which were widely available through dead drops and were referred as much cheaper than opioids. PWUD often injected methadone (any type) mixed with pharmacy drugs – mainly Sonnat (zopiclone, hypnotic medication) and Dimedrol (diphenhydramine, antihistamine medication), to prolong methadone effect. They also used pregabalin-based drugs (Lirika, Gabana) to relieve the withdrawal syndrome.

According to many participants, since mid-March, with the strict lockdown, buying drugs through dead drops became especially problematic. In addition to unavailable public transportation, there were a lot of police on the streets, and due to the social distancing "*every PWUD was in sight*". Therefore, during the strict lockdown, especially in April-May, while the use of illicit methadone decreased, a lot of PWUD turned to methadone (and to less extent buprenorphine) easily available for purchase at pharmacies using prescriptions obtained from private physicians, or from other clients of these physicians.

"*A number of people buying street methadone decreased by 2-3 times. It was more difficult to get, it is expensive, and people switched to the more convenient option – medical one*". (Female, 45).

In addition, since most patients of the governmental OST sites were transferred to 10-day take-home doses, there were indications that this could increase availability of the medicinal opioids on the illicit market. "*What we often see is - a person receives the pills for 10 days, and after 2-3 days the medication is over, and he comes for the next 10-day pills with a visible withdrawal*" (OST physician). Given that the average dose at Kyiv OST sites exceeds 100mg/day,[31] insufficient dosing is an unlikely reason of withdrawal in most cases.

According to both PWUD and service providers, Kyiv quickly responded to the increased demand for medical methadone: many private physician sites were newly opened (at least 40 in Kyiv City), often offering flexible price discounts to attract new customers. Therefore, the share of medical methadone on the drug scene increased quickly, and "*one person often became a client of 2-3 private methadone sites buying pills cheaper and reselling them for his mates*" (PWUD community representative). As many PWUD respondents mentioned, "*a person would buy a package of 40 25-mg methadone pills for 152 UAH* [~5 EUR]*, and resell it by 30 UAH* [~1 EUR] *per a pill. On the black market, 1 pill of methadone could cost up to 100 UAH* [~4 EUR]". (Female, 37).

At the same time, some PWUD reported that the dealers of illicit methadone also quickly adjusted to the situation, providing dead drops in the walking distance of a customer's place. Many PWUD reported they were still buying drugs from their trusted dealers. "*Nothing has changed for me. I have always bought from the same*

dealer for many years; now he puts dead drops as close to my house as possible, I even do not need to walk far." (Female, 34).

In June, after the operation of the public transportation restored and metro re-opened (May 22), the situation on the drug scene started gradually going back to the pre-lockdown period. In July-August, the availability of all types of drugs returned to the pre-COVID levels. The most popular types of drugs reported in the interviews were the same as before the pandemic, with "*illicit methadone occupying estimated 70% of the scene*", according to the providers. Still, methadone from private physicians remained popular, and "*most of those who moved from illicit to medical methadone, remained on it. It's comfortable for people, the purity is predictable, and no need to run around…*" (PWUD community representative).

The PWUD respondents echoed the providers: many switched from illicit methadone to medical methadone. At first, PWUD who were used to illicit methadone, complained about a lack of effect or a smaller effect of medical methadone, so "*people tried to adjust, combining program methadone with Dimedrol or Sonnat, to increase and prolong the effect*" (Female, 45). However, as respondents suggested, for many using medical methadone appeared to be more convenient, so when the drugs availability returned to per-COVID, many stayed on medical methadone or combined both types.

"*I use pills from the paid program on the working days, and for the weekend we buy crystal methadone - to inject, to relax a little bit*". (Female, 54).

«*Even before [COVID], I was sick and tired of running around looking for dead drops, to dig the soil in front of the police. During lockdown I switched to the pharmacy methadone. This works much better for me. So, lockdown helped me*". (Male, 42).

"*People understood that medical methadone is much cheaper, there is less criminal activity involved, you have to steal less frequently… This is really more convenient*". (Female, 45).

Only one participant reported that during lockdown he was not able to get medical methadone, so started buying illicit methadone through dead drops (Male, 33).

Quantitative results:

The use of heroin, homemade opioids (historically the drug of choice in Ukraine) and other drugs (MDMA, LSD, others) was negligible. Use of amphetamine fluctuated and mostly remained low at about 10%, then reduced to 4-7% in July-August and September. Among other substances, there seems to be a decline in use of cannabis (from 20% in April to 13% in September, Figure 7). Antihistamines, mostly used as an adjuvant to injected opioids, also decreased from 20% in April to 13-15% in September. Alcohol consumption increased in April to 46% compared to pre-COVID level (37%), but then steadily decreased to about 30% in the last rounds of the survey. This reduction was statistically significant (aOR=0.9 [0.8-1.0]).

Qualitative results:

According to the PWUD community representative and other interview participants, and in line with the surveys data, the percent of PWUD using bath salts was rather small, but it remained stable even during lockdown. The salts are considered the cheapest and probably most easily accessible drugs. Regarding the use of additional substances, the respondents reported that, with less availability of illicit methadone in April-May and decreased income for many PWUD, both PWUD who switched to medical methadone and who tried to decrease frequency of injecting, started using more alcohol and pharmacy drugs. This confirms the trend shown in the surveys.

Quantitative results:

The subjective perceptions of the trends in accessibility of drugs and their purity among cohort participants changed over time (Figures 10-11). Apparently, in the initial period of the epidemic, many users experienced harder access to their main drug of choice. Over time, the proportion of participants reporting that access became harder in the past two weeks declined from 39% at baseline to 4% in June, and then to 0% in late September. This trend was highly statistically significant (aOR=0.7 [0.6-0.8]). After initial improvement in April-June, there are no apparent trends in purity of drugs, with fluctuations between 8 and 20% reporting worse purity.

