International Journal of Drug Policy 116 (2023) 104044

Contents lists available at ScienceDirect

International Journal of Drug Policy

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

Research Paper

Hepatitis C treatment uptake among people who inject drugs in Oslo, Norway: A registry-based study

Kristian Braathen Malme[a,b,*], Kjersti Ulstein[c], Ane-Kristine Finbråten[d], Linda Elise Couëssurel Wüsthoff[e,f], Knut Boe Kielland[g], Joakim Hauge[g], Olav Dalgard[a,b], Håvard Midgard[a,h]

[a] Department of Infectious Diseases, Akershus University Hospital, Lørenskog, Norway
[b] Institute of Clinical Medicine, University of Oslo, Norway
[c] Agency for Social and Welfare Services, City of Oslo, Norway
[d] Unger-Vetlesen Institute, Lovisenberg Diaconal Hospital, Oslo, Norway
[e] Norwegian Centre for Addiction Research, Institute of Clinical Medicine, University of Oslo, Norway
[f] Unit for Clinical Research on Addictions, Oslo University Hospital Health Trust, Oslo, Norway
[g] Norwegian National Advisory Unit on Concurrent Substance Abuse and Mental Health Disorders, Innlandet Hospital Trust, Brumundal, Norway
[h] Department of Gastroenterology, Oslo University Hospital, Oslo, Norway

ARTICLE INFO

Keywords:
Hepatitis C virus elimination
Hepatitis C virus treatment
People who inject drugs
Direct-acting antivirals

ABSTRACT

Background: Improving HCV treatment uptake among people who inject drugs (PWID) is crucial to achieving the WHO elimination targets. The aims were to evaluate HCV treatment uptake and HCV RNA prevalence in a large cohort of PWID in Norway.

Methods: Registry-based observational study where all users of the City of Oslo's low-threshold social and health services for PWID between 2010–2016 (n = 5330) were linked to HCV notifications (1990–2019) and dispensions of HCV treatment, opioid agonist treatment (OAT) and benzodiazepines (2004–2019). Cases were weighted to account for spontaneous HCV clearance. Treatment rates were calculated using person-time of observation, and factors associated with treatment uptake were analysed using logistic regression. HCV RNA prevalence was estimated among individuals alive by the end of 2019.

Results: Among 2436 participants with chronic HCV infection (mean age 46.8 years, 30.7% female, 73.3% OAT), 1118 (45.9%) had received HCV treatment between 2010–2019 (88.7% DAA-based). Treatment rates increased from 1.4/100 PY (95% CI 1.1–1.8) in the pre-DAA period (2010–2013) to 3.5/100 PY (95% CI 3.0–4.0) in the early DAA period (2014–2016; fibrosis restrictions) and 18.4/100 PY (95% CI 17.2–19.7) in the late DAA period (2017–2019; no restrictions). Treatment rates for 2018 and 2019 exceeded a previously modelled elimination threshold of 50/1000 PWID. Treatment uptake was less likely among women (aOR 0.74; 95% CI 0.62–0.89) and those aged 40–49 years (aOR 0.74; 95% CI 0.56–0.97), and more likely among participants with current OAT (aOR 1.21; 95% CI 1.01–1.45). The estimated HCV RNA prevalence by the end of 2019 was 23.6% (95% CI 22.3–24.9).

Conclusion: Although HCV treatment uptake among PWID increased, strategies to improve treatment among women and individuals not engaged in OAT should be addressed.

Abbreviations: aOR, adjusted odds ratio; CI, confidence intervals; DAA, direct-acting antivirals; DAC, Daclatasvir; DAS, Dasabuvir; EBR, Elbasvir; GZR, Grazoprevir; HCV, hepatitis C virus; IFN, Interferon; IQR, Interquartile range; LDV, Ledipasvir; MSIS, The Norwegian Surveillance System for Communicable Diseases; NA, not applicable; NorPD, The Norwegian Prescription Database; OAT, opioid agonist therapy; OMB, Ombitasvir; PIB, Pibrentasvir; PWID, people who inject drugs; PY, person years; RBV, Ribavirin; RTV, Ritonavir, SD, standard deviation; SIM, Simeprevir; SOF, Sofosbuvir; VEL, Velpatasvir; VOX, Voxilaprevir.

* Corresponding author.
E-mail address: krimal@ahus.no (K.B. Malme).

https://doi.org/10.1016/j.drugpo.2023.104044

Introduction

Globally, 58 million people were estimated to be living with chronic hepatitis C virus (HCV) infection in 2019 (WHO, 2021). Two-thirds of the HCV disease burden in Western Europe can be attributed to injecting drug use (Degenhardt et al., 2016). Although harm reduction interventions such as opioid agonist therapy (OAT) and needle and syringe provision can prevent new HCV infections (Platt et al., 2017), transmission continues to occur among people who inject drugs (PWID) (Grebely et al., 2019). Comprised of approximately 8500 individuals, Norway has seen a relatively stable but aging population of PWID during the last decade, as mean age of first injection has increased significantly during the last 30 years (Bretteville-Jensen, 2009).

Historically, HCV treatment uptake among PWID has been low (Alavi et al., 2014; Iversen et al., 2014; Kielland, Amundsen, & Dalgard, 2014). HCV treatment uptake among OAT patients living with chronic HCV infection in Norway was only 14% during the last 10 years before the availability of direct-acting antiviral (DAA) therapy (Midgard, Bramness, Skurtveit, Haukeland, & Dalgard, 2016). The introduction of DAAs in 2014 changed the HCV treatment paradigm, providing a virologic cure in more than 95% of individuals after 8–12 weeks of oral treatment (Gotte & Feld, 2016). Several trials have shown high efficacy of DAA treatment among PWID, including trials that included people with recent injecting drug use (Dore et al., 2016; Grebely et al., 2018; Grebely et al., 2018; Hajarizadeh et al., 2018; Midgard et al., 2021).

Scaled-up HCV treatment among PWID will be crucial to achieving the World Health Organization's goal of eliminating HCV infection as a major public health threat by 2030 (Day et al., 2019; WHO, 2016, 2022). Mathemathical modeling of the HCV epidemic in Norway has shown that annual treatment rates of at least 50 per 1000 PWID will be needed to achieve substantial reductions in viremic prevalence (Fraser et al., 2018). Although treatment uptake among PWID in many settings has increased in the DAA era (Bajis et al., 2020; Bardsley et al., 2021; Bartlett et al., 2019; Falade-Nwulia et al., 2020; Valerio et al., 2020; Valerio et al., 2020), few studies have documented this in the most marginalized populations with ongoing injecting drug use. As previous studies have been limited by selection biases or lacking behavioural data, (Grebely et al., 2017; Grebely, Hajarizadeh, Lazarus, Bruneau, & Treloar, 2019), more data concerning HCV treatment uptake among PWID is needed to better understand the challenges that remain in this population.

The high quality of Norwegian health registries provides opportunities for linkage of a well-defined cohort of PWID to registries with population-level coverage, providing robust data on HCV status and drug dispensions in a marginalized group. This study aimed to document HCV treatment uptake and associated factors in a large cohort of people who engaged in injection drug use between 2010–2016. Furthermore, the study aimed to estimate HCV RNA prevalence by the end of the study period in the same population.

Materials and methods

Data sources

This was an observational cohort study based on linked data from the following sources:

The Agency for Welfare and Social Services in the City of Oslo. The Agency provides extensive low-threshold services for PWID, including short-term accommodation, a drug consumption room, and low-threshold health clinics. The initial study cohort was defined as all registered users of the drug consumption room, five low-threshold health clinics, and six short-term housing facilities between 1 January 2010 and 31 December 2016. These services were chosen because they exclusively serve individuals with ongoing injecting drug use and share the same electronic files.

The Norwegian Surveillance System for Communicable Diseases (MSIS). Notification of HCV infection from clinicians and laboratories has been mandatory since 1990. From 1990–2008 only cases of acute infection were registered, but since 2008 HCV infections have been registered based on detection of HCV RNA or anti-HCV antibodies. Since 2016 all notifications have been based on the detection of HCV RNA. Suspected mode of transmission, place of residence, country of birth, notification date, and detection method is registered for all notifications. HCV notification data were extracted for all study participants between 1 January 1990 and 31 December 2019.

The Norwegian Prescription Database (NorPD). NorPD was established in January 2004 and contains data on all prescription drugs dispensed from all pharmacies in Norway. The registry has nationwide coverage, encompassing the entire Norwegian population (5.3 million inhabitants). Date of dispension and detailed drug information is registered for all dispensions. This database also contains information regarding year and month of death for individuals that resides or has resided in Norway with dispensions of prescription drugs. These data are derived from the National Population Register. All prescription drugs in Norway are classified according to the Anatomical Therapeutic Chemical (ATC) Classification System. Quantities of dispensed drugs are measured as the number of defined daily doses (DDDs), the assumed average dose per day used for its main indication in adults, as determined by the World Health Organization Collaborating centre for Drug Statistics Methodology (WHOCC, 2020). We extracted data on dispensions for HCV treatment and OAT for all study participants between 1 January 2004 and 31 December 2019. As a previous study had indicated that concurrent use of benzodiazepines and z-hypnotics was associated with HCV testing and treatment (Midgard et al., 2016), data on dispensions of benzodiazepines and z-hypnotics was also extracted.

The Agency for Welfare and Social Services in the City of Oslo extracted data on use of the different low-threshold services from their electronic patient file system (Rusdata). These data, containing birth- and social security number, were sent to the Norwegian Institute for Public Health, where linkage to the Norwegian Surveillance System for Communicable Diseases (MSIS) was performed. These data were linked to the Norwegian prescription database (also managed by the Norwegian Institute of Public Health) and anonymized. In the files every individual has a separate serial number and contain no person-identifiable information.

The study period was defined as 1 January 2010 - 31 December 2019.

Study setting

During the study period, treatment for HCV infection underwent a paradigm shift, with pegylated interferon and ribavirin being replaced with DAA treatment from early 2014. Concurrently, models of HCV care for PWID in Norway changed. Shifting from a traditional specialist healthcare-oriented model of care, HCV treatment has increasingly been offered in low-threshold settings and outreach practices during the last years.

HCV genotypes 3 and 1 are most common in Norway. Due to high drug costs, DAA treatment was restricted to patients with significant liver fibrosis between 2014 and 2016. From 2017, the cost of DAAs for genotypes 1 and 4 fell sharply, enabling fibrosis restrictions for these genotypes to be lifted. From 2018 DAAs were offered for all HCV patients in Norway without restrictions. The cost of HCV treatment was covered by Social Security until 2016 and by the regional Health Trusts from 2016.

By the end of 2021, approximately 4500 individuals were living with chronic HCV infection in Norway (data on file).

Study population

The final study population was defined by linkage of the initial study cohort to MSIS for HCV status and to NorPD for dispension data. Of

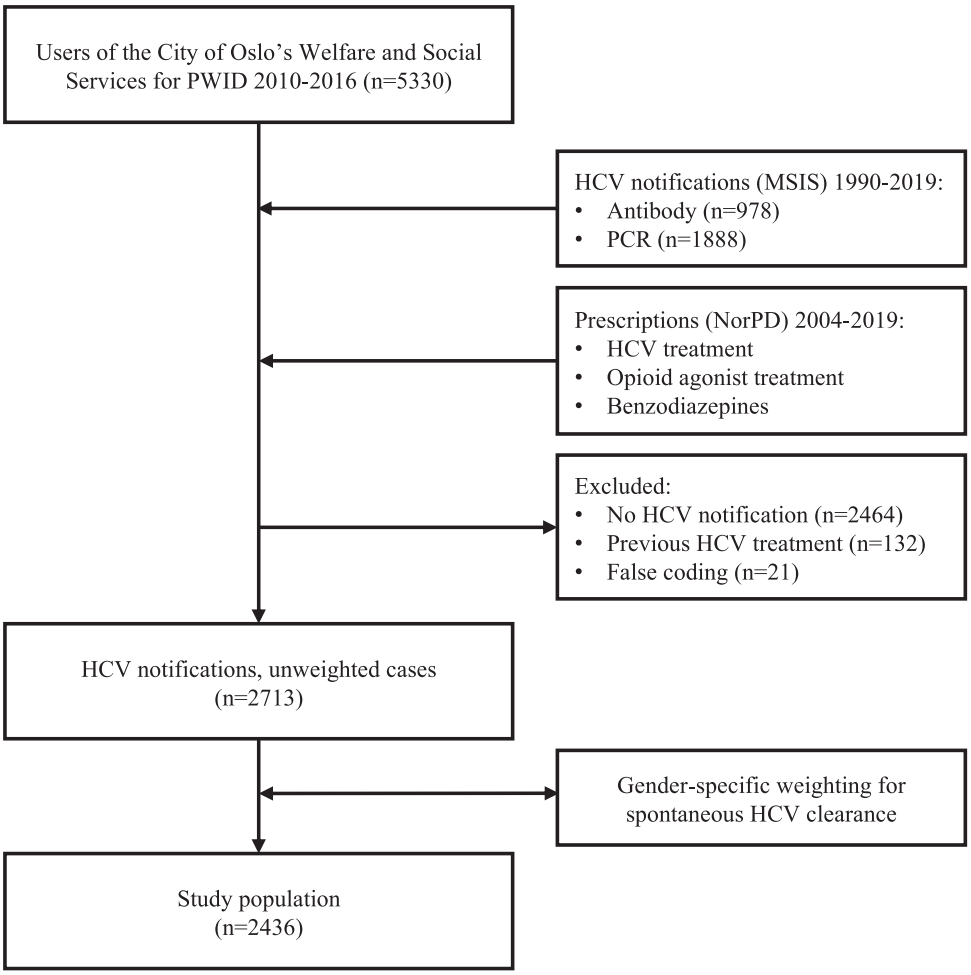

Fig. 1. Flowchart of the study population.

the initial cohort identified as users of the low-threshold services for PWID (n = 5330), we excluded individuals without HCV notification (n = 2464), individuals with HCV treatment before first contact with the services (n = 132), and individuals who were registered as users of the services after death, thus assumed to be a result of registration error (n = 21). As no behavioural data was accessible, all participants were counted as PWID independent of the time of contact with the low-threshold services.

To account for spontaneous HCV clearance, adjustments were made to more accurately estimate the population with chronic HCV infection. Although estimates of spontaneous clearance rates vary (Aisyah, Shallcross, Hully, O'Brien, & Hayward, 2018; Kåberg, Navér, Hammarberg, & Weiland, 2018; Micallef, Kaldor, & Dore, 2006; Smith, Jordan, Frank, & Hagan, 2016; Valerio et al., 2020), we chose to base our adjustments on a recent study with high coverage of HCV RNA, where spontaneous clearance rates of 25% for men and 34% for women were reported (Bartlett et al., 2019). Sex-specific importance weights were assigned to all cases using a previously described method (Heather Valerio et al., 2020). Cases were weighted 1 if HCV notifications were based on HCV RNA (n = 1888) or if HCV treatment had been received (i.e., confirmed chronic HCV infection). Cases with HCV notifications based on anti-HCV antibodies alone (n = 978) were weighted based on the following formula:

$$x = 1.0 - \frac{Total\ HCV\ antibody\ notifications * spontaneous\ clearance\ rate}{Total\ HCV\ antibody\ notifications - treated\ HCV\ antibody\ notifications}$$

This resulted in a weight of 0.63 for untreated women and 0.70 for untreated men with HCV notifications based on anti-HCV antibodies. Cases registered without a test method (n = 65) were assumed to be based on anti-HCV if they were registered at a time when HCV RNA was not available or if they had not received treatment for HCV infection. The importance weighted study population was comprised of 2436 individuals living with chronic HCV infection, that had not previously undergone HCV treatment. 354 of the participants included in the study population deceased during the study period. A flowchart describing the derivation of the importance weighted study population is shown in Fig. 1.

Exposure variables

Age and sex were obtained from the electronic files of the Agency for Welfare and Social Services. Sex was derived from the birth- and social security number. Age was defined as age at the end of 2019 or death, whatever occurred first, and categorized as <30, 30–39, 40–49, 50–59, and ≥60 years. Year and month of death was extracted from NorPD. For a minority of individuals (n = 96) with no dispensions, we did not find a way to obtain data concerning death (if this had occurred or not), this has been listed as missing data. Country of birth was provided by the MSIS register.

The number of visits at each type of low-threshold service was calculated for all participants based on the Agency for Welfare and Social Services files. Participants were stratified according to the following categories: no use (never use), moderate use (1–9 visits/year), and frequent use (≥10 visits/yr), focusing on the year with the highest number of visits. These cut-offs were established in consensus with local partners with experience from the various services.

Exposure to HCV treatment was defined as having been dispensed ribavirin or DAAs. Ribavirin without concurrent dispension of DAAs was used as a proxy for interferon-based treatment as interferon was pre-

scribed for other medical conditions in Norway at that time, and as it would not have been possible to differentiate this from prescription due to HCV treatment. The timepoint of HCV treatment uptake was defined as the date of the first dispension of HCV treatment.

Exposure to OAT was defined as having been dispensed methadone, levomethadone, buprenorphine, or buprenorphine-naloxone. Participants were stratified to the following categories: a) never (no dispensations), b) former (dispensations of OAT only prior to the first contact with the low-threshold services), and c) current (OAT dispensations during the study period). Exposure to benzodiazepines and/or z-hypnotics was defined as having been prescribed diazepam, oxazepam, alprazolam, nitrazepam, midazolam, clonazepam, zopiclone, or zolpidem. We calculated median OAT and benzodiazepine doses per year and stratified participants according to the following categories: no dispensions, moderate use (total defined daily doses (DDDs)/year <median), and high use (total DDDs/year >median).

Relevant ATC codes are listed in the Supplementary Materials.

Outcomes

The primary outcome was HCV treatment uptake, defined as the first dispension of HCV treatment between 2010–2019 in the importance-weighted study population. Secondary outcomes were 1) factors associated with treatment uptake in the same population, and 2) HCV RNA prevalence among registered users of the low-threshold services alive by the end of 2019.

Statistical analysis

Categorical data were summarized and reported as N (%), continuous data as median (IQR) or mean (SD) appropriate. Cumulative overall and DAA treatment uptake was calculated in the importance-weighted study population and stratified according to age groups, sex, use of low-threshold services, country of birth, OAT, and benzodiazepine use.

Annual treatment uptake was calculated in the importance-weighted study population using person-time of observation and reported as incidence rates per 100 person-years (PY) with 95% Poisson confidence intervals (CI). The observation time for each participant was defined as the time from first contact with low-threshold services or from HCV notification (if notification occurred later) to the time of HCV treatment, death, or 31 December 2019 (whatever occurred first). Treatment rates were reported for each year and according to the pre-DAA period (2010–2013), early DAA period (2014–2016; fibrosis restrictions), and late DAA period (2017–2019; no restrictions). Annual treatment rates per 1000 PWID with Poisson 95% CIs were calculated as the number of treatments per 1000 registered unweighted users of the low-threshold services each year.

Logistic regression analysis reporting odds ratios (OR) and 95% CIs was used to evaluate factors associated with overall treatment uptake. An additional model was specified to identify factors associated with DAA treatment uptake. For this analysis, individuals who received interferon-based treatment (n = 126) or died before 2014 (n = 109) were excluded. Factors significant at the 0.100 level in unadjusted analysis in addition to age and sex were considered for inclusion in the adjusted analyses. The adjusted models were tested for collinearity using variance-covariance matrices, and the best fit models were deduced based on likelihood ratio tests and pseudo R squared.

HCV RNA prevalence estimates with Clopper-Pearson exact 95% CIs were calculated as the importance weighted number of untreated individuals with HCV notification divided by the total number of registered users of the low-threshold services for PWID. For this analysis, individuals without HCV notification were weighted 1. Prevalence estimates were reported among individuals alive by 31 December 2019 and stratified by subgroups of interest.

To investigate the effect of importance-weighting on effect sizes and statistical significance, a sensitivity analysis was performed comparing weighted and unweighted results of the logistic regression analyses.

All analyses were performed in STATA v.17.0 (College Station, TX, USA).

Results

Study population

Of 5330 registered users of the low-threshold services for PWID, we identified 2713 previously untreated individuals living with chronic HCV infection. After applying sex-specific importance weights, the final study population estimated to have chronic HCV infection comprised of 2436 individuals (Fig. 1). Characteristics of study participants are shown in Table 1. The mean age was 46.8 years, 30.7% were female, 91.1% were born in Norway, 73.3% were current OAT recipients, and 86.7% had moderate or extensive benzodiazepine use. Use of short-term accomodation, the drug consumption room, and low-threshold health clinics was registered in 51.3%, 50.7%, and 68.5% of the participants, respectively.

The median observation time was 5.6 years among treated individuals and 5.9 years among untreated. The size of the study population changed during the study period, with individuals entering and exiting throughout, including 354 (14.5%) individuals who died during the study period. Mortality was lower (4.8%) among individuals treated for HCV infection than among untreated individuals (22.7%).

HCV treatment uptake

Overall, 1118 of 2436 individuals (45.9%) had received HCV treatment during the study period. The majority of treatments (842 of 1118) were registered in 2017 – 2019, peaking at 369 treatments in 2018 (Fig. 2). Treatment was interferon-based in 126 cases (11.3%) and DAA-based in 992 cases (88.7%) with sofosbuvir/velpatasvir being the most frequent regimen (41.3%).

Table 2 shows cumulative overall and DAA treatment uptake in different subgroups. Treatment uptake was lowest among individuals below 30 years (39.1% overall; 37.1% DAA) and highest among those 60 years or older (50.8% overall; 50.4% DAA). Treatment uptake was lower among women (40.7% overall; 38.0% DAA) than among men (48.2% overall; 47.7% DAA). Overall and DAA

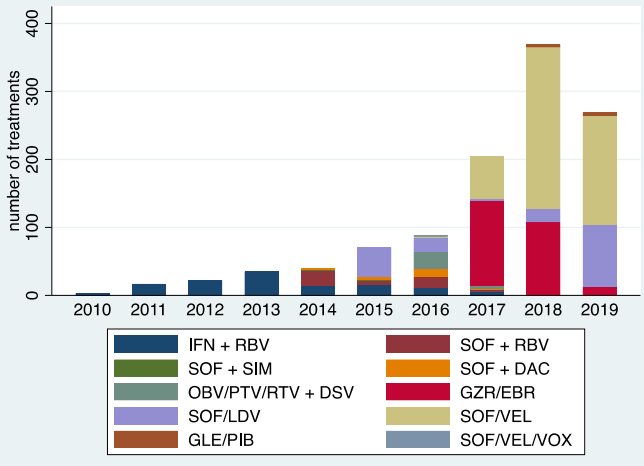

Fig. 2. Annual number of HCV treatments among users of low-threshold services for people who inject drugs in Oslo between 2013 and 2019, stratified by treatment regimen.

Table 1
Characteristics of the importance weighted study population of HCV RNA positive users of low-threshold services for people who inject drugs in Oslo between 2010 and 2019.

Characteristic, *n* (col%)	Total	Treated	Untreated
Total	2436 (100)	1118 (45.9)	1318 (54.1)
Age groups			
20–29	94 (3.9)	37 (3.3)	58 (4.4)
30–39	561 (23.0)	265 (23.7)	295 (22.4)
40–49	748 (30.7)	320 (28.6)	428 (32.5)
50–59	761 (31.2)	358 (32.0)	403 (30.6)
≥ 60	272 (11.2)	138 (12.4)	134 (10.1)
Mean age (SD)	46.8 (10.2)	47.1 (10.3)	46.5 (10.1)
Sex			
Male	1689 (69.3)	814 (72.8)	875 (66.4)
Female	747 (30.7)	304 (27.2)	443 (33.6)
Country of birth[1]			
Norway	2172 (91.1)	1014 (91.4)	1158 (90.9)
Other	213 (8.9)	96 (8.6)	116 (9.1)
Deceased during study period[2]	354 (14.5)	54 (4.8)	300 (22.7)
Observation time, median years (IQR)	5.8 (3.7–7.5)	5.6 (2.9–7.7)	5.9 (4.1–7.0)
Short-term accommodation			
No use	1188 (48.7)	557 (49.8)	631 (47.9)
Moderate use	1074 (44.1)	488 (43.7)	586 (44.4)
Frequent use	174 (7.2)	73 (6.5)	101 (7.7)
Short-term accommodation, median number of visits (IQR)	0.6 (0.0- 3.0)	1.0 (0.0–3.0)	0.6 (0.0–3.0)
Drug consumption room			
No use	1201 (49.3)	543 (48.6)	658 (49.9)
Moderate use	610 (25.1)	277 (24.8)	333 (25.3)
Frequent use	625 (25.6)	298 (26.6)	327 (24.8)
Drug consumption room, median number of visits (IQR)	0.6 (0.0–17.5)	1.0 (0.0–21.0)	0.6 (0.0–14.5)
Low-threshold health clinics			
No use	769 (31.5)	355 (31.8)	414 (31.4)
Moderate use	1242 (51.1)	566 (50.6)	676 (51.3)
Frequent use	425 (17.4)	197 (17.6)	228 (17.3)
Low-threshold health clinics, median number of visits (IQR)	2.0 (0.0–8.8)	2.0 (0.0–9.0)	2.0 (0.0–8.0)
Overall use of low-threshold services			
One service	1180 (48.5)	535 (47.9)	645 (48.9)
Two services	798 (32.7)	385 (34.4)	413 (31.3)
All three services	458 (18.8)	198 (17.7)	260 (19.8)
OAT status			
Never	595 (24.4)	258 (23.1)	337 (25.6)
Former	75 (3.1)	27 (2.4)	48 (3.6)
Current	1766 (72.5)	833 (74.5)	933 (70.8)
OAT dispensions			
No dispensions	595 (24.4)	258 (23.1)	337 (25.5)
Moderate	768 (31.5)	373 (33.4)	395 (30.0)
High	1073 (44.1)	487 (43.5)	586 (44.5)
Main OAT drug[3]			
Methadone-based	944 (51.5)	429 (50.1)	515 (52.8)
Buprenorphine-based	886 (48.5)	423 (49.9)	463 (47.2)
OAT dose, median DDD/year (IQR)	548 (317- 865)	594 (358–957)	505 (285–806)
Benzodiazepine dispensions			
No dispensions	324 (13.3)	138 (12.3)	186 (14.1)
Moderate	982 (40.3)	467 (41.8)	515 (39.1)
High	1130 (46.4)	513 (45.9)	617 (46.8)
Main benzodiazepine[4]			
Diazepame	526 (26.0)	231 (24.7)	295 (27.0)
Oxazepame	899 (44.3)	425 (45.4)	474 (43.4)
Alprasolame	86 (4.2)	38 (4.1)	48 (4.4)
Nitrazepame	111 (5.5)	51 (5.4)	60 (5.5)
Z-hypnotics	237 (11.7)	120 (12.8)	117 (10.8)
Clonazepame	169 (8.3)	72 (7.6)	97 (8.9)
Benzodiazepine dose, median DDD/year (IQR)	182 (51–441)	199 (56–481)	170 (45–415)

Data are presented as n (%) unless otherwise indicated.
Abbreviations: IQR, interquartile range; HCV, hepatitis C virus; PWID, people who inject drugs; OAT, opioid agonist therapy; PCR, polymerase chain reaction; SD, standard deviation.
[1] Missing data for 51 participants.
[2] Missing data for 96 persons.
[3] Among those with OAT dispensions, and in cases where types of OAT were not equal in use.
[4] Among those with benzodiazepine dispensions, and in cases where types of benzodiazepines were not equal in use.

treatment uptake among individuals who were alive by 31 December 2019 was 51.1% (1074 of 2101) and 48.4% (963 of 1990), respectively.

Fig. 3 shows annual HCV treatment rates per 100 PY and per 1000 PWID between 2010 and 2019. Annual treatment rates increased from 1.4/100 PY (95% CI 1.1–1.8) in the pre-DAA period (2010–2013) to 3.5/100 PY (95% CI 3.0–4.0) in the early DAA period (2014–2016) and 18.4/100 PY (95% CI 17.2–19.7) in the late DAA period (2017–2019), peaking at 24.1/100 PY (95% CI 21.7–26.7) in 2018 (Fig. 3A-B). Annual treatment rates per 1000 PWID (infected or uninfected) were

Table 2
Cumulative HCV treatment uptake (overall and DAA) among users of low-threshold services for people who inject drugs in Oslo between 2010 and 2019. Overall treatment uptake includes participants having been dispensed interferon-based treatment.

Characteristic, *n* (%)	Overall treatment uptake	DAA treatment uptake
Total	1118/2436 (45.9)	992/2218 (44.7)
Age groups		
20–29	37 (39.1)	30 (37.1)
30–39	265 (47.3)	215 (43.8)
40–49	320 (42.8)	278 (41.4)
50–59	358 (47.0)	336 (47.3)
≥ 60	138 (50.8)	133 (50.4)
Sex		
Male	814 (48.2)	733 (47.7)
Female	304 (40.7)	259 (38.0)
Country of birth		
Norway	1014 (46.7)	899 (45.5)
Other	96 (45.2)	87 (44.5)
Short-term accommodation		
No use	557 (46.9)	478 (45.5)
Moderate use	488 (45.4)	443 (44.3)
Frequent use	73 (41.9)	71 (42.4)
Drug consumption room		
No use	543 (45.2)	479 (43.7)
Moderate use	277 (45.4)	241 (44.2)
Frequent use	298 (47.7)	272 (47.2)
Low-threshold health clinics		
No use	335 (46.1)	310 (44.7)
Moderate use	566 (45.6)	497 (44.2)
Frequent use	197 (46.3)	185 (46.1)
Use of low-threshold services		
One service	535 (45.3)	464 (43.9)
Two services	385 (48.3)	339 (46.8)
All three services	198 (43.2)	189 (43.3)
OAT status		
Never/former	285 (42.6)	240 (41.3)
Current	833 (47.2)	752 (45.9)
OAT dispensions		
No dispensions	258 (43.4)	218 (41.6)
Moderate	373 (48.6)	339 (48.0)
High	487 (45.4)	435 (44.1)
Main OAT drug[1]		
Methadone-based	429 (45.4)	398 (45.4)
Buprenorphine-based	423 (47.8)	368 (45.6)
Benzodiazepine dispensions		
No dispensions	138 (42.5)	119 (40.2)
Moderate	467 (47.6)	409 (46.1)
High	513 (45.4)	464 (44.8)

[1] Among those with OAT dispensions, and in cases where types of OAT were not equal in use.

below 10 in the pre-DAA period but exceeded the previously modelled elimination threshold of 50 per 1000 PWID in 2018 and 2019 (Fig. 3C).

Factors associated with treatment uptake

In adjusted logistic regression analysis (Table 3), the odds of overall treatment uptake were lower among those aged 40–49 years compared to those above 60 years (aOR 0.74; 95% CI 0.56–0.97) and lower among women than among men (aOR 0.74; 95% CI 0.62–0.89). The odds of overall treatment uptake were higher among participants with current OAT (aOR 1.21; 95% CI 1.01–1.45) compared to those with never or former OAT.

DAA treatment uptake (Table 3) was similarly negatively associated with female sex (aOR 0.68; 95% CI 0.56–0.82) and more clearly associated with age; the odds of DAA treatment increased by 10% for each 10-year increment in age (aOR 1.10; 95% 1.01–1.19). Treatment uptake was not associated with country of origin, benzodiazepine use, OAT status, or with the use of any of the low-threshold services.

HCV RNA prevalence estimates

Among 4354 individuals who were alive by 31 December 2019, 1027 were estimated to still have untreated chronic HCV infection, for an overall HCV RNA prevalence of 23.6% (95% CI 22.3–24.9). The estimated HCV RNA prevalence was higher among women (33.0%; 95% CI 30.3–35.8) than among men (20.3%; 95% CI 19.0–21.8) and higher among those with a history of OAT (32.3%; 95% CI 30.4–34.2) than among those without (13.2%; 95% CI 11.7–14.8). HCV RNA prevalence was lowest among individuals 60 years or older (18.0%; 95% CI 15.0–21.4) and highest among those aged 40–49 years (26.6%; 95% CI 24.1–29.1). Fig. 4 illustrates overall treatment uptake and corresponding HCV RNA prevalence estimates by the end of the study period for selected subgroups.

Sensitivity analysis

Unweighted analysis of treatment uptake yielded generally lower rates than weighted analysis, but relative proportions across subgroups were not affected by weighting (Supplementary Table 1). In logistic regression analysis of factors associated with overall and DAA treatment uptake, unweighted results for age and sex were comparable to weighted results with similar effect sizes and CIs (Supplementary Table 2). The factor most impacted by importance-weighting was OAT, and this factor did not reach significance in unweighted analysis.

Discussion

In this registry-based observational study of people who engaged in injection drug use between 2010–2016 with a HCV notification between 1990–2019, cumulative HCV treatment uptake between 2010–2019 was 45.9%. Treatment rates increased from 1.4/100 PY in the pre-DAA period to 18.4/100 PY in the late DAA period and exceeded a previously modelled elimination threshold of 50/1000 PWID in 2018 and 2019 (Fraser et al., 2018). Treatment uptake was less likely among women and those aged 40–49 years and more likely among participants with current OAT. The estimated HCV RNA prevalence among those alive by the end of 2019 was 23.6%. This study documents the effect of DAAs on HCV treatment uptake in Norway and provides valuable insights that could inform HCV elimination efforts internationally.

HCV treatment uptake was higher than in recent studies from the US and Canada (Bartlett et al., 2022; Corcorran, Tsui, Scott, Dombrowski, & Glick, 2021; Falade-Nwulia et al., 2020; Socías et al., 2019) but in line with findings from other regions with unrestricted access to DAAs, such as New South Wales in Australia (Valerio et al., 2020). The low pre-DAA treatment rates are similar to results from a previous study among OAT recipients in Norway (Midgard et al., 2016), reflective of a period dominated by barriers to HCV care. It should be noted that patients treated with interferon in monotherapy due to contraindications for ribavirin may have been missed, as our definition of interferon-treatment rests on the dispension of ribavirin alone. Although treatment rates increased in the early DAA-era, it was first when fibrosis restrictions were lifted in 2017 that treatment rates increased sharply, exceeding a previously modelled HCV elimination threshold of 50 pr 1000 PWID (Fraser et al., 2018). In addition to unrestricticted access to treatment, improved experience with HCV care among healthcare providers and patients becoming more aware of treatment options may have contributed to the increasing uptake. Sustaining an elimination threshold of 50 pr 1000 PWID could pose a significant challenge in a remaining HCV population that may be dominated by individuals that are unsuccessfully reached with testing and treatment. Therefore, new models of care better adapted to this group are needed. Mean age and distribution of participants based on sex in the cohort was similar to findings in a recent report documenting OAT use nationwide (Beck et al., 2022), indicating that our findings are generalizable on a national level.

Table 3
Logistic regression analysis of factors associated with HCV treatment uptake in the DAA era among users of low-threshold services for people who inject drugs in Oslo.

	Overall treatment uptake				DAA treatment uptake			
Factor	Unadjusted OR (95% CI)	p	Adjusted OR (95% CI)	*p*	Unadjusted OR (95% CI)	*p*	Adjusted OR (95% CI)	*p*
Age groups							NA	NA
20–29	0.62 (0.39–1.00)	0.052	0.69 (0.43–1.12)	0.131	0.58 (0.35–0.97)	0.036		
30–39	0.87 (0.65–1.16)	0.345	0.89 (0.67–1.19)	0.435	0.76 (0.57–1.03)	0.079		
40–49	0.73 (0.55–0.96)	0.024	0.74 (0.56–0.97)	0.031	0.69 (0.52–0.92)	0.012		
50–59	0.86 (0.65–1.14)	0.294	0.88 (0.67–1.16)	0.364	0.88 (0.66–1.17)	0.384		
≥60	1				1			
Age (per 10- year increment)	1.05 (0.97–1.14)	0.185	NA	NA	1.11 (1.02–1.21)	0.012	1.10 (1.01–1.19)	0.027
Sex								
Male	1		1		1		1	
Female	0.74 (0.62–0.88)	0.001	0.74 (0.62–0.89)	0.001	0.67 (0.56–0.81)	<0.001	0.68 (0.56–0.82)	<0.001
Country of birth								
Norway	1		NA	NA	1		NA	NA
Other	0.94 (0.71–1.25)	0.684			0.96 (0.71–1.29)	0.772		
Short-term accomodation								
No use	1		NA	NA	1		NA	NA
Moderate use	0.94 (0.80–1.11)	0.495			0.95 (0.80–1.14)	0.600		
Frequent use	0.82 (0.59–1.13)	0.217			0.88 (0.63–1.22)	0.449		
Drug consumption room								
No use	1		NA	NA	1		NA	NA
Moderate use	1.01 (0.83–1.23)	0.939			1.02 (0.83–1.25)	0.869		
Frequent use	1.10 (0.91–1.34)	0.314			1.15 (0.94–1.41)	0.182		
Low-threshold health clinics								
No use	1		NA	NA	1		NA	NA
Moderate use	0.98 (0.81–1.17)	0.789			0.98 (0.81–1.19)	0.841		
Frequent use	1.00 (0.79–1.27)	0.972			1.06 (0.83–1.35)	0.656		
Use of low- threshold services								
One service	1		NA	NA	1		NA	NA
Two services	1.13 (0.94–1.35)	0.199			1.13 (0.93–1.36)	0.222		
Three services	0.92 (0.74–1.40)	0.433			0.98 (0.78–1.23)	0.852		
OAT status								
Never/former	1		1		1		1	
Current	1.20 (1.01–1.44)	0.043	1.21 (1.01–1.45)	0.043	1.21 (1.00–1.46)	0.053	1.21 (1.00–1.47)	0.055
Benzodiazepine dispensions								
No dispensions	1		NA	NA	1		NA	NA
Moderate	1.22 (0.95–1.58)	0.116			1.27 (0.97–1.66)	0.078		
High	1.12 (0.88–1.44)	0.358			1.21 (0.93–1.57)	0.157		

Treatment uptake was lower among women than men, consistent with international studies (Corcorran et al., 2021; Iversen et al., 2014; Rojas et al., 2019; Heather Valerio et al., 2020; H. Valerio et al., 2020). The reason is probably multifactorial, but women may face additional individual and structural barriers to care, including increased stigma. Men are more likely to use illicit drugs and alcohol, but women are as likely as men to develop substance use disorders (SAMHSA, 2017). Women tend to initiate substance use later than men but progress faster from initiation to chronic use and to the development of substance-related adverse consequences, often referred to as "telescoping" (Piazza, Vrbka, & Yeager, 1989; SAMHSA, 2017). In addition, women with substance use carry a higher burden of psychiatric comorbidities (Kaló, 2020) and are more at risk of engaging in injection risk behavior (Des Jarlais, Feelemyer, Modi, Arasteh, & Hagan, 2012; Karlsson et al., 2017). Women who inject drugs are also particularly vulnerable due to sex work, physical and sexual violence, stigma, and discrimination (Roberts, Mathers, & Degenhardt, 2010; SAMHSA, 2017). A study from the pre-DAA era found that even if women were more proactive in health-seeking behavior than men, they were not more likely to receive HCV treatment (Temple-Smith et al., 2007). The female participants in this study had higher mean age than males (47.1 years vs 46.0), and a higher percentage were registered with Norway as country of birth (Supplementary Table 3). Furthermore, there were fewer females registered as frequent users of the drug consupmtion room and short-term accommodation, and a higher number of female participants had a high number of benzodiazepine dispensions compared to men.

Participants with OAT dispensions during the observation period had higher odds of treatment compared to those with no or previous OAT. This is in line with previous studies (Socías et al., 2019; H. Valerio et al., 2020), including a recent cohort study from Canada in which HCV-positive individuals with current OAT were 84% more likely to initiate HCV treatment compared to those not engaged in OAT (Bartlett et al., 2022). OAT could serve as a facilitator for health seeking behavior (Degenhardt et al., 2019; Ferraro et al., 2021). In the context of HCV care, the multidisciplinary nature of OAT programs could provide a platform for testing and linkage to care for PWID. In a recent randomized controlled trial from Norway (Fadnes et al., 2021), integrated HCV treatment in OAT was superior to standard of care with regards to treatment uptake and virologic response. Therefore, increasing OAT uptake among PWID and integrating HCV care in OAT could be key to enhance HCV treatment in marginalized populations.

Treatment uptake was associated with increasing age, as also demonstrated in previous studies (Aas et al., 2020; Corcorran et al., 2021). This age effect could be explained by several factors, including longer time in the cohort (i.e., longer duration of HCV infection) among older individuals and increased opportunities for linkage to care, but also the fact that early DAA era fibrosis restrictions prioritized older individuals with more advanced liver disease. Although this is encouraging from an individual health perspective, it is disappointing from a public health perspective that treatment uptake was lower among younger individuals who may contribute to higher transmission risk (Page et al., 2019; Roy, Boudreau, & Boivin, 2009). Younger individuals with injecting drug use may have additional vulnerabilities, making it less likely that they are reached with HCV testing and treatment (Prussing, Bornschlegel, & Balter, 2015; Sundsbø, 2013). In addition, several of the low-threshold services may not be adopted to these indi-

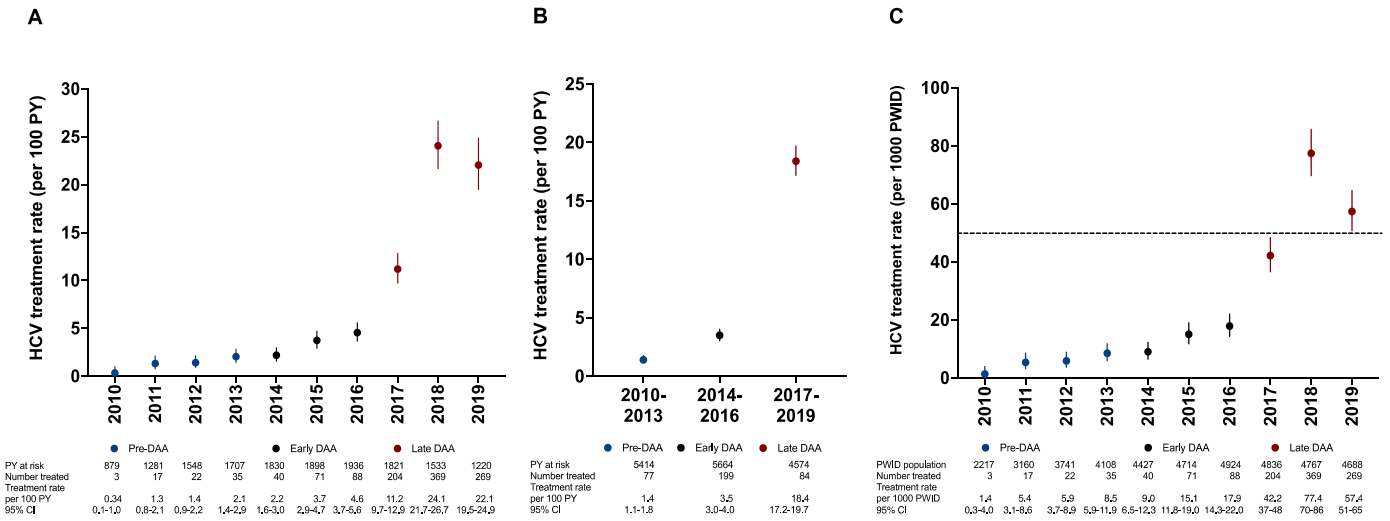

Fig. 3. HCV treatment rates among users of low-threshold services for people who inject drugs in Oslo. (A) Annual rates per 100 PY between 2010 and 2019. (B) Rates per 100 PY according to time periods. (C) Annual rates per 1000 people who inject drugs between 2010 and 2019. Dots indicate point estimates and bars indicate 95% Poisson confidence intervals. The dotted line in (C) indicate a previously modelled elimination threshold.

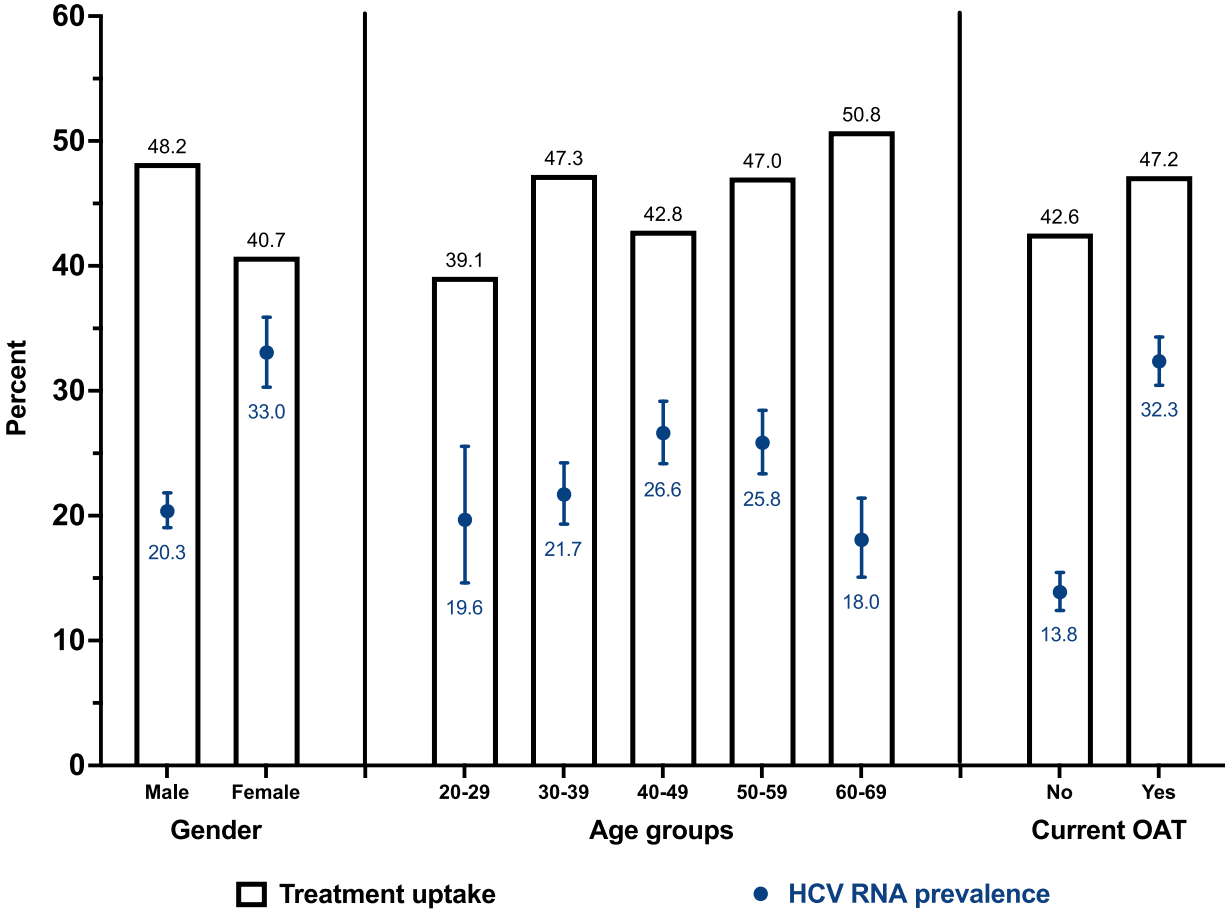

Fig. 4. Overall treatment uptake and corresponding HCV RNA prevalence estimates in the study cohort by 31 December 2019 according to sex, age and opioid agonist treatment status. Gray bars represent treatment uptake and bludots represent prevalence estimates with 95% CI. .

viduals, often practicing referral to collaborating services to guide them away from the injecting drug scene. This is in contrast to policies for other age groups where retention and proximity have been key strategies (Sundsbø, 2013).

One could assume that being in contact with the various health and social services would increase the probability of linkage to HCV care. Therefore, a surprising finding was the lack of association between use of low-threshold services and treatment uptake. This could be explained by increased somatic, psychiatric, and addiction-related comorbidities among frequent users of the health services, who may be additionally marginalized and have a lower likelihood of being reached. Another explanation could be that the low-threshold services simply fail to meet

the needs of the clients with regards to HCV testing and linkage to care. To facilitate access to HCV treatment, we believe all low-threshold services should offer HCV testing and swift provision of treatment in a systematic fashion, and consider point-of care HCV testing for broader implementation.

Estimated HCV RNA prevalence among individuals alive at the end of the study period was 23.6%. This is almost one-half of the estimated prevalence in 2018 ("The Norwegian Directorate of Health. Hepatitt C skal elimineres som folkehelseproblem," 2018) and highlights the impact of DAAs in this population. However, it is still discouraging that HCV RNA prevalence estimates in most subgroups were relatively high, and a stark reminder that if high-income countries are to succeed in HCV elimination, people with ongoing injecting drug use are in dire need of attention and customized models of care.

This study demonstrates the importance of unrestricted DAA access among PWID, but also reveals the need for strategies directly addressing women with HCV. Future research is needed to increase our understanding of sex-specific barriers to HCV care and factors associated with HCV care.

A key strength of the study is the inclusion of a large and representative sample of PWID with evidence of ongoing injecting drug use. This has provided credible estimates of treatment uptake anchored in a target-population for HCV elimination. Another strength is the use of sex-specific weighting, adding accuracy and robustness to the estimate of the population living with chronic HCV infection.

A limitation of our study, caused by the methodology, is that we only included individuals engaged in low-threshold care. By omitting to include individuals not engaged in these services, we risk selection bias. Another limitation is that the registry-based method only allowed for registration of dispensions, and that actual intake of drugs has not been measured. A potential bias regarding treatment rates for 2017–2019 is that the study did not recruit participants after 2016. Unless individuals recruited to the low-threshold services after 2016 were treated with the same rates, estimated treatment uptake for the last three years has been overestimated. Furthermore, as no participants were included after 2016, our findings regarding DAA uptake in 2017–2019 does not constitute recent HCV infections. As a longer duration of HCV infection is associated with a higher probability of receiving treatment, this may have added to overestimation of treatment rates from 2017–2019. A limitation is that the lack of clinically relevant background variables (i.e., stage of liver disease, alcohol consumption, housing status) may have hampered the analysis of factors associated with treatment uptake. Another limitation of the study rests on the definition on some of our time-varying variables, such as age, OAT use, and the use of low-threshold services. As age was defined at the end of the study cohort or death, age given at the time of treatment uptake will for the vast majority be somewhat overestimated. Furthermore, our definition of “current OAT” has limitiations and could be regarded as misleading, as HCV treatment may have been administered to some participants prior to first dispension of OAT. Lastly, a limitiation of our study rests on the definition of all participants being counted as PWID, independent of the time of contact with the low-threshold services. By avoiding to discriminate between recent and distant use of these services, potential findings of importance may have been missed.

In conclusion, this observational study has demonstrated increased HCV treatment uptake among PWID after the introduction of DAAs, exceeding previously established elimination thresholds. However, strategies targeting women and individuals not engaged in OAT are needed to maintain momentum in HCV elimination efforts.

Ethics approval

The authors declare that they have obtained ethics approval from an appropriately constituted ethics committee/institutional review board where the research entailed animal or human participation. This study was approved by the Regional committees for medical and health research ethics (REK) in Norway in 2014 (ref. number: 2014/461), and was conducted in accordance with the Declaration of Helsinki. Permission was given to collect data without informed consent from patients.

Funding sources

This research received funding from the following sources. KM receives research grants from the South-Eastern Norway Regional Health Authority, grant number: 2020011.

The funding sponsor has not been involved in study design, collection of data, analysis/interpretation of data, in the writing of the article, or in the decision to submit the article for publication.

Declarations of Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests. K.M., A.F., L.W., and K.B.K. have no conflicts of interest. K.U. has received lecture grants from Gilead and MSD. J.H. is an industry-sector Ph.D-student funded by AbbVie and the Norwegian Research Council. No funding was received from AbbVie related to this study. O.D. has received lecture, research support and consultancy fees from MSD and Abbvie. H.M. has received lecture and consultancy fees from Gilead, MSD and Abbvie.

No pharmaceutical grants were received in the development of this study.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.drugpo.2023.104044.

References

Aas, C. F., Vold, J. H., Skurtveit, S., Odsbu, I., Chalabianloo, F., Lim, A. G., Johansson, K. A., & Fadnes, L. T. (2020). Uptake and predictors of direct-acting antiviral treatment for hepatitis C among people receiving opioid agonist therapy in Sweden and Norway: A drug utilization study from 2014 to 2017. *Substance Abuse Treatment, Prevention, and Policy, 15*(1), 44. 10.1186/s13011-020-00286-2.

Aisyah, D. N., Shallcross, L., Hully, A. J., O'Brien, A., & Hayward, A. (2018). Assessing hepatitis C spontaneous clearance and understanding associated factors—A systematic review and meta-analysis. *Journal of Viral Hepatitis, 25*(6), 680–698.

Alavi, M., Raffa, J. D., Deans, G. D., Lai, C., Krajden, M., Dore, G. J., Tyndall, M. W., & Grebely, J. (2014). Continued low uptake of treatment for hepatitis C virus infection in a large community-based cohort of inner city residents. *Liver International, 34*(8), 1198–1206. 10.1111/liv.12370.

Bajis, S., Grebely, J., Hajarizadeh, B., Applegate, T., Marshall, A. D., Ellen Harrod, M., Byrne, J., Bath, N., Read, P., Edwards, M., Gorton, C., Hayllar, J., Cock, V., Peterson, S., Thomson, C., Weltman, M., Jefferies, M., Wood, W., Haber, P., Ezard, N., Martinello, M., Maher, L., & Dore, G. J. (2020). Hepatitis C virus testing, liver disease assessment and treatment uptake among people who inject drugs pre- and post-universal access to direct-acting antiviral treatment in Australia: The LiveRLife study. *Journal of Viral Hepatitis, 27*(3), 281–293. 10.1111/jvh.13233.

Bardsley, M., Heinsbroek, E., Harris, R., Croxford, S., Edmundson, C., Hope, V., Hassan, N., Ijaz, S., Mandal, S., & Shute, J. (2021). The impact of direct-acting antivirals on hepatitis C viraemia among people who inject drugs in England; real-world data 2011–2018. *Journal of viral hepatitis, 28*(10), 1452–1463.

Bartlett, S. R., Wong, S., Yu, A., Pearce, M., MacIsaac, J., Nouch, S., Adu, P., Wilton, J., Samji, H., Clementi, E., Velasquez, H., Jeong, D., Binka, M., Alvarez, M., Wong, J., Buxton, J., Krajden, M., & Janjua, N. Z. (2022). The impact of current opioid agonist therapy on Hepatitis C virus treatment initiation among people who use drugs from the direct-acting antiviral (DAA) Era: A population-based study. *Clinical Infectious Diseases, 74*(4), 575–583. 10.1093/cid/ciab546.

Bartlett, S. R., Yu, A., Chapinal, N., Rossi, C., Butt, Z., Wong, S., Darvishian, M., Gilbert, M., Wong, J., Binka, M., Alvarez, M., Tyndall, M., Krajden, M., & Janjua, N. Z. (2019). The population level care cascade for hepatitis C in British Columbia, Canada as of 2018: Impact of direct acting antivirals. *Liver International, 39*(12), 2261–2272. 10.1111/liv.14227.

Beck, AB., Lobmaier, P., Skeie, I., Lillevold, PH., & Clausen, T. (2022). SERAF RAPPORT 2/2022 - Statusrapport 2021. *Siste året med gamle LAR-retningslinjer. UiO: Det medisinske fakultet.*

Bretteville-Jensen, A. A. (2009). *Forbruk av heroin i Norge*. SIRUS, Statens institutt for rusmiddelforskning https://www.fhi.no/globalassets/dokumenterfiler/rapporter/2009-og-eldre/forbruk_heroin_norge2009.pdf.

Corcorran, M. A., Tsui, J. I., Scott, J. D., Dombrowski, J. C., & Glick, S. N. (2021). Age and gender-specific hepatitis C continuum of care and predictors of direct acting antiviral treatment among persons who inject drugs in Seattle, Washington. *Drug and Alcohol Dependence, 220*, Article 108525. 10.1016/j.drugalcdep.2021.108525.

Day, E., Hellard, M., Treloar, C., Bruneau, J., Martin, N. K., Øvrehus, A., Dalgard, O., Lloyd, A., Dillon, J., Hickman, M., Byrne, J., Litwin, A., Maticic, M., Bruggmann, P., Midgard, H., Norton, B., Trooskin, S., Lazarus, J. V., Grebely, J., & Users, t. I. N. o. H. i. S (2019). Hepatitis C elimination among people who inject drugs: Challenges and recommendations for action within a health systems framework. *Liver International, 39*(1), 20–30. 10.1111/liv.13949.

Degenhardt, L., Charlson, F., Stanaway, J., Larney, S., Alexander, L. T., Hickman, M., Cowie, B., Hall, W. D., Strang, J., & Whiteford, H. (2016). Estimating the burden of disease attributable to injecting drug use as a risk factor for HIV, hepatitis C, and hepatitis B: Findings from the Global Burden of Disease Study 2013. *The Lancet infectious diseases, 16*(12), 1385–1398. https://www.thelancet.com/pdfs/journals/laninf/PIIS1473-3099(16)30325-5.pdf.

Degenhardt, L., Grebely, J., Stone, J., Hickman, M., Vickerman, P., Marshall, B. D., Bruneau, J., Altice, F. L., Henderson, G., & Rahimi-Movaghar, A. (2019). Global patterns of opioid use and dependence: Harms to populations, interventions, and future action. *The Lancet, 394*(10208), 1560–1579.

Des Jarlais, D. C., Feelemyer, J. P., Modi, S. N., Arasteh, K., & Hagan, H. (2012). Are females who inject drugs at higher risk for HIV infection than males who inject drugs: An international systematic review of high seroprevalence areas. *Drug and Alcohol Dependence, 124*(1-2), 95–107.

Dore, G. J., Altice, F., Litwin, A. H., Dalgard, O., Gane, E. J., Shibolet, O., Luetkemeyer, A., Nahass, R., Peng, C.-Y., & Conway, B. (2016). Elbasvir–grazoprevir to treat hepatitis C virus infection in persons receiving opioid agonist therapy: A randomized trial. *Annals of internal medicine, 165*(9), 625–634.

Fadnes, L. T., Aas, C. F., Vold, J. H., Leiva, R. A., Ohldieck, C., Chalabianloo, F., Skurtveit, S., Lygren, O. J., Dalgård, O., Vickerman, P., Midgard, H., Løberg, E. M., & Johansson, K. A. (2021). Integrