JOINT ACTION ON HIV AND CO-INFECTION PREVENTION AND HARM REDUCTION

# Epidemiological Research to Estimate the Number of High Risk Drug Users in Lithuania

RESEARCH REPORT

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# Executive Summary

In Lithuania, high-risk drug use has been dominated by injecting of heroin since about 2000. Newly diagnosed HIV cases among people who inject drugs (PWID) have peaked in 2002 and 2009 and drug-related deaths have been on increase. A limited provision of harm reduction interventions has been reported. In order to assess the coverage of NSPs and OST, up-to-date estimates of high-risk drug users (HRDU) and PWID were needed.

Indirect prevalence estimation methods (HIV- and mortality multiplier, capture-recapture, truncated Poisson and multivariate indicator method) were used to obtain annual estimates of the population of high-risk drug users in Lithuania in 2015/2016. The coverage of NSPs and OST (number of syringes per injector per year and percentage of opioid users in substitution programs in each year) was estimated, using service data.

Between 8 371 and 10 474 PWID and between 4 854 and 12 444 high-risk opioid users (HROU) were estimated in Lithuania in 2015/2016. This constitutes around 4.4-5.3 PWID and around 2.5-6.5 HROU per 1 000 population aged 15-64. An average PWID in Lithuania obtained 19-29 syringes via needle and syringe programs (NSP) in 2015 or 2016 and 9.9-25.5% of HROUs were in opioid substitution treatment (OST) in the study period.

In conclusion, the current prevalence of high-risk drug use in Lithuania is comparable to other European countries (or, for injecting drug use it is above average), but the coverage of NSPs and OST services in this population is lower than in most countries of the EU and warrants further investment/development.

## List of abbreviations

CRM – capture-recapture method

HM – HIV multiplier (method)

HRAU – high risk amphetamine use

HRAUs – high risk amphetamine users

HRDU – high risk drug use

HRDUs – high risk drug users

HROU – high risk drug use

HROUs – high risk drug users

PWID – people who use drugs

MM – mortality multiplier (method)

MIM – multivariate indicator method

NSP – needle-syringe programs

OST – opioid substitution treatment

TP – Truncated Poisson (method)

# Section 1. Background

Estimates of high-risk drug use prevalence indicate the extent of the drug problem and provide the necessary information for monitoring of the phenomenon. High-risk drug use estimates can be used as denominators or multipliers for further analyses and studies. For instance, such denominators are used in studies assessing the coverage of interventions such as drug treatment and harm reduction. This is particularly helpful in the planning of appropriate services. Indirect methods using statistical extrapolations are the most used methods to estimate total populations with high-risk drug use including hidden populations and are in general, for this purpose, considered more reliable than surveys(1). The European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) recommends that countries produce such estimates at least every three years, but ideally biannually. Some countries produce estimates annually.

Despite this, the most recent Lithuanian estimate of prevalence of problem drug use dates back to the year 2007, i.e. is now approximately ten years old.

The present study took place within the Joint Action on HIV and Co-infection Prevention and Harm reduction project (HAREACT) funded by the European Commission. This study aimed at constructing more recent high-risk drug use prevalence estimates, taking into account the drug epidemiological situation in Lithuania and the need to inform policy-making, especially in terms of treatment need and the need for harm-reduction interventions as means of HIV prevention.

## Drug epidemiological situation in Lithuania (prevalence and patterns of drug use)

Similarly, to most former Soviet Union (fSU) and Scandinavian countries, the "big picture" of drug use in Lithuania is characterised by relatively low level of low-frequency (or, "recreational") drug use in the general population compared to the rest of the European Union (EU) in case of cannabis, cocaine and MDMA, and comparable or higher levels of amphetamines use. However, focusing on the youngest age groups surveyed, according to the ESPAD[1] study, 15-16 years old Lithuanians were quite close to the European average; even slightly above the average in all categories of surveyed drug, alcohol and tobacco use except for self-reported alcohol use in the last 30 days, which was much lower in Lithuania than the average of the surveyed countries (2).

However, more intensive forms of drug use often follow their own course in terms of prevalence and there is no direct relationship between the indicators "drug use in the general population" and "problem drug use". Older studies placed Lithuania at the lower bound of the prevalence spectrum across Europe with the rate of below three cases (2.4) per 1000 population aged 15-64 based on Lithuanian estimate of "problem drug use" (mainly opioids use or poly-drug use) from 2007 (3).

Lithuania was one of the EU countries where the "heroin epidemic" struck among the last, even later than in some "newer" EU member states which joined the EU in 2004. By many indicators (overdose deaths, treatment demand, etc.), the first peak of problems related to heroin and other opioids was observed around the year 2000, similarly to Latvia, Estonia and non-EU countries to the east of the Baltic states. Unfortunately, HIV infections related to intravenous drug use were soon spread in the country too, with a first peak in 2002 (a year later than in Estonia and Latvia), second peak in 2009 and an on-going, though possibly decreasing, transmission to date(4). In 2002, a rapid increase in the number of HIV diagnoses in Lithuania was observed due to HIV outbreak in Alytus prison (299 new HIV cases in prison where drug use was recognised as the main mode of transmission). During the whole HIV

[1] The European School Survey Project on Alcohol and Other Drugs

reporting period (1988-to date) in Lithuania, 61.5% of all HIV diagnoses were registered among IDUs. Since 2004, HIV has spread mainly via injecting equipment in the IDUs population (5).

The available data suggest that the population of more intensive users of drugs who might also experience considerable problems related to their use is mostly composed of opioid users (for the most part, users of street heroin, which was recently found to be diluted by fentanyls). In the latest published report from Lithuania to the EMCDDA (6), heroin users formed almost 90% of all users requesting treatment due to their drug use. Most of these (again, around 90%) injected their drug. Thus, non-injecting heroin use is present in the Lithuanian drug scene too. According to anecdotal evidence, this could be in the beginning of their drug using career. There is no evidence of long-term heroin users who do not inject. There exist also high-risk amphetamine use but indications are that many, especially the more intensive ones and injectors, might be using opioids as well (7). In a 2016 data set of treatment episodes funded by public insurance (SVEIDRA), requests for treatment due to amphetamines formed 1.5% of all treatment episodes. Altogether, looking at first treatment episode of persons treated in 2016, there were 122 individuals who asked for treatment due to amphetamines. There were almost no amphetamine-related deaths in the mortality register of Lithuania in the last two years, and neither these were identified in any other available national-level data source (however, information on the substance/s used is often missing). Only one local data set from Vilnius (police-ordered urine testing) contained a significant number of amphetamines-positive records. There were also few intensive cocaine users in the existing data sources (15 cases in treatment TDI data (8) in 2015, and 12 in 2016 in the SVEIDRA data set; treatments delivered by private medical-care subjects were not included in the SVEIDRA data set). The existing data sources suggest that intensive use of amphetamines and/or cocaine exists, but most importantly for the present study, its prevalence probably cannot be reliably estimated based on the existing data sources.

Therefore, the present study focused on the prevalence of opioid use and injecting drug use, although it was also attempted to obtain estimates of high-risk amphetamines users.

Looking into the characteristics of opioid users, according to the data sources with longest and most consistent trends (drug treatment and mortality, (8, 9)), users are less often female than in the EU on average, apart from treatment, where females form about one fifth with a stable proportion. Also, their mean age is lower than in most EU countries, however, they are following the trend of ageing as elsewhere in the EU. The largest proportion of opioid users is currently in their thirties (according to the treatment and mortality data; the deceased are slightly older than those treated(8, 9)). As mentioned earlier, there are incident cases reported, but there are indications that the incidence rate is relatively low, without any observable "new waves" of heroin or opioids use epidemic.

On 31 December 2015, there were 596 individuals in opioid substitution treatment (OST) and 200 630 syringes were distributed to users through needle and syringe programmes (NSPs). In the same year, there were 12 low-threshold units, including three mobile outreach needle/syringe distribution and exchange points, operating in nine cities in Lithuania(6). Moreover, syringes are available for purchase in pharmacies. In a 2014 study, 58% injectors were (also) buying syringes from pharmacies, while 65% were acquiring them from NSPs (10). There are neither drug consumption rooms nor diamorphine programmes available in Lithuania. Take-home naloxone programmes for the prevention of opioid overdose deaths are available but limited. There is neither substitution treatment nor NSPs in prisons.

The study detailed in this report aimed to obtain (i) up-to-date prevalence estimates of HRDU (PWID and HROU) at the national and sub-national level, and (ii) the current coverage of OST and NSP programs in the HRDU population.

## Data sources and methods

All descriptions and issues pertaining to data sources and methodology can be found in Annex 1 to this report.

# Section 2: National estimates

## Estimates of populations with high-risk opioid use (HROU)

### Mortality Multiplier (MM)

In 2016,102 people died of opioid overdose (as identified in death certificates recorded in the data set of the Lithuanian Institute of Hygiene). The application of the mortality multiplier method yielded an estimate of 6 543 opioid users in the year 2016, with a confidence interval of 4 454 – 10 851 persons[2].

In 2015, between 109 opioids-poisoning-related deaths were identified. Using the calculated mortality rate (in Annex 1), the estimate was 6 296 of probably injecting opioid users in the year 2015. The corresponding confidence limits were 4 760 – 11 596.

#### *Sensitivity analyses*

The mortality multiplier is generally known to be more applicable to injecting opioid users because benchmark (users who died of opioid overdose) is likely to be composed almost exclusively of opioid injectors, given the dramatic difference in risk of overdose between injecting and non-injecting use of opioids (11, 12).

According to the Treatment Demand Indicator data, 87.2% of opioid users who were asking for treatment in 2015, injected their substance (8). Assuming that the obtained estimates formed 87.2% of the total population of opioid users, injectors and non-injectors, the 100% can be easily calculated. Thus, in 2016, the estimated number of all opioid users (injecting and non-injecting) was estimated to be 7 503 persons (5 108 – 12 444) and in the year 2015, this was 7 220 (5 459 – 13 298).

Another known possible source of uncertainty in the performed calculations comes from an estimate of the proportion of overdose deaths out of all recorded mortality among those treated under the public health insurance system to obtain the overdose mortality rate (detailed calculations can be found in Annex 1). As this was not known, the proportion found in a pooled analysis of mortality cohort studies from EU countries was used. This was 34.9% (13). However, an earlier publication based on a similar analysis suggested that the proportion varied by study markedly and ranged from 14.9% to 63.6%, with 70% of studies ranging from 33.1% to 54% (14). Thus, in a second sensitivity analysis, we have applied the extremes of an interval of values of 70% studies, in order to avoid outliers (which have a higher chance to be unreliable figures due to artefact in the data or similar). Should these be used as basis for calculation of the overdose mortality rate, the results could range from 1.52% to 2.48%. The lower limit of this range was included in the confidence interval for the overdose mortality rate in Lithuania. The higher proportion would have led to a lower overall estimate (namely 4 113 in 2016 and 4 395 in 2015), which would have moderately widened the confidence intervals obtained for the above estimate.

### Capture-recapture method (CRM)

In the performed two-source CRM, 24 matches were identified (i.e. 24 individuals were found in both data sets – SVEIDRA and drug related deaths - DRD). 1369 individuals were in the 2016 SVEIDRA (national-level data, opioids only). 117 were in the 2016 DRD (national-level data, opioids mentioned in the death certificate). A Table below summarises the obtained results and corresponding confidence

[2] Rates per 1000 inhabitants aged 15-64 as well as the respective population sizes can be found in Tables 9, 10 and 11 at the end of the document.

intervals. About 22-22.6% of the estimated population was observed at the data sources employed in the analysis.

Table 1. Estimates of total population of opioid users from SVEIDRA and DRD data sets (both from 2016), using several two-source capture-recapture estimators

| Estimator | Central estimate | Lower limit of 95% CI based on normal approximation to binomial | Upper limit of 95% CI based on normal approximation to binomial | Lower limit of 95% CI based on the Bootstrap method | Upper limit of 95% CI based on the Bootstrap method |
|---|---|---|---|---|---|
| Lincoln-Petersen | 6 674 | 4 293 | 9 054 | 4 854 | 10 011 |
| Chapman | 6 465 | 4 279 | 8 652 | 4 754 | 9 508 |
| Bailey | 6 462 | 4 257 | 8 667 | 4 751 | 9 502 |

## Estimates of populations of people who inject drugs (PWID)

### HIV Multiplier (HM)

Using 10.75% as the national HIV prevalence and the estimate of people who live with HIV (PLWH) who were infected by intravenous drug use (details can be found in Annex 1), the population of PWID could be estimated to be 13 786 (13 237 - 13 963).

Using 12.5%, the HIV prevalence from the highest quality multi-city study available, the population of PWID could be estimated to be 11 856 (11 384 – 12 008).

These estimates would be best referred to as 2015 estimates because the benchmark was based on the 2015 data and the multipliers are not expected to change dramatically in only few years according to HIV-related data in the country (albeit their use might omit possible significant local HIV infection outbreaks, which were not recorded in the reference period).

### *Sensitivity analysis*

One strong assumption that had to be made in the above HIV multiplier analyses is that all people living with HIV who were infected by intravenous drug use were still current injectors in 2015. However, part of them might have ceased injection, especially after receiving such diagnosis and with the help of effective drug treatment (e.g. opioid substitution treatment programmes).

There exists one study of PLWH in Lithuania; its data collection is dating to a similar period of time to that in the HIV prevalence studies above - 2012-2013 (15). From the 127 PLWH involved in the study, 76.4% had been infected by intravenous drug use and 39.3% self-reported last month drug use (there was no data on injecting or last year drug use). If all drug use took place among those infected by injecting drug use, just over half (51.4%) of these respondents would be continued drug user and, potentially, injectors. However, some individuals might have injected earlier in the last year and thus might still be current injectors. As this was a small study relying on self-report, we used the results (approx. 50 %) as an upper limit of PLWH infected by intravenous drug use who did not inject in the last month.

Table 2 below summarises the adjusted estimates from the performed sensitivity analysis assuming 10%, 25% and 50% as rates of cessation of current injection.

Table 2. Results of sensitivity analysis assuming various rates of PLWH who ceased current injection (2015 estimates).

| Rates of cessation of current injecting applied in the sensitivity analysis | 10.75% HIV prevalence | | | 12.5% HIV prevalence | | |
|---|---|---|---|---|---|---|
| 10% not currently injecting | 12 409 | 11 926 | 12 567 | 10 672 | 10 256 | 10 808 |
| 25% not currently injecting | 10 344 | 9 926 | 10 474 | 8 896 | 8 536 | 9 008 |
| 50% not currently injecting | 6 893 | 6 619 | 6 981 | 5 928 | 5 692 | 6 004 |

**Multivariate Indicator Method (MIM)**

The estimates of PWID obtained by means of the multivariate indicator method, for the 60 municipalities of Lithuania can be found in the table below.

Table 3. Estimated populations of PWID by Multivariate Indicator Method in Lithuanian municipalities.

| Municipality name | Estimated PWID | Estimated 95% CI | | Anchor point |
|---|---|---|---|---|
| Akmenė d. mun. | 24.67 | 12.86 | 36.49 | |
| Alytus d. mun. | 20.56 | 10.72 | 30.41 | |
| Alytus t. mun. | 131.60 | 68.58 | 194.62 | 100 |
| Anykščiai d. mun. | 8.22 | 4.29 | 12.16 | |
| Birštonas mun. | 8.22 | 4.29 | 12.16 | |
| Biržai d. mun. | 20.56 | 10.72 | 30.41 | |
| Druskininkai mun. | 94.59 | 49.29 | 139.88 | |
| Elektrėnai mun. | 57.57 | 30.00 | 85.15 | |
| Ignalina d. mun. | 28.79 | 15.00 | 42.57 | |
| Jonava d. mun. | 135.71 | 70.72 | 200.70 | |
| Joniškis d. mun. | 12.34 | 6.43 | 18.25 | |
| Jurbarkas d. mun. | 37.01 | 19.29 | 54.74 | |
| Kaišiadoriai d. mun. | 37.01 | 19.29 | 54.74 | |
| Kalvarija mun. | 16.45 | 8.57 | 24.33 | |
| Kaunas c. mun. | 645.66 | 336.47 | 954.85 | 802 |
| Kaunas d. mun. | 119.26 | 62.15 | 176.37 | |
| Kazlų Rūda mun. | 0.00 | 0.00 | 0.00 | |
| Kėdainiai d. mun. | 156.27 | 81.44 | 231.11 | |

| | | | | |
|---|---|---|---|---|
| Kelmė d. mun. | 4.11 | 2.14 | 6.08 | |
| Klaipėda c. mun. | 477.04 | 248.61 | 705.49 | 1425 |
| Klaipėda d. mun. | 32.90 | 17.15 | 48.65 | |
| Kretinga d. mun. | 24.67 | 12.86 | 36.49 | |
| Kupiškis d. mun. | 24.67 | 12.86 | 36.49 | |
| Lazdijai d. mun. | 16.45 | 8.57 | 24.33 | |
| Marijampolė mun. | 53.46 | 27.86 | 79.06 | |
| Mažeikiai d. mun. | 65.80 | 34.29 | 97.31 | |
| Molėtai d. mun. | 78.14 | 40.72 | 115.56 | |
| Neringa mun. | 0.00 | 0.00 | 0.00 | |
| Pagėgiai mun. | 12.33 | 6.43 | 18.25 | |
| Pakruojis d. mun. | 8.22 | 4.29 | 12.16 | |
| Palanga t. mun. | 24.67 | 12.86 | 36.49 | |
| Panevėžys d. mun. | 41.12 | 21.43 | 60.82 | |
| Panevėžys c. mun. | 250.86 | 130.73 | 370.99 | |
| Pasvalys d. mun. | 28.79 | 15.00 | 42.57 | |
| Plungė d. mun. | 24.67 | 12.86 | 36.49 | |
| Prienai d. mun. | 32.90 | 17.15 | 48.65 | |
| Radviliškis d. mun. | 32.90 | 17.15 | 48.65 | |
| Raseiniai d. mun. | 20.56 | 10.72 | 30.41 | |
| Rietavas mun. | 0.00 | 0.00 | 0.00 | |
| Rokiškis d. mun. | 49.35 | 25.72 | 72.98 | |
| Šakiai d. mun. | 41.12 | 21.43 | 60.82 | |
| Šalčininkai d. mun. | 94.59 | 49.29 | 139.88 | |
| Šiauliai c. mun. | 180.95 | 94.30 | 267.60 | |
| Šiauliai d. mun. | 41.12 | 21.43 | 60.82 | |
| Šilalė d. mun. | 8.22 | 4.29 | 12.16 | |
| Šilutė d. mun. | 37.01 | 19.29 | 54.73 | |

| | | | | |
|---|---|---|---|---|
| Širvintos d. mun. | 16.45 | 8.57 | 24.33 | |
| Skuodas d.mun. | 0.00 | 0.00 | 0.00 | |
| Švenčionys d. mun. | 69.91 | 36.43 | 103.39 | |
| Tauragė d. mun. | 32.90 | 17.15 | 48.65 | |
| Telšiai d. mun. | 102.81 | 53.58 | 152.05 | |
| Trakai d. mun. | 102.81 | 53.58 | 152.05 | |
| Ukmergė d. mun. | 82.25 | 42.86 | 121.64 | |
| Utena d. mun. | 41.12 | 21.43 | 60.82 | |
| Varėna d. mun. | 61.69 | 32.15 | 91.23 | |
| Vilkaviškis d. mun. | 37.01 | 19.29 | 54.74 | |
| Vilnius c. mun. | 3643.67 | 1898.83 | 5388.51 | 3493 |
| Vilnius d. mun. | 378.35 | 197.17 | 559.53 | |
| Visaginas mun. | 111.04 | 57.87 | 164.21 | |
| Zarasai d. mun. | 20.56 | 10.72 | 30.41 | |

The fit of the linear regression model was good with R square of 0.936 (adjusted R square of 0.915), F=44.166 and p=0.007.

Sum of the estimates by municipalities was 7962 (6845 - 9079). Adding up estimates by municipalities with anchor points (four original estimates) results in a PWID prevalence estimate of 8868 PWID in Lithuania (8 371 – 9 364) in 2016[3].

## Estimates of populations with high-risk amphetamines use (HRAU)

A preliminary estimate of high-risk users of amphetamines (who primarily use amphetamines and don`t use opioids) was obtained.

Applying an inverted proportion of treated users living outside of Vilnius to Vilnius estimates of high-risk amphetamines use (see below) resulted in an estimated population of high-risk amphetamines users of 4 742 – 7 000 in 2016 and 4 795 – 6345 in 2015.

## Synthesis of national estimates

Concerning the HROU estimates, both used methods were considered methodologically and statistically approximately equal. The sensitivity analysis of the mortality multiplier (2015 and 2016) resulted in annual estimates of 7 220 and 7 503 users with wide intervals, ranging between 5 108 (or even 4 113 according to one sensitivity analysis) and 13 298 individuals (see Table 9); the intervals overlapped at 5 459-12 444 HROU. The two-source capture-recapture method estimates (2016) calculated by three estimators had their midpoints ranging from 6 462 to 6 674 individuals. Their confidence intervals overlapped between 4 854 and 8 652 HROU.

[3] Alytus anchor point was based on 2015 data, but all other anchor points and the distribution of patients according to municipalities was based on 2016 data. Thus, this estimate is best interpreted as 2016 estimate.

As regards PWID, an estimated number by multivariate indicator method was 8 868 (8 371 – 9 364) in 2016. For 2015, a different set of data was available such that allowed for the use of HIV multiplier method. While the sensitivity analysis for 2015 yielded a wide range of estimates (6 004-12 409 PWID), the available evidence seemed most in support of the 25% of injecting-infected people living with HIV having not injected in 2015 – 25% is the mid-point between the 51.4% self-reported abstinence from drugs in the past month (15) and the anecdotal evidence from drug service staff in Lithuania that among HIV positive individuals who continue to frequent harm-reduction services, injecting cessation is rather low. This proportion yielded between 8 536 and 10 474 PWID in Lithuania in 2015. As a range obtained by the two methods, the annual prevalence of PWID was estimated to be between 8 371 and 10 474 individuals in 2015-2016.

The corresponding prevalence rates were about 2.5-6.5 HROU and about 4.4-5.3 PWID per 1000 population in Lithuania aged 15-64.

## Section 3: Sub-national estimates

### Vilnius

#### Estimates of populations with high-risk opioid use (HROU)

***Mortality multiplier (MM)***

68 persons died in larger Vilnius where opioid use or dependence was mentioned on the death certificate. Out of them, 55 died from opioids overdose. Using the annual overdose mortality rate in Lithuania - 1.62% (0.94% - 2.29%) (see Annex 1), this gives an estimate of 3 395 (2 402- 5 851) opioid users in Vilnius in 2016[4].

Sensitivity analysis

Given the fact that mortality multiplier generally gives an estimate closer to injecting opioid use, an additional analysis was performed to extrapolate the results to non-injecting opioid users. According to the Treatment Demand Indicator data set, 87.2% of opioid users asking for treatment inject their substance. This leads to an extrapolation of 3 893 (2 755 – 6 710) injecting and non-injecting opioid users in Vilnius in 2016.

***Capture-recapture method (CRC)***

**A) Drug-related deaths, urine testing and court-ordered treatment data**

Log-linear models were fit. The results are summarised in Table 4.

Table 4. Results of log-linear models based on drug-related deaths, police-referred urine testing and court-ordered treatment data (2016).

| Model | df | Missing cell est. | Low | High | P | G2 | AIC | BIC |
|---|---|---|---|---|---|---|---|---|
| p1p2p3 | 3 | 1788 | 1020 | 3137 | 0.524 | 2.238 | -3.762 | 4.456 |
| p1p2p3 p1*p3 | 2 | 1674 | 954 | 2940 | 0.856 | 0.311 | -3.689 | 1.214 |

[4] Rates per 1000 inhabitants aged 15-64 as well as the respective population sizes can be found in Tables 9, 10 and 11 at the end of the document.

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| p1p2p3 p1*p2 | 2 | 1634 | 668 | 3992 | 0.337 | 2.175 | -1.825 | 3.078 |
| p1p2p3 p2*p3 | 2 | 2076 | 1017 | 4239 | 0.422 | 1.723 | -2.277 | 2.626 |
| p1p2p3 p1*p3 p1*p2 | 1 | 1361 | 556 | 3328 | 1.000 | 0 | -2 | 0.228 |
| p1p2p3 p1*p3 p2*p3 | 1 | 1884 | 922 | 3847 | 1.000 | 0 | -2 | 0.228 |
| p1p2p3 p2*p3 p1*p2 | 1 | na | na | Na | 0.562 | 0.336 | -1.664 | 0.564 |

Explanation: p1 DRD, p2 urine testing, p3 probation

According to the Akaike Information Criterion (AIC), the best model would be "the independence model". It is also logical theoretically, as there should be little or no interaction between dying of opioid overdose, being sent by police for urine testing and having a court-ordered treatment. However, this model has the highest Bayes Information Criterion (BIC). The second model, with an interaction between drug related deaths and court-ordered treatment has a better balance between the two indices. In any case, both models gave very similar estimates whose confidence intervals overlap significantly (which applies to most fitted models).

We can thus conclude that around 1 674 opioid users (954 – 2940) are missing from the observations made by the three data sources used in this estimation procedure. From that it follows that together with the 409 observed cases, there should be about 2 083 HROUs in larger Vilnius (1 363 – 3 349).

### B) SVEIDRA, police-referred urine testing and court-ordered treatment/probation data

Log-linear models were fit. The results are summarised in Table 5.

Table 5. Results of log-linear models based on **SVEIDRA, police-referred urine testing and court-ordered treatment/probation data.**

| Model | df | Missing cell est. | Low | high | P | G2 | AIC | BIC |
|---|---|---|---|---|---|---|---|---|
| p1p2p3 | 3 | 815 | 652 | 1018 | <0.001 | 23.255 | 17.255 | 25.473 |
| p1p2p3 p1*p3 | 2 | 925 | 732 | 1169 | 0.012 | 8.851 | 4.851 | 9.754 |
| p1p2p3 p1*p2 | 2 | 316 | 141 | 704 | <0.001 | 16.397 | 12.397 | 17.300 |
| p1p2p3 p2*p3 | 2 | 837 | 667 | 1049 | <0.001 | 21.097 | 17.097 | 22.000 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| p1p2p3<br>p1*p3<br>p1*p2 | 1 | na | Na | Na | 0.015 | 5.860 | 3.860 | 6.0884 |
| p1p2p3<br>p1*p3<br>p2*p3 | 1 | 957 | 754 | 1216 | 0.012 | 6.296 | 4.296 | 6.5244 |
| p1p2p3<br>p2*p3<br>p1*p2 | 1 | 338 | 143 | 799 | <0.001 | 16.202 | 14.202 | 16.430 |

Explanation: p1 SVEIDRA, p2 urine testing, p3 probation

In the case of SVEIDRA, urine testing and probation data, which were matched by and reduced to solely date of birth and gender, the model with the lowest AIC and BIC indices is actually a model which gives completely off-the-scale estimates (in billions). This is probably the result of over-fitting. The second-best model with estimates of the missing cell of 957 (754-1 216) is with interactions between SVEIDRA and court-ordered treatment and urine testing and court-ordered treatment. As there is no reason to believe that police-ordered urine testing should in any way depend/be dependent upon appearing in the SVEIDRA data set of treatments covered from the public health insurance, we chose a model, which is third best according to the indices, but it is more logical, suggesting only an interaction between SVEIDRA and court-ordered treatment (with the missing cell estimates of 925, 732 - 1 169). It may happen that people in court-ordered treatment will be covered from public health insurance and thus appear also in this data source or that a compulsory treatment brings a person closer to other health care services which will be covered from public health insurance. In any case, the second best and third best models have very similar results.

We can thus conclude that according to this estimation procedure, together with 979 individuals identified in the used data sources, we estimate 1 904 opioid users in greater Vilnius, ranging from 1 711 to 2 148.

### C) SVEIDRA drug treatment modalities used as separate data sources

Log-linear models were fit. The results are summarised in Table 6.

Table 6. Results of log-linear models based on **using treatment modalities in SVEIDRA as separate data sources.**

| Model | df | Missing cell est. | Low | high | P | G2 | AIC | BIC |
|---|---|---|---|---|---|---|---|---|
| p1p2p3 | 3 | 108 | 87 | 134 | <0.001 | 65.554 | 59.554 | 67.772 |
| p1p2p3<br>p1*p3 | 2 | 193 | 147 | 253 | <0.001 | 31.838 | 27.838 | 32.741 |
| p1p2p3<br>p1*p2 | 2 | 86 | 68 | 108 | <0.001 | 27.865 | 23.865 | 28.768 |
| p1p2p3<br>p2*p3 | 2 | 91 | 66 | 125 | <0.001 | 63.273 | 59.273 | 64.176 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| p1p2p3<br>p1*p3<br>p1*p2 | 1 | 139 | 103 | 187 | 0.014 | 6.037 | 4.037 | 6.265 |
| p1p2p3<br>p1*p3<br>p2*p3 | 1 | 928 | 327 | 2639 | <0.001 | 16.868 | 14.868 | 17.096 |
| p1p2p3<br>p2*p3<br>p1*p2 | 1 | 115 | 84 | 158 | 1 | 0 | -2 | 0.228 |
| p1p2p3<br>p2*p3<br>p1*p2<br><br>p1*p3 | 0 | 406 | 141 | 1164 | na | 0 | 0 | 0 |

Explanation: p1 OST, p2 inpatient treatment, p3 non-OST out-patient treatment

In the case of using drug treatment modalities in SVEIDRA as separate data sources, the model with best AIC and BIC would be the one in the row before last row in the table. However, from the clinical practice, we know that p3 (non-OST outpatient treatment) serves as some kind of waiting modality or preparation modality for entering either inpatient or OST treatment. Thus, the chosen model should reflect this by including an interaction term between OST and p3, and also inpatient treatment and p3. This will be either the saturated model with all two-way interactions or the model including p1*p3 and p2*p3 interaction. We choose to opt for the simpler model giving a missing cell estimate of 928 (327-2 639). This means that the resulting estimate for Vilnius is 1 736 (1 135 – 3 447) opioid users. It is important to mention that this estimate needs a different interpretation from the previous figures. According to the CRC assumptions, these individuals should come from a homogeneous group, i.e. whose members have the same probability of "being captured". Thus, it can be interpreted as individuals who will at some point appear in treatment.

### Estimates of populations of people who inject drugs (PWID)

#### *Truncated Poisson methods (TPM)*

In the Demetra programme, 468 individuals came only once to the programme, while 216 were seen by the programme twice. An average number of visits per client was 7.048, very close to the estimated parameter $\theta$_hat, which was 7.042, indicating a good fit of the Poisson distribution. Zelterman's estimator has returned an estimate of 2 218 PWID (2 201 – 2 236). Chao's estimator has given an estimate of 1 844 PWID with a 95% confidence interval of 1 770 – 1 931.

In the Republican Centre for Addictive Disorders RCAD mobile unit, 1 158 individuals came only once to the programme, while 220 were seen by the programme twice. An average number of visits per client was 1.966, again close to the estimated parameter $\theta$_hat, which was 1.548. Zelterman's estimator has returned an estimate of 5 454 PWID (4 891 – 6 163). Chao's estimator has given an estimate of 4 772 PWID with a 95% confidence interval of 4 433 – 5 152.

It is important to note that the RCAD mobile unit operates at two places and receives a significant number of clients from abroad or other parts of the country. Thus, the distribution of visits was skewed by this. Unfortunately, there is no data as to what proportion of the visits are paid by the "travellers" as opposed to local PWID.

Sensitivity analysis

While the Truncated Poisson estimates from the Demetra programme might be to a certain extent biased downwards (due to stable clients, and clients to some extent limited by the single location of the programme), the RCAD mobile unit estimates are expected to be biased upwards, due to significant inclusion of "travellers" which the programme reports to see, usually from abroad. These individuals will be generally seen only once. Thus, we performed a sensitivity analysis assuming that 400 such "travellers" contacted the programme in the year 2015 (and thus need to be excluded from calculations). If this was the case, the number of one-time visitors of the programme from Vilnius itself would shrink to 758. Estimated population of PWID in Vilnius would thus be 3 007 according to Zelterman estimator (2 979 – 3 250). According to Chao's estimator, this will be 2 630 (2 468 – 2 815). If only 200 visitors would come from such "travellers" population, then the estimates would be 4 138 (3 780 – 4 572) according to Zelterman and 3 610 (3 367 – 3 884) according to Chao.

Another possibility of finding the best estimate of PWID for Vilnius could be a weighted average of the estimates provided by the two programmes – one mobile and open with many one-time clients, the second one more localised and closed with a set of its "loyal" clients. This would, based on the Chao estimator, give an estimate of 3 494 (3 239 – 3 789) PWID. In the case of Zelterman estimator, the weighted average would result in 4 041 PWID.

### High-risk amphetamines users estimates

A preliminary estimate of high-risk users of amphetamines (likely without combination with opioids) was obtained.

#### *Capture-recapture method (CRM)*

The results obtained using combinations of three estimators and two methods to derive confidence intervals are summarised in Table 7. The observed population in relation to the resulting estimates was 9-12% in 2016 and 13-17% in 2015.

Table 7. Results of a Capture-recapture analysis based on data from public drug treatment (SVEIDRA) and police-referred drug testing

| | 2016 | | | 2015 | | |
|---|---|---|---|---|---|---|
| Estimator | Central estimate | Lower and upper limit of 95% CI based on normal approximation to binomial | Lower and upper limit of 95% CI based on the Bootstrap method | Central estimate | Lower and upper limit of 95% CI based on normal approximation to binomial | Lower and upper limit of 95% CI based on the Bootstrap method |
| Lincoln-Petersen | 1 750 | 633 - 2 867 | 700 - Inf | 1 269 | 474 - 2 867 | 544 - Inf |
| Chapman | 1 217 | 100 - 2 334 | 608 - 3 635 | 993 | 198 - 1 788 | 496 - 3 975 |
| Bailey | 1 176 | 37 - 2 315 | 588 - 3 528 | 959 | 130 - 1 787 | 479 - 3 834 |

## Klaipeda

### Estimates of populations with high-risk opioid use (HROU)

*Mortality Multiplier method*

14 people died in the city of Klaipeda due to opioid overdose in 2016. Using the national estimates of annual mortality rate from SVEIDRA data set as in the case of Vilnius, this gives estimates of 864 (611 – 1 489) opioid users for 2016[5].

Sensitivity analysis

Given the fact that mortality multiplier generally tends to give an estimate of injecting opioid use, an additional analysis was performed to extrapolate the results to non-injecting users of opioids. According to the Treatment Demand Indicator data, 87.2% of opioid users asking for treatment inject their substance. This leads to an extrapolation of 991 (701 – 1708) opioid users in Klaipeda in 2016.

### Estimates of populations of people who inject drugs (PWID)

*Truncated Poisson method (TPM)*

At Klaipeda's NSP, 374 individuals came to the programme only once, while 121 were seen by the programme twice. An average number of visits per client was 6.352, very close to the estimated parameter θ_hat, which was 6.341, indicating a good fit of the Poisson distribution. Zelterman's estimator has returned an estimate of 1 778 PWID (1 748 – 1 809). Chao's estimator has given an estimate of 1 425 PWID with a 95% confidence interval of 1 327 – 1 542.

## Kaunas

### Estimates of populations with high-risk opioid use (HROU)

*Mortality Multiplier (MM)*

13 people died in the city of Kaunas due to opioid overdose in 2016. Using the same national estimate of annual overdose mortality rate in Lithuania as in the case of the previous cities, this gives an estimate of 802 opioid users with a confidence interval of 568 – 1 383 cases[6].

Sensitivity analysis

Given the fact that mortality multiplier generally tends to give an estimate of injecting opioid use, an additional analysis was performed to extrapolate the results to non-injecting users of opioids. According to the Treatment Demand Indicator data, 87.2% of opioid users asking for treatment inject their substance. This leads to an extrapolation of 920 (651 – 1 586) opioid users in Kaunas in 2016.

### Estimates of populations of people who inject drugs (PWID)

*Truncated Poisson method*

At Kaunas' NSP, 34 individuals came only once to the programme, while 13 were seen by the programme twice. An average number of visits per client was 22.496, which was equal to the estimated parameter θ_hat, indicating a good fit of the Poisson distribution. Zelterman's estimator has returned an estimate of 249 PWID (248.81 – 248.82). Chao's estimator has given an estimate of 177 PWID with a 95% confidence interval of 158 – 212.

[5] Rates per 1000 inhabitants aged 15-64 as well as the respective population sizes can be found in Tables 9, 10 and 11 at the end of the document.

[6] Rates per 1000 inhabitants aged 15-64 as well as the respective population sizes can be found in Tables 9, 10 and 11 at the end of the document.

## Alytus

### Estimates of populations of people who inject drugs (PWID)

*Truncated Poisson method*

At Alytus' NSP, 16 individuals came only once to the programme, and also 16 were seen by the programme twice. An average number of visits per client was 33.8587, which was equal to the estimated parameter θ_hat, indicating a good fit of the Poisson distribution. Zelterman's estimator has returned an estimate of 106 PWID (106 – 106)[7]. Chao's estimator has given an estimate of 100 PWID with a 95% confidence interval of 96 – 109.

## Section 4. Estimates of coverage

The obtained estimates of prevalence of opioid use and injecting drug use allow us to make certain estimates of the coverage by interventions, although not without assumptions, limitations – and caution needed while interpreting them (see Discussion for more details).

It was estimated by means of the HIV multiplier (HM) method that there were about 8 536 - 10 474 of current injectors in Lithuania in 2015. Given the fact that 200 630 syringes were distributed among people who inject drugs in the country in the same year, the number of syringes per user were most probably in the bracket of 19 to 24 syringes per year.

An estimate by the Multivariate Indicator Method suggested a prevalence of 8 868 (8 371 – 9 364) PWID in Lithuania in 2016. As 240 061 syringes were distributed in 2016 around the country, this would lead to an estimate of 27 (26 - 29) of syringes per user per year.

The mortality multiplier method and further sensitivity analysis suggested that there might be annually between 6 462 and 7 503 HROUs in Lithuania in the years 2015 and 2016 (with confidence intervals ranging from 4 257 to 13 298). As there were up to 1 231 and 1393 persons treated in OST in 2016 and 2015, this leads to estimates of coverage of opioid substitution treatment of 19.3% (10.5-25.5%) of HROU in treatment in 2015 and 16.4% (9.9 --24.1%) in 2016 according to MM-based estimates and 14.2-25.4% in 2016 according to CRC estimates (see Table 8).

Table 8. Summary of NSP and OST coverage estimates

| | Needle and syringe programmes | | Opioid substitution treatment | | |
|---|---|---|---|---|---|
| Target population | People who inject drugs (PWID) | | High risk opioid users (HROU) | | |
| Year | 2015 | 2016 | 2015 | 2016 | |
| Service provision records (no.) | 200 630 | 240 061 | 1393[8] | 1 231[6] | |
| Estimated population | 8 536 - 10 474 | 8 868 (8 371 – 9 364) | 7 220 (5 459 – 13 298) | 7 503 (5 108 – 12 444) | 4 854 - 8 652 |
| Method and interval type | HM, sensitivity analysis interval | MIM, 95% confidence interval | MM, sensitivity analysis interval | MM, sensitivity analysis interval | CRC, overlap of confidence intervals |

[7] Rates per 1000 inhabitants aged 15-64 as well as the respective population sizes can be found in Tables 9, 10 and 11 at the end of the document.

[8] This figure contains double-counts, however, according to anecdotal evidence from RPLC Vilnius, these should be rather few.

| | | | | | |
|---|---|---|---|---|---|
| Coverage (no. of syringes per year per user and % of estimated HROU in OST) | 19 – 24 | 27 (26 – 29) | 19.3% (10.5-25.5%) | 16.4% (9.9 - 24.1%) | 14.2%-25.4% |

## Discussion

In Lithuania, the up-to-now available estimates of prevalence of high-risk drug use were ten years old and therefore it was difficult to understand the present magnitude of the phenomenon as well as coverage of interventions provided to high-risk drug users in order to pursue policy goals, such as HIV prevention.

Therefore, the estimates contained in this report contribute to the knowledge of the phenomenon.

Based on the data available for the years 2015 and 2016, it was estimated that there were between 6 462 and 7 503 HROUs in Lithuania in the years 2015 and 2016 (with confidence intervals ranging from 4 257 to 13 298) and 8 371 - 10 474 of people who inject drugs, according to the present analysis. Lithuania's estimated rate of high-risk opioid use (with central estimates around 3.4-3.9 per 1000 aged 15-64) is slightly higher than the median of other European countries (3.1 per 1000 population) according to the most recent figures (16). The Lithuanian estimate of people who inject drugs (around 4.4-5.3 per 100 aged 15-64), on the other hand, seems higher than the recent figure in two thirds of European countries with available data; 4.9 per 1000 population being the third quartile of the EU data distribution (17). The present study suggests that compared to other Baltic states, Lithuania has lower prevalence rates of HROU, but the confidence intervals of the estimates overlap. Latvia's 2014 study on high-risk opioid use resulted in rates of 4.7 (3.4-7.5) of HROUs per 1000 inhabitants aged 15-64. The prevalence of PWID in other Baltic states is also higher than in Lithuania, although Estonian confidence intervals overlap with the Lithuanian ones. The most recent studies of PWID prevalence in Latvia and Estonia (2012 and 2009) resulted in rates 9.2 (7.3-11.7) and 5.9 (4.3-10.8) people who inject drugs per 1000 inhabitants aged 15-64 (16, 17).

The obtained opioid estimate is lower than the estimate of drug injectors in the same period although confidence intervals of the estimates overlap. Multiple studies show that the mortality multiplier method used to obtain the opioid estimate almost always results in lower estimates than other methods (18). Therefore, its result can be generally interpreted rather as the lower bound of prevalence. In the case of Lithuania though, it is important to take into account the fact that the number of opioid-related poisoning deaths could be overestimated, which could in turn lead to a higher estimate. This is because the benchmark used included all poisoning deaths with the code T40.6 (poisoning with other narcotics). There was anecdotal evidence available that poisonings with new fentanyls will be recorded under this code, but occasionally, other substances, possibly non-opioids, could be included. Thus, type of method used does not fully explain the fact that injecting estimates are higher than opioid estimates. It is also possible that non-opioid injectors exist (in particular, injectors of amphetamines), but their exact prevalence is difficult to assess as they appear in the existing data sources only in small numbers. However, it was possible to obtain a preliminary estimate of population of high-risk amphetamines users. This would be between 4 742 and 7 000 individuals in Lithuania in total, including injecting and non-injecting users of amphetamines. This preliminary estimate has to be interpreted with caution, as the overlap used to calculate it by means of two-source capture-recapture was small and would be sensitive to very small changes in this number, e.g. 1-2 cases. Therefore, the confidence intervals obtained for the Vilnius estimate, which served as a basis for national extrapolation, were very wide. Also, the extrapolation to national level itself required a multiplier of 4 to 5. On the other hand, the results on the national level as well as for Vilnius were consistent between 2015 and 2016. The proportion of injectors among amphetamine users in drug treatment was found to be 26.7% (8), which in combination with the above estimates means around 1 200 to 1 800 amphetamines injectors nationwide. Taking together 6 300 to 6 500 opioids injectors (the results of the mortality multiplier method before sensitivity analysis) and 1 200 to 1 800 amphetamine injectors, adds up to 7 500 – 8 300 injectors, which reaches the lower limit of the obtained estimates of PWID. However, it has to be kept in mind that only 60 amphetamine users and no methamphetamine were treated (8) and it is difficult to assess, how representative these were of the entire population of amphetamines users in the country. Additional studies would be needed to understand what proportion of amphetamines users inject their substance and what is the overlap between opioids use and

amphetamines use. Interestingly, the available PWID estimate from Latvia is also considerably higher than HROU estimate for the same country.

Also, various subnational estimates were obtained, mainly for Vilnius but also for several other cities.

Comparing obtained estimates to the existing data can give a very crude idea of their validity. In the case of national estimates, it seems realistic that there would be approximately 6 462 – 7 503 opioid users in the country, given there were 2 268 opioid users entering treatment in 2015 according to the Treatment Demand Indicator of the EMCDDA. This was confirmed by two-source capture-recapture estimates, which were based on overlapping, but not the same data as the mortality multiplier estimate. Also, an estimate of 8 371 to 10 474 people who inject drugs, seems realistic compared to the count of 3 053 clients who contacted needle and syringe programmes in the country in 2015 and so is the estimate of almost 9 000 people who inject drugs provided by another method. It can also be noted that the ratio between opioid users seeking treatment and people who inject drugs seeking clean needles is almost the same as the ratio between the estimated population of HROU and the estimated population of PWID.

In case of subnational estimates, there are two which "stand out" of the pattern of comparison with other data. Firstly, it is the Kaunas estimate of 177-249 people who inject drugs obtained by the Truncated Poisson method using data from one needle and syringe programme (0.9-1.3 per 1000 inhabitants aged 15-64). This seems to be too low, compared to a mortality multiplier estimate of opioid injectors for the same city and year (802 opioid injectors with a confidence interval of 568 – 1 383 or 4.2, 3.0-7.3 per 1000 inhabitants aged 15-64) and also compared to the treated population in the SVEIDRA data set due to opioid use (125, compared with Klaipeda – 39 and Vilnius city – 732 and Vilnius region - 72) and, similarly, treated population due to combined opioids, amphetamines and polydrug use (157, compared with Klaipeda – 116 and Vilnius city – 886 and Vilnius region - 92). It is likely that the data for the Truncated Poisson estimate came from a small NSP with "loyal" clients and thus this estimate should not be used as representative of the entire city. Also, in the application of Multivariate Indicator Method to estimate national prevalence of injecting drug use, the mortality estimate for Kaunas was used instead of the Truncated Poisson estimate. While it is likely only an estimate of opioid injection, it was still considered closer to the real prevalence of PWID, than the likely underestimated value derived from the needle and syringe program data.

On the other hand, the estimate of people who inject drugs obtained by the Truncated Poisson method for Klaipeda, seems to be a possible overestimate (1 425 by Chao estimator and 1 778 by Zelterman estimator – 14.1 and 17.6 per 1000 inhabitants aged 15-64). On the other hand, the estimate of 864 opioid users, possibly injectors (611 – 1 489), i.e. 8.8 (6.2-15.2) per 1000 inhabitants aged 15-64, by the mortality multiplier method for the same city might be an underestimate if looked at as indicator of injecting prevalence, compared to the fact that there were 847 individual clients using the Klaipeda's NSP's services. One possibility is that there exists a sizeable population of amphetamines injectors in the city. Another possibility is that there could be an artefact in the records of needle and syringe programmes – either a large number of individuals travelling from other places to use the programme services or a number of clients reporting a different personal identifier every time they contact the programme. Also, the population rates produced by the two "off-scale" estimates for Kaunas and Klaipeda are unrealistically low and high.

The estimates for Vilnius referring to years 2015 and 2016 range between less than 2 000 and more than 3 000 opioid users and between less than 2 000 and more than 5 000 people who inject drugs. After careful consideration and a series of sensitivity analyses, we would recommend using the estimate based on mortality multiplier and sensitivity analysis (3 893, 2 755 – 6 710; i.e. 10.6, 7.5-18.2 per 1000 inhabitants aged 15-64) as a conservative (possibly lower) estimate of the prevalence of high-risk opioid use referring to the year 2016. In the case of estimate of prevalence of drug injection, it seems most reasonable to use either the weighted average of the two Truncated Poisson estimates based on two different needle and syringe programmes (Chao: 3 493, 3 239-3 789, Zelterman: 4 041, i.e. 9.4, 8.8-10.2 0r 10.9 per 1000 inhabitants aged 15-64) or the

interval based on sensitivity analysis of the RPLC mobile unit-based estimate, assuming that 200 programme visitors were "travellers" and did not dwell and use drugs in the area for more than a very short period of time (3 610, 3 367-3 884, 4 138, 3 780-4 572, corresponding to 11.2, 10.2-12.4 and 9.8, 9.1-10.5 per 1000 inhabitants aged 15-64). Sensitivity analysis has proven that the estimate was in fact considerably sensitive to the number of "travellers" who appear in the data set. A recommendation for the future data collections would be to also collect a variable of whether the user attending the NSP resides in Vilnius or not. This would make future estimations easier. Alternatively, this parameter can be obtained by a one-time data collection conducted, for example, in a single week and applied as a correction factor in the estimation phase.

No matter how useful indirect estimates might be, they do not come without limitations. Limitations are based on a set of assumptions the methods rely on and on the limitations related to the data sources themselves (data availability and quality and the type of clients the services manage to cater for and thus will appear in the data sets generated by these services).

Among general limitations, which apply to all estimates, belong biases stemming from the fact that important subgroups with differences in "catchability" or probability to appear in the data sources exist within the data sets. This becomes a problem in situations when there is no data to analyse the data sets while controlling for these subgroups. A general problem, encountered also by other studies, is the inclusion of opioid users who quit heroin use and are stabilised in opioid substitution treatment (OST) programmes. These individuals might appear less often on other lists due to, for example, their lower probability of dying or getting involved with the police. It was not possible in the datasets utilised in this study to distinguish the stabilised OST clients. However, evidence based on empirical data existed in the largest Lithuanian drug treatment centre that they should form up to one third of all OST clients. Other subgroups included Roma ethnic group, which was, according to the anecdotal evidence and some empirical data available, underrepresented in most data sources (but in particular drug treatment) in Lithuania. Another important group was composed of Russian-speaking drug users, a common phenomenon in the Baltic states. This group was also to some extent underrepresented in treatment and other data sources, as suggested by the available evidence. However, neither Roma population nor Russian-speaking drug users were identifiable in the available data sets (i.e. no information on ethnicity which would identify either of the two groups was available in the existing data sets).

Another limitation of the estimates, in situations where data from public health insurance-covered treatment (SVEIDRA) was used is that this data set does not include episodes of private treatments. In 2016, 209 clients were treated with buprenorphine substitution in two private clinics (19). However, it is not clear how many of them also appeared in the public health insurance treatment data set (SVEIDRA). This may have led to underestimation of prevalence where SVEIDRA data set was used and not more than two data sources in total were employed in the analysis.

In case of multiplier estimates, there can virtually never exist a perfect match between benchmark and multiplier. For instance, HIV prevalence estimates we used were obtained from the sample of current injectors, while the number of people living with HIV in Lithuania represents those, in whom intravenous drug use was determined as a route of HIV infection transmission at the time of the diagnosis. The proportion of current injectors among the PLWH at the time of the study was not precisely known. It had to be only roughly estimated in the sensitivity analysis. In case of mortality multiplier, it is known that opioid overdose deaths cases are almost exclusively from among people who injected the drug (11, 12), while drug treatment records include around 10% of non-injecting opioid users (according to other data sources). Moreover, users in treatment might be heavier users than those from hidden populations, and thus might have higher rates of injecting than the "street population" or users who have not made it to treatment yet.

Truncated Poisson estimates might be considerably sensitive to heterogeneity (as proven in the case of mobile unit of needle and syringe programme which served also quite a number of one-time clients from other countries or cities).

The capture-recapture method relies on several assumptions, out of which many are not fully complied with in the real life. Mainly, the population of drug users we aim to estimate is not closed (there are "entries" by new users as well as "departures" by users who cease use or die). Also, the "capture probabilities" will naturally differ within the sample. For instance, in case of data set with drug-related deaths, after a person dies, he or she has zero probability of appearing at any other data source. This means that in addition to capture probabilities being different among individuals whose data was used in the estimation process, they are also not constant over time. Moreover, all-way dependence between data sources cannot be checked, although from knowledge of the situation, it was not assumed to exist in the performed three-source analyses (except of the one using three treatment modalities as three different data sources where the known dependence among data sources has limited the interpretation of the estimate, as explained above). However, "all-way dependence" cannot be excluded in the two-source analyses performed.

Finally, we have got to one of the main purposes of the estimation of high-risk drug use prevalence and that is the estimation of coverage of effective interventions.

The estimated syringe coverage per user of 19-29 syringes per year is indeed low in comparison to the EU standards (20). The number of distributed syringes has increased in 2016, however, still does not reach 2009 levels and EMCDDA's arbitrary but useful zone of medium syringe coverage per user per year (which is at least 100 syringes per user per year). To correctly interpret this finding in relation to HIV spread, it is also important to take into account parallel syringe acquisition in pharmacies. This was occurring in case of 58% of users in one Lithuanian multi-city study(10). Moreover, a user usually reuses his or her own used syringe. However, the same study which was just mentioned also found a very high-risk behaviour of sharing needles in 21.5% of surveyed NSP clients. This was mainly receptive sharing. Another aspect to consider is that what we are using as a denominator in the calculations of coverage are only estimates and not real counts and might thus be overestimates or underestimates. However, even if all 3 053 individuals who contacted NSPs around Lithuania in 2015 were the only injecting users in the country (which is a completely unrealistic assumption used here only for illustration), still the number of syringes distributed per injecting drug user would be only 66, which still falls under the EMCDDA zone of low syringe coverage (below 100 per year per user). In 2016, although the number of syringes of distributed was higher, the number of clients who visited NSPs was even higher and thus this extreme example might lead to an even lower figure. Thus, for an effective campaign to bring HIV spread among PWID close to a halt, an increase in syringe coverage is definitely a must.

Coverage of opioid users by opioid substitution treatment of 9.9-25.5% calculated by the present study is also in the zone of low coverage of the EMCDDA (20), although it's upper limit is relatively close to the lower bound of "medium coverage" postulated by the same institution. However, it also has to be taken into account that it is likely that the estimate of coverage produced is an overestimate due to the fact that available figures of clients treated in OST in 2015 and 2016 were known to contain some double-counts, although anecdotal evidence suggested these should be rather few.

Laying side by side the fact that needle and syringe programmes and opioid substitution treatment are interventions effective in the prevention of HIV spread (e.g. (21-23)) and the estimates of their coverage calculated above, it becomes clear that there is still room for improvement for Lithuania in the coverage of these efficient and life-saving interventions for people who inject drugs and opioid users.

Furthermore, the available data sources were explored, and methodology was developed, applicable under the Lithuanian conditions, which can be replicated and further developed in the future in order to provide regular estimates of the population of high-risk drug users in the country.

## Summary tables of estimates with rates per 1000 population aged 15-64.

### Table 9. National estimates

| Method | Population definition | year | Prevalence | | | Rates per 1000 population aged 15-64. (1 948 685 in 2015 and 1 916 284 in 2016) | | |
|---|---|---|---|---|---|---|---|---|
| | | | central | lower | upper | central | lower | upper |
| HM, 10.75% prevalence | PWID | 2015 | 13 786 | 13 237 | 13 963 | 7.07 | 6.79 | 7.17 |
| HM, 12.5% prevalence | PWID | 2015 | 11 856 | 11 384 | 12 008 | 6.08 | 5.84 | 6.16 |
| HM, sensitivity analysis, 10% PLWH ceased injection, 10.75% prevalence | PWID | 2015 | 12 409 | 11 926 | 12 567 | 6.37 | 6.12 | 6.45 |
| HM, sensitivity analysis, 10% PLWH ceased injection, 12.5% prevalence | PWID | 2015 | 10 672 | 10 256 | 10 808 | 5.48 | 5.26 | 5.55 |
| HM, sensitivity analysis, 25% PLWH ceased injection, 10.75% prevalence | PWID | 2015 | 10 344 | 9 926 | 10 474 | 5.31 | 5.09 | 5.37 |
| HM, sensitivity analysis, 25% PLWH ceased injection, 12.5% prevalence | PWID | 2015 | 8 896 | 8 536 | 9 008 | 4.57 | 4.38 | 4.62 |
| HM, sensitivity analysis, 50% PLWH ceased injection, 10.75% prevalence | PWID | 2015 | 6 893 | 6 619 | 6 981 | 3.54 | 3.40 | 3.58 |
| HM, sensitivity analysis, 50% PLWH ceased injection, 12.5% prevalence | PWID | 2015 | 5 928 | 5 692 | 6 004 | 3.04 | 2.92 | 3.08 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| MIM | PWID | 2016 | 8 868 | 8 371 | 9 364 | 4.63 | 4.37 | 4.89 |
| MM | Opioid injectors | 2015 | 6 296 | 4 760 | 11 596 | 3.36 | 2.29 | 5.57 |
| MM | Opioid injectors | 2016 | 6 543 | 4 454 | 10 851 | 3.07 | 2.17 | 5.28 |
| MM sensitivity analysis | Opioid users | 2015 | 7 220 | 5 459 | 13 298 | 3.71 | 2.80 | 6.82 |
| MM sensitivity analysis | Opioid users | 2016 | 7 503 | 5 108 | 12 444 | 3.92 | 2.67 | 6.49 |
| 2-source CRC, SVEIDRA and DRD, Lincoln-Petersen estimator | Opioid users | 2016 | 6 674 | 4 293 | 9 054 | 3.48 | 2.24 | 4.72 |
| as above; confidence intervals generated via bootstrapping | Opioid users | 2016 | | 4 854 | 10 011 | | 2.53 | 5.22 |
| 2-source CRC, SVEIDRA and DRD, Chapman estimator | Opioid users | 2016 | 6465 | 4 279 | 8 652 | 3.37 | 2.23 | 4.51 |
| as above; confidence intervals generated via bootstrapping | Opioid users | 2016 | | 4 754 | 9 508 | | 2.48 | 4.96 |
| 2-source CRC, SVEIDRA and DRD, Bailey estimator | Opioid users | 2016 | 6 462 | 4 257 | 8 667 | 3.37 | 2.22 | 4.52 |
| as above; confidence intervals generated via bootstrapping | Opioid users | 2016 | | 4 751 | 9 502 | | 2.48 | 4.96 |
| 2-source CRC, Lincoln-Petersen estimate of Vilnius extrapolated to national level | Amps users | 2015 | 6 345 | | | 3.26 | | |
| 2-source CRC, Chapman estimate of Vilnius extrapolated to national level | Amp users | 2015 | 4 965 | | | 2.55 | | |
| 2-source CRC, Bailey estimate of Vilnius extrapolated to national level | Amp users | 2015 | 4 795 | | | 2.46 | | |
| 2-source CRC, Lincoln-Petersen estimate of Vilnius extrapolated to national level | Amp users | 2016 | 7 000 | | | 3.65 | | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| 2-source CRC, Chapman estimate of Vilnius extrapolated to national level | Amp users | 2016 | 4 868 | | | 2.54 | | |
| 2-source CRC, Bailey estimate of Vilnius extrapolated to national level | Amp users | 2016 | 4 742 | | | 2.47 | | |

## Table 10. Vilnius estimates.

| Method | Estimated population | year | Prevalence | | | Rates per 1000 population aged 15-64 (370 116 in 2015 and 370 116 in 2016) | | |
|---|---|---|---|---|---|---|---|---|
| | | | center | lower | upper | center | lower | upper |
| MM | Opioid injectors | 2016 | 3395 | 2402 | 5851 | 9.22 | 6.52 | 15.88 |
| MM, sensitivity analysis adding non-injectors | Opioid users | 2016 | 3893 | 2755 | 6710 | 10.57 | 7.48 | 18.21 |
| CRC (DRD, urine testing, probation) | Opioid users | 2016 | 2083 | 1363 | 3349 | 5.65 | 3.70 | 9.09 |
| CRC (SVEIDRA, urine testing, probation) | Opioid users | 2016 | 1904 | 1711 | 2148 | 5.17 | 4.64 | 5.83 |
| CRC (SVEIDRA OST, SVEIDRA inpatient, SVEIDRA outpatient non-OST) | Opioid users | 2016 | 1736 | 1135 | 3345 | 4.71 | 3.08 | 9.08 |
| TP, (Demetra NEP) Zelterman | PWID | 2015 | 2218 | 2201 | 2236 | 5.99 | 5.95 | 6.04 |
| TP, (Demetra NEP) Chao | PWID | 2015 | 1844 | 1770 | 1931 | 4.98 | 4.78 | 5.22 |
| TP, (RPLC NEP) Zelterman | PWID | 2015 | 5454 | 4891 | 6163 | 14.74 | 13.21 | 16.65 |
| TP, (RPLC NEP) Chao | PWID | 2015 | 4772 | 4433 | 5152 | 12.89 | 11.98 | 13.92 |
| TP, Weighted average of Chao estimates for Demetra and RPLC | PWID | 2015 | 3493 | 3239 | 3789 | 9.44 | 8.75 | 10.24 |
| TP, Weighted average of Zelterman estimates for Demetra and RPLC | PWID | 2015 | 4041 | | | 10.92 | | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| TP, (RPLC NEP) Zelterman, sensitivity analysis with 200 travellers | PWID | 2015 | 4138 | 3780 | 4572 | 11.18 | 10.21 | 12.35 |
| TP, (RPLC NEP) Chao, sensitivity analysis with 200 travellers | PWID | 2015 | 3610 | 3367 | 3884 | 9.75 | 9.10 | 10.49 |
| TP, (RPLC NEP) Zelterman, sensitivity analysis with 400 travellers | PWID | 2015 | 3007 | 2979 | 3250 | 8.12 | 8.05 | 8.78 |
| TP, (RPLC NEP) Chao, sensitivity analysis with 400 travellers | PWID | 2015 | 2630 | 2468 | 2815 | 7.11 | 6.67 | 7.61 |
| 2-source CRC, Lincoln-Petersen estimate | Amphetamines users | 2015 | 1269 | 474 | 2867 | 3.43 | 1.28 | 7.75 |
| as above; confidence intervals generated via bootstrapping | Amphetamines users | | | 544 | Inf | | 1.47 | Na |
| 2-source CRC, Chapman estimate | Amphetamines users | 2015 | 993 | 198 | 1788 | 2.68 | 0.53 | 4.83 |
| as above; confidence intervals generated via bootstrapping | Amphetamines users | | | 496 | 3975 | | 1.34 | 10.74 |
| 2-source CRC, Bailey estimate | Amphetamines users | 2015 | 959 | 130 | 1787 | 2.59 | 0.35 | 4.83 |
| as above; confidence intervals generated via bootstrapping | Amphetamines users | | | 479 | 3834 | | 1.29 | 10.36 |
| 2-source CRC, Lincoln-Petersen estimate | Amphetamines users | 2016 | 1750 | 633 | 2867 | 4.75 | 1.71 | 7.75 |
| as above; confidence intervals generated via bootstrapping | Amphetamines users | | | 700 | Inf | | 1.89 | na |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| 2-source CRC, Chapman estimate | Amphetamines users | 2016 | 1217 | 100 | 2334 | 3.30 | 0.27 | 6.31 |
| as above; confidence intervals generated via bootstrapping | Amphetamines users | | | 608 | 3635 | | 1.64 | 9.82 |
| 2-source CRC, Bailey estimate | Amphetamines users | 2016 | 1176 | 37 | 2315 | 3.19 | 0.10 | 6.25 |
| as above; confidence intervals generated via bootstrapping | Amphetamines users | | | 588 | 3528 | | 1.59 | 9.53 |

**Table 11. Other sub-national estimates.**

| Cities | Method | Estimated population | year | Prevalence | | | Rates per 1000 population aged 15-64. | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | center | lower | upper | center | lower | Upper |
| Klaipeda<br><br>101 282 inhabitants aged 15-64 in 2015 and 98 077 in 2016 | MM | Opioid injectors | 2016 | 864 | 611 | 1489 | 8.81 | 6.23 | 15.18 |
| | MM, sensitivity analysis adding non-injectors | Opioid users | 2016 | 991 | 701 | 1708 | 10.10 | 7.15 | 17.41 |
| | TP, NEP visits, Zelterman | PWID | 2015 | 1778 | 1748 | 1809 | 17.55 | 17.26 | 17.86 |
| | TP, NEP visits, Chao | PWID | 2015 | 1425 | 1327 | 1542 | 14.07 | 13.10 | 15.22 |
| Kaunas<br><br>195 006 inhabitants aged 15-64 in 2015 and 189 891 in 2016 | MM | Opioid injectors | 2016 | 802 | 568 | 1383 | 4.22 | 2.99 | 7.28 |
| | MM, sensitivity analysis adding non-injectors | Opioid users | 2016 | 920 | 651 | 1586 | 4.84 | 3.43 | 8.35 |
| | TP, NEP visits, Zelterman | PWID | 2015 | 249 | 249 | 249 | 1.28 | 1.28 | 1.28 |
| | TP, NEP visits, Chao | PWID | 2015 | 177 | 158 | 212 | 0.91 | 0.81 | 1.09 |
| Alytus<br><br>35 473 inhabitants aged 15-64 in 2016 | TP, NEP visits, Zelterman | PWID | 2016 | 106 | 106 | 106 | 2.99 | 2.99 | 2.99 |
| | TP, NEP visits, Chao | PWID | 2016 | 100 | 96 | 109 | 2.82 | 2.71 | 3.07 |

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