Qualitative results:

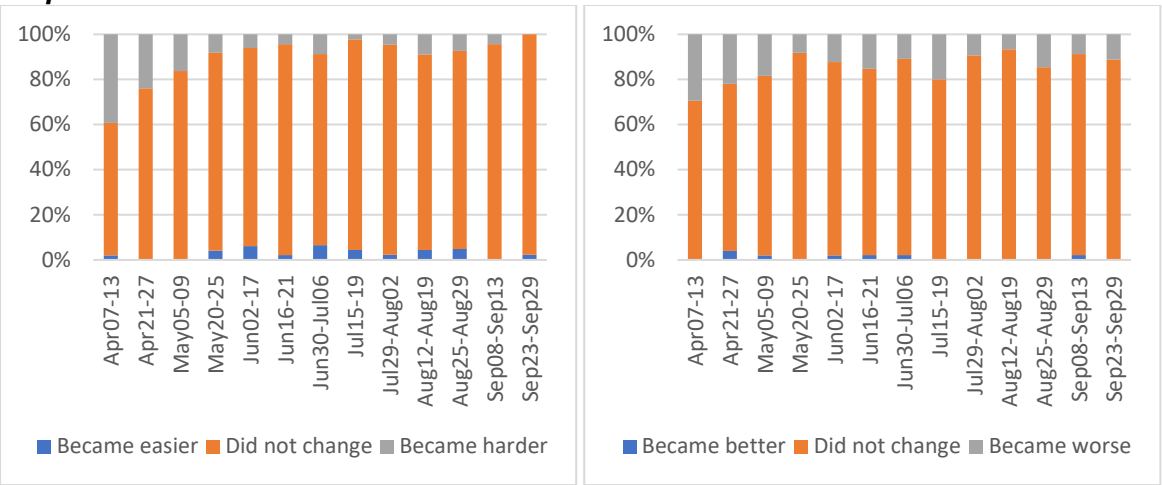
A specific theme that emerged in the interviews was the worsened purity of illicit methadone during and post-lockdown period. Some "online sources" (darknet websites or Telegram channels) disappeared or were inactive during lockdown. At the same time, both services providers and PWUD reported that in July-September a lot of new dealers appeared on the market, and most of them had access to the base of the PWUD phone numbers, as the PWUD received text messages all the time from new sellers offering drugs at cheaper price. However, often it was "kidalovo" (cheating) – the purity of drugs was unacceptable, or it was not a drug at all.

"*When trusted sellers disappeared, we had to refer to new ones. I once paid for two checks (0.25 gr), and what I got? Just a cooking salt! It was a real frustration, when everything aches, and you spent all your money for nothing*". (Female, 42).

"*You could lose 1000 Hryvnia* [~30 EUR] *on one day and get nothing… This was the most negative thing during all these months*." (Female, 54).

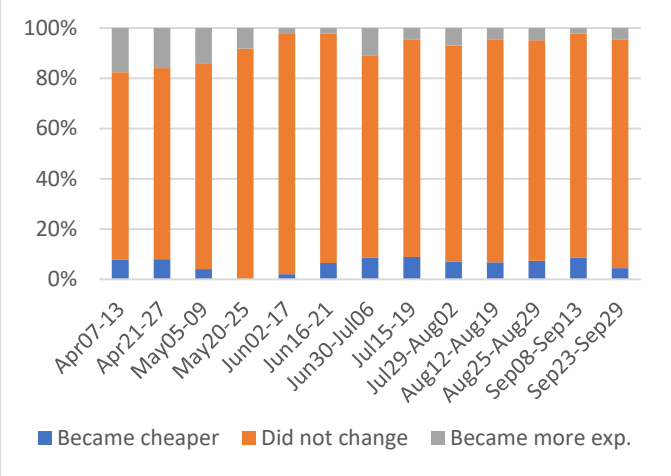
In general, according to the respondents, during the lockdown, people started using more drugs of unknown composition or purity; they "would use everything they had access to" (PWUD community representative), including alcohol. People experimented with the use of substances to achieve desired effect; they reported adding pharmacy drugs more often, mixing available methadone (either illicit or medicinal) with Dimedrol, Sonnat, etc. they also used more low alcohol drinks (canned gin-tonic, etc.). Some PWUD reported they started a day with "Lirika" in the morning (to cope with abstinent syndrome), added Sonnat and Dimedrol, and later - Methadone. According to the PWUD community representative, this polydrug use (including alcohol) may be the reason of the increase in the number of fatal overdoses in June.

Figures 10-11. Perception of trend in access to (left) and purity of the drug of choice (right) in the past two weeks.



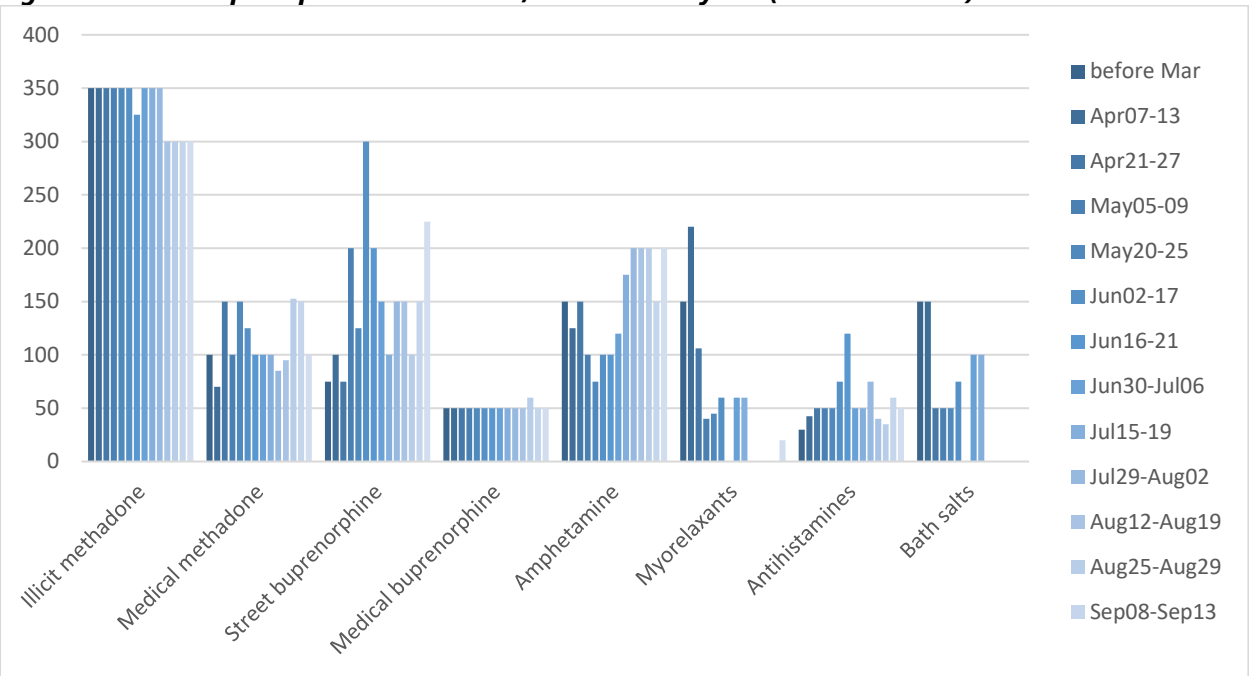
Similarly, the proportion reporting higher prices for the main drug was 18% at baseline, and declined to about 4% since June, with one spike to 11% in late June (aOR=0.8 [0.7-0.9]) (Figure 12).

Figure 12. Perception of trend in price of the drug of choice in the past two weeks.



However, the actual prices per standard dose fluctuated without any obvious trend (Figure 13). The frequency of use did not change significantly. Median frequency was once a day and 7 days per week for most of injecting drugs, with exception of illicit methadone which is injected 3-5 times per week.

Figure 13. Median price per standard dose, Ukrainian Hryvna (1EUR ~ 33UAH).



Qualitative results:

According to the qualitative data, in the beginning of the lockdown (March and April), the price for the illicit drugs increased slightly. However, according to all respondents, in June the prices started going back to the pre-COVID level. "*Before the epidemic, one dead drop (0,25 gr of illicit methadone and 2 pills of Dimedrol) cost 300 Hryvnia* [~9EUR]*; then the price grew to 340-400 Hryvnia* [~10-12EUR]*, without Dimedrol. In July-August, the price returned to 300* [~9EUR] *again, and the purity improved*". (Female, 42). This point of view was echoed by the majority of the PWUD participants.

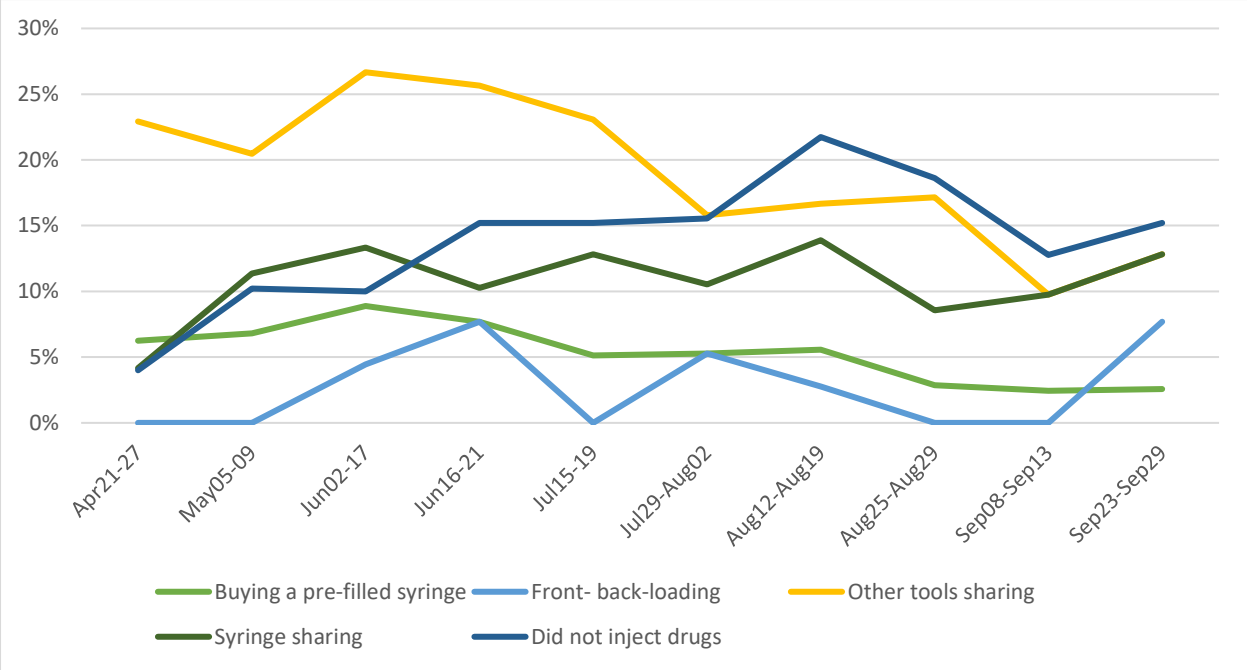
According to the PWUD, in August and September, the sellers even somewhat decreased the prices, as "*people now have less money*". As a part of competition for the client, "the dealers now add different "bonuses", when you buy methadone, - such as 2 pills of Sonnat or Dimedrol for free". (Male, 36).

4.4 TRENDS IN INJECTING RISK BEHAVIOURS

There was a consistent increase in the proportion of users who did not inject, from 4% at baseline to 22% in August, which then again decreased to 15% (Figure 14). The proportion sharing syringes at least once in the past 2 weeks was relatively stable, between 4% in April to 15% in July, confirmed by the insignificant test of trend (aOR=1.0 [1.0-1.1]). Sharing of other tools declined from the maximum of 27% in early June to 13% in the last round of the survey, and this trend was statistically significant (aOR=0.9 [0.8-1.0]). The lower probability of sharing syringes and other tools was significantly associated with longer duration of drug use (syringe sharing aOR=0.9 [0.8-1.0], tools sharing aOR=0.8 [0.7-1.0]). Front- and back-

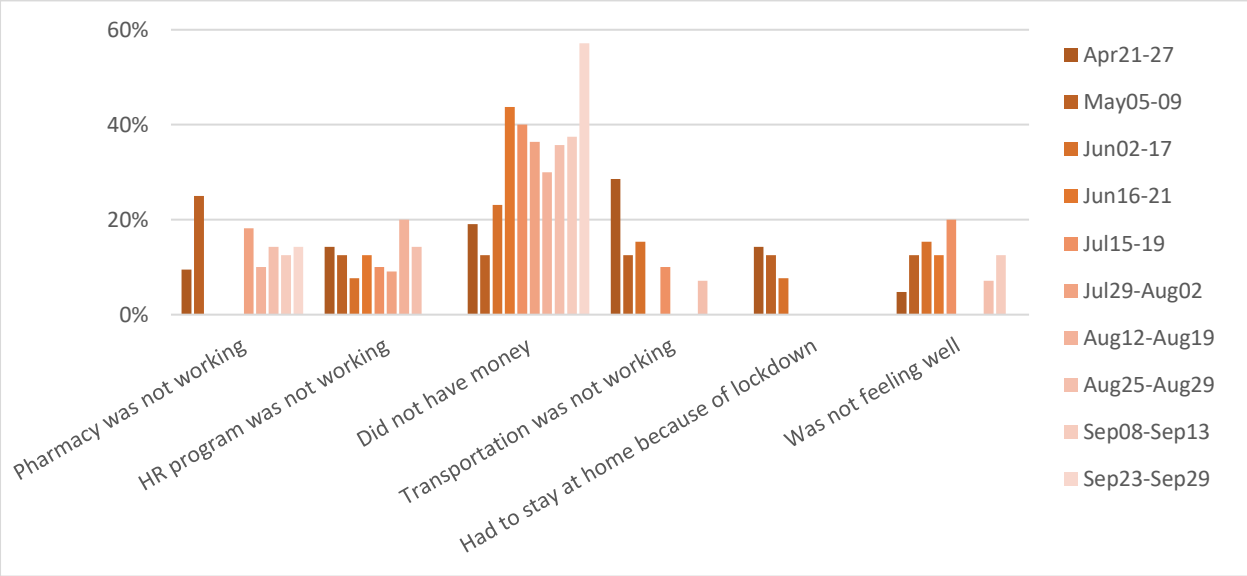
loading practice was not consistent, ranging from 0 to 9%. Buying in pre-filled syringes gradually declined from 9% to 3%.

Figure 14. Injecting risk behaviours in the past two weeks.



The proportion of PWID who reported always having a new syringe for injection in the past two weeks increased from 74% at baseline to 87% in the last round, and this trend was significant (aOR=1.2 [1.0-1.3]), with higher odds among those with longer drug use careers (aOR=1.3 [1.1-1.6]). Among those who reported not always having a new syringe for injection (N=7-21 across rounds), the most common reason was not having enough money (Figure 15). The proportion indicating unavailability of transportation and having the stay home because of the lockdown as reasons for not having clean syringes was 29% and 14% in April, respectively, with both declining to 0% in June.

Figure 15. Reasons for not having a clean syringe for each injection in the past two weeks.



Qualitative results:

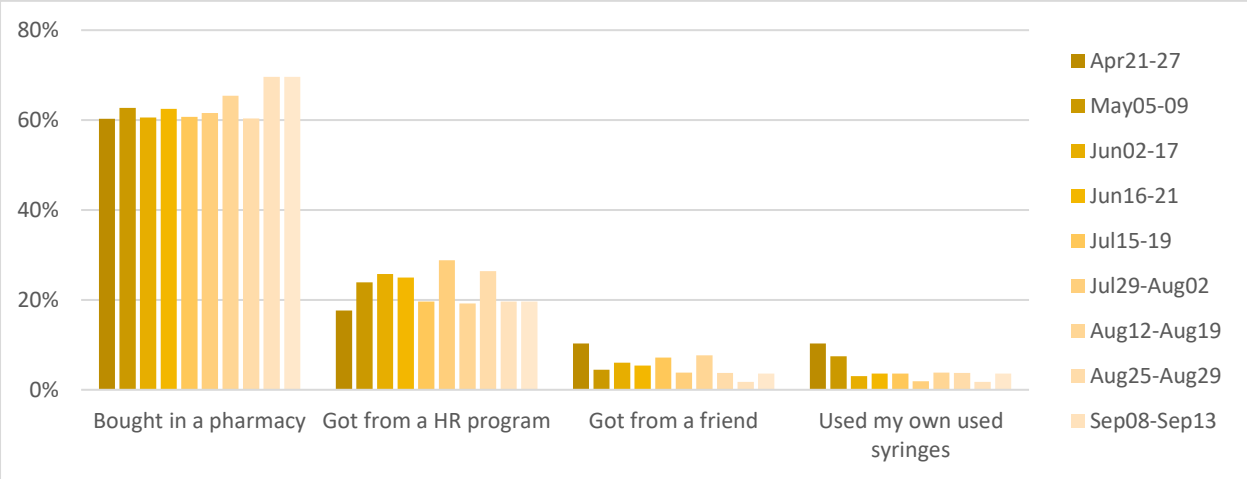
The reduced access to clean syringes at HR programs during strict lockdown was confirmed by the qualitative interviews participants – both PWUD and the PWUD community representative. Harm reduction programs did not provide face masks or disinfectants for the clients, so most PWUD have no access to these protective measures. Regarding COVID-specific risks, no social distancing was respected during drug purchase, preparation or use. Many respondents (even in October cycle of the interviews) reported they "did not believe in COVID".

The PWUD community representative emphasized that during the strict lockdown, "*as more police were in the streets, and every drug user was in plain sight, more arrests happened – so people tried to buy drug and to use it immediately, not to carry it on them. In summer, they did it in the parks or in the house entrance. This often leads to a riskier drug use*".

4.5 TRENDS IN AVAILABILITY OF SERVICES

The main source of syringes for injection in our sample was pharmacies (60% of participants or more were buying syringes in the past 2 weeks), followed by harm reduction programs (about 20%), and then less common sources like getting from friends. The sources of syringes did not change substantially over the study period (Figure 16). Use of harm reduction programs to obtain syringes did not change notably over time.

Figure 16. Sources of syringes for drug injection in the past two weeks.



Overall, 50-60% of participants were using any services at harm reduction programs in the past 2 weeks across all assessment points, without a notable trend. About 25% of those who used harm reduction reported poorer access "in the past 2 weeks" at baseline. This proportion decreased to 4% in June, and then fluctuated at around 6-7% (Figure 17).

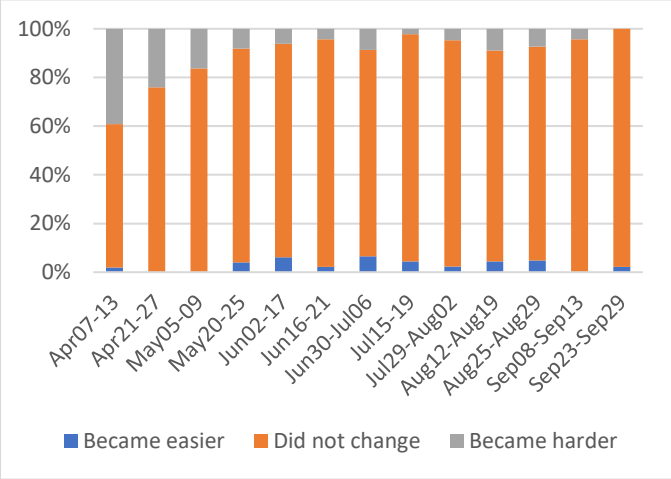
Qualitative results:

The participants of qualitative interviews also perceived this trend: during the strict lockdown in April-May, HR services (needle and syringes programs) tried to respond flexibly to the client needs, bringing the services as close to the clients as possible. Outreach workers provided syringes and other basic services at many points across

the city – on the street near private methadone sites and pharmacies. However, working hours and a number of locations were reduced, and many PWUD reported "*the HR site where I used to go for syringes was closed*" (Male, 40). In general, with restrictions on movement and shutdown of the public transportation, in March-May people have less access to HR services. Typical response of the PWUD participants was, "*Before COVID, I received syringes from NGO; during lockdown, I bought syringes at the pharmacy*". (Male, 33).

In August-September, HR services provided their services in full; protective masks and disinfectants for clients became available. According to the HR provider, "*some clients got lost during COVID; also, it is clear that NGOs do not reach a significant part of the PWUD community*".

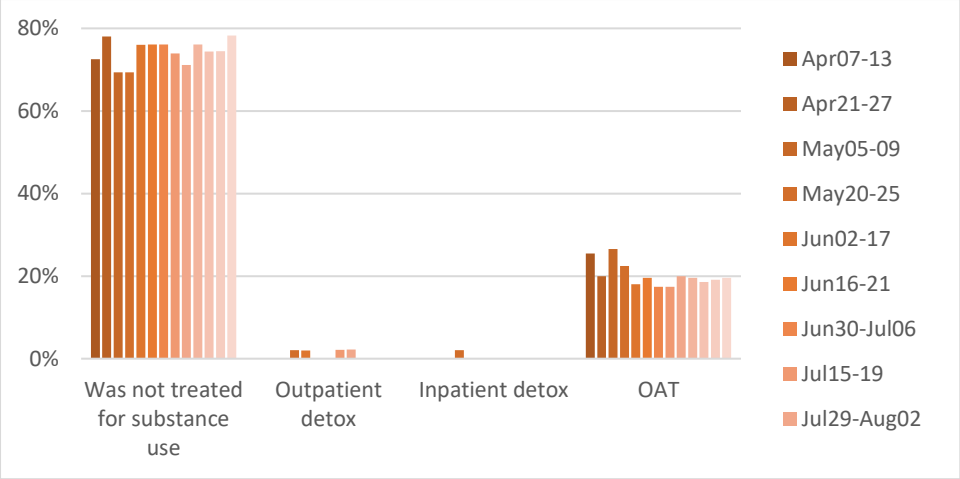
Figure 17. Perception of trend in access to harm reduction services in the past two weeks.



The governmental OST programs quickly responded to the epidemic. Before the COVID-19, about 50-60% of the OST clients in the free programs received methadone/buprenorphine every day on-site. Following the letter of the MoH in March, recommending universal transfer to take-home administration for up to 10-days, nearly 90% of patients were transferred.

In our cohort, the proportion of participants who reported receiving OST in a governmental clinic was 25% at baseline, 27% in May, and then declined to 20% in the last round (Figure 18). This trend was significant (aOR=0.8 [0.7-0.9]), while controlling for the effect of lifetime exposure to OST. Use of other treatment options was negligible.

Figure 18. Substance use treatment experience in the past two weeks.



Qualitative results:

Data from the qualitative interviews confirmed that during the COVID-19 epidemic, narcological dispensaries (government clinics) stopped accepting new patients to the free OST sites or for the detox programs. In April, the demand for the free OST program has notably increased in Kyiv; "*for the first time since 2013, there was a waiting list to start OST*" (OST physician). This, however, may have been a motivation for the people who wanted to join the OST but were unable to do so, to turn to the private physicians. As explained before, these private physicians had been authorised to issue prescriptions for methadone and buprenorphine for a fee.

Regarding the existing patients on OST, both physicians-narcologists mentioned that the transfer of patients to take-home dispensing played a positive role in supporting retention in OST, which was perceived as high during the strict lockdown and during the whole study period. However, patients who previously received liquid methadone and were transferred to take-home tablets, reported they liked the quality of liquid methadone better[3].

Since June, some OST participants who had to adjust the dose or were suspected to be non-adherent on the OST take-home mode, were transferred back to the daily on-site treatment; still, as of August and September, "*80% OST patients stayed on the take-home doses, which is significantly more that before the COVID*" (OST physician).

In June, the Kyiv City "Sociotherapy" Clinic started accepting new patients to OST and detox programs. However, a required (expensive) test for coronavirus hindered PWUD access to this treatment programme. According to the PWUD community representative, this was a serious barrier for PWUD, and of those 20 people who were on a waiting list to start OST, only four enrolled in the program. Overall, OST sites returned to "normal" operation, providing all standard services, such as HIV tests and TB examinations. In August and September, the COVID test became free for PWUD

[3] Overall, it is a common opinion among clients, that methadone from Ukrainian manufacturers has lower than declared dosing. The lab tests did not confirm that though. Since liquid methadone is imported, it is considered to be higher quality by clients.

who wanted to start OST, so 40 new patients were enrolled for methadone OST during these two months.

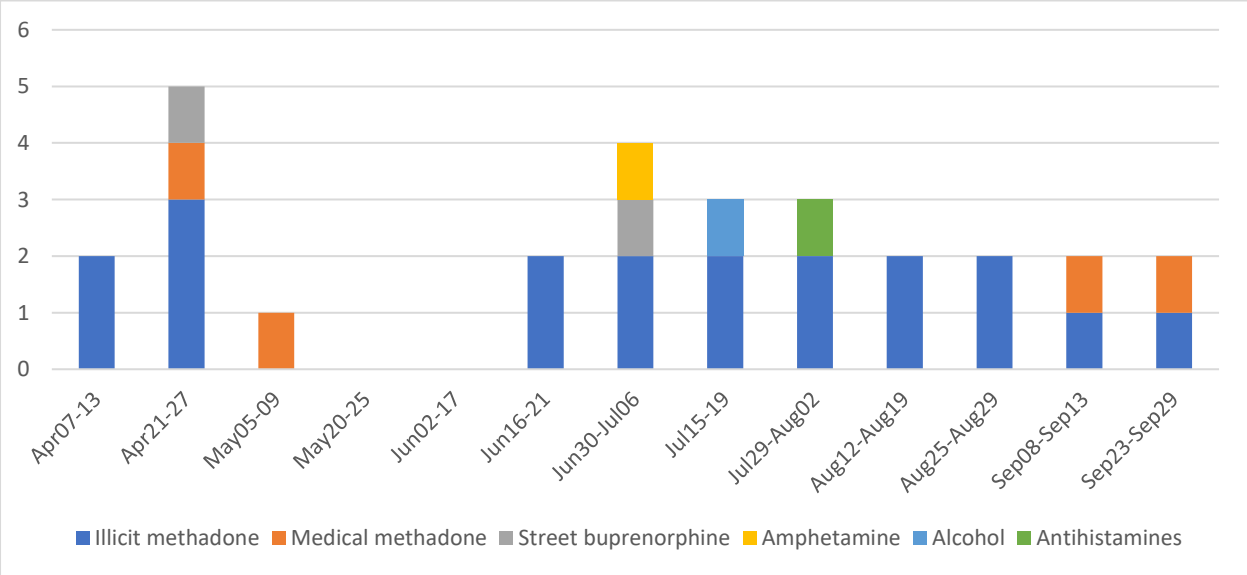
The providers emphasized the availability of both methadone and buprenorphine at the OST sites, and their capacity to enroll new patients. Free treatment for Hepatitis C is also available for the OST patients. According to the OST physician, "*a good news is that community organizations actively referred new clients for OST since September*". However, a need to visit a public OST site daily for six months before receiving take-home doses, was reported as a barrier by PWUD and community representative. Limited number of OST sites in Kyiv leads to long commute for many potential clients, representing another barrier. Therefore, many PWUD preferred to buy prescriptions for methadone from private providers, who are much more geographically accessible.

According to the qualitative data, as the access to drugs decreased, many people tried to reduce the frequency of drug use, and some drug users even tried to quit using drugs through rehabilitation. Despite all structural barriers, according to the information from the DU community, very rarely PWID successfully quit using drugs. Only one qualitative interview participant reported that when there was no money to buy drugs, he entered rehab with 12-Step program in May and since that time has "*kept sober*", having completely quit using opioids. As he reported, "*the epidemic helped him to quit using drugs*" (Male, 37).

4.6 Trends in overdoses

There was no major increase or decrease in the number of overdoses experienced by the cohort participants that would correlate with the trends in corresponding drug use. The total reported number of overdoses experienced in each two-week assessment period varied from 0 to 5 (Figure 19).

Figure 19. Number of overdoses experienced in two weeks prior to each assessment by cause



Qualitative results:

The qualitative interview participants suggested that in their practice they observed a notable increase in overdoses during the first months of the lockdown and in May in particular. The narcologist mentioned that only among the patients of the Sociotherapy Clinic in Kyiv, 4 people died from an overdose in April-May. According to the community representative, in Dnipro, a city with similar to Kyiv drug scene, eleven overdoses were reported among the clients of HR sites in May, 4 of which were fatal. The harm reduction provider reported that his colleagues in other regions were observing an increased number of overdoses allegedly caused by street methadone in August. The respondents-narcologists associate these overdoses with unknown purity of drugs bought through dead drops from new dealers. PWUD associated overdose incidence mostly with mixing methadone with alcohol. "*Several my friends died of overdose during this lockdown. They added alcohol to this street methadone, that's why.*" (Male, 51).

5 CONCLUSIONS

The triangulation of findings from all three components of the study with other available data sources leads to the following conclusions. In the initial phase of the lockdown, March-April 2020, many PWUD faced disruptions in access to their drugs of choice via usual sources. This was primarily related to the closure of public transportation, loss of income, and increased visibility to the police. A minority of PWUD reported a decrease in purity of their main drug or increased prices. In May-June, the society continued to adapt and the lockdown measures were gradually revoked. This led to stabilization of the drug scene and returning of usual patterns. The proportion of participants reporting decreasing access to their drug of choice was minimal starting since June.

We observed a major shift in opioid use that remained in place until the end of the study. The use of illicit methadone, the most commonly used injecting drug in the past several years in Kyiv, decreased from 70% in the past 14 days prior to lockdown to 50% in the last interview round. At the same time, the use of prescription methadone tablets purchased by PWUD in pharmacies went up from 12% in March to almost 40% in June and with some fluctuation remained at that level since then. The practice of issuing prescriptions for methadone or buprenorphine by private medical providers for a fee, legally framed as "detoxification", was not regulated in terms of quality standards by any normative document at the time of the study. Due to the obvious advantages for clients, namely the anonymity, absence of supervision of medication use, and possibility of illegal income from reselling, this service gained unprecedented popularity in Kyiv and other large cities of Ukraine. A significant amount of medications obtained by prescription was resold to other PWUD. Despite the fact that prescription methadone was often used orally, the lack of clinical assessment and supervision when the patient is not stabilized creates a possibility of overdose and increases severity of opioid dependence.

The main injection risk behavior, syringe sharing, was not very prevalent (at 10-15% in the past 14 days) and did not change significantly during duration of the study, even though the

availability of clean syringes for each injection was lower at in the initial period of the epidemic. Sharing of other tools like containers or cottons was more frequent (up to 27%), and decreased during the observation period, possibly due to the decreased use of illicit methadone.

The majority of PWUD obtain syringes from pharmacies, and lockdown restrictions contributed to the lower availability of clean syringes in the beginning of the epidemic. Other reports indicate that harm reduction programs remained an important source of sterile injection equipment and other services for PWUD for more than a half of participants throughout the study. Of those who used services of harm reduction programs, about a third experienced reduced access to services in April, which was then quickly restored by May (Figure 17). Harm reduction providers made significant efforts to adapt services to the epidemic context. The increased use of mobile clinics, outreach and condom vending machines helped to sustain coverage of PWUD with clean syringes, condoms, HIV testing and counseling.[32]

The reduced access to OST programs, leading to the slowdown of new patient enrolment nationally and decrease in OST coverage in our cohort in Kyiv, can be explained by several factors. First, the lockdown restrictions such as closure of public transportation could reduce physical accessibility of the OST programs and lead to dropout. To mitigate that, the OST providers were instructed to transfer patients on take-home administration, to reduce the risk of COVID-19 transmission. Admission of new patients was complicated by the new requirement to undergo testing for SARS-CoV-2 at their own expense. Lastly, the growing availability and use of paid prescriptions for methadone and buprenorphine could prevent PWUD from going (back) to the public OST clinic. It has to be noted, however, that overall OST coverage in Kyiv and Ukraine increased over the six month duration of the study,[31] although the pace of scale up has been slower than needed to reach the ambitious targets of the National Strategy.[33]

The findings of this study have a number of important public health implications. Access to illicit drugs, sterile injection equipment and health services for PWUD may again be affected if the lockdown is introduced in response to the continuing COVID-19 pandemic or other possible global health emergencies. To mitigate the potential health risks, harm reduction programs should use the lessons learned and roll out the best practice models to ensure uninterrupted access to key services, such as provision of sterile needles and syringes, overdose prevention, and HIV testing and treatment. The public OST program should be decentralized to a larger network of health care institutions to achieve better geographic availability, programme coverage and to reduce the risk of dropout in case of transportation closure. The shift to take home provision of OST medications is an effective measure to prevent dropout and transmission of SARS-CoV-2, and should continue to be used widely until the pandemic is under control. The practice of issuing prescriptions for OST medications by private physicians does not aim to achieve OST treatment goals and poses health risks. The recently approved Standards of care for opioid use disorders[30] should be enforced to minimize this practice.

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6 ANNEX

Table. Significance of trend in selected indicators. Results from the mixed effect models adjusted for duration of drug use, sex, and OST experience.

Outcomes	Predictors	Coef.	Standard error	p-value	aOR (95% CI)
Illicit methadone use	Duration of drug use	0.04	0.12	0.715	1.0 (0.8-1.3)
	Sex (male vs. female)	-4.59	1.87	0.014	0.0 (0.0-0.4)
	Lifetime OST exposure	-3.39	1.94	0.080	0.0 (0.0-1.5)
	Assessment number	**-0.22**	**0.05**	**0.000**	**0.8 (0.7-0.9)**
Medical methadone use	Duration of drug use	0.02	0.10	0.860	1.0 (0.8-1.2)
	Sex (male vs. female)	-2.00	1.82	0.272	0.1 (0.0-4.8)
	Lifetime OST exposure	5.90	2.09	0.005	3.6E+2
	Assessment number	**0.08**	**0.04**	**0.058**	**1.1 (1.0-1.2)**
Alcohol use	Duration of drug use	-0.14	0.07	0.032	0.9 (0.8-1.0)
	Sex (male vs. female)	0.11	1.01	0.913	1.1 (0.2-8.1)
	Lifetime OST exposure	-1.10	0.98	0.260	0.3 (0.0-2.3)
	Assessment number	**-0.09**	**0.04**	**0.007**	**0.9 (0.8-1.0)**
Medical methadone injecting use	Duration of drug use	-0.35	0.17	0.043	0.7 (0.5-1.0)
	Sex (male vs. female)	1.18	2.37	0.617	3.3 (0.0-339.2)
	Lifetime OST exposure	-3.31	2.30	0.149	0.0 (0.0-3.3)
	Assessment number	**-0.12**	**0.08**	**0.144**	**0.9 (0.8-1.0)**
Illicit methadone obtained from dead drops	Duration of drug use	0.12	0.12	0.287	1.1 (0.9-1.4)
	Sex (male vs. female)	-3.83	1.93	0.048	0.0 (0.0-1.0)
	Lifetime OST exposure	-0.24	1.98	0.905	0.8 (0.0-38.3)
	Assessment number	**-0.32**	**0.08**	**0.000**	**0.7 (0.6-0.8)**
Price becoming more expensive	Duration of drug use	-0.02	0.05	0.686	1.0 (0.9-1.1)
	Sex (male vs. female)	-0.43	0.81	0.595	0.7 (0.1-3.2)
	Lifetime OST exposure	0.79	0.77	0.301	2.2 (0.5-9.9)
	Assessment number	**-0.21**	**0.05**	**0.000**	**0.8 (0.7-0.9)**
Access to substances becoming harder	Duration of drug use	0.09	0.05	0.089	1.1 (1.0-1.2)
	Sex (male vs. female)	-0.05	0.75	0.948	1.0 (0.2-4.2)
	Lifetime OST exposure	0.68	0.71	0.342	2.0 (0.5-8.0)
	Assessment number	**-0.42**	**0.07**	**0.000**	**0.7 (0.6-0.8)**
Harm reduction access becoming worse	Duration of drug use	0.00	0.05	0.985	1.0 (0.9-1.1)
	Sex (male vs. female)	0.27	0.83	0.747	1.3 (0.3-6.6)
	Lifetime OST exposure	1.23	0.75	0.103	3.4 (0.8-15.0)
	Assessment number	**-0.20**	**0.05**	**0.000**	**0.8 (0.7-0.9)**
Being on OST	Duration of drug use	0.03	0.14	0.817	1.0 (0.8-1.4)
	Sex (male vs. female)	-0.80	2.10	0.704	0.5 (0.0-27.5)
	Lifetime OST exposure	10.04	2.64	0.000	2.3E+4
	Assessment number	**-0.20**	**0.07**	**0.007**	**0.8 (0.7-0.9)**
Syringe sharing	Duration of drug use	-0.11	0.05	0.029	0.9 (0.8-1.0)
	Sex (male vs. female)	0.32	0.79	0.690	1.4 (0.3-6.5)
	Lifetime OST exposure	0.59	0.73	0.419	1.8 (0.4-7.6)
	Assessment number	**0.04**	**0.05**	**0.363**	**1.0 (1.0-1.1)**
Injection tools sharing	Duration of drug use	-0.18	0.07	0.016	0.8 (0.7-1.0)
	Sex (male vs. female)	-0.60	1.01	0.551	0.5 (0.1-4.0)
	Lifetime OST exposure	-0.76	0.97	0.434	0.5 (0.1-3.1)
	Assessment number	**-0.15**	**0.05**	**0.004**	**0.9 (0.8-1.0)**
Always having a new syringe for injection	Duration of drug use	0.25	0.10	0.012	1.3 (1.1-1.6)
	Sex (male vs. female)	-0.28	1.31	0.832	0.8 (0.1-9.9)
	Lifetime OST exposure	-1.87	1.26	0.136	0.2 (0.0-1.8)
	Assessment number	**0.14**	**0.05**	**0.009**	**1.2 (1.0-1.3)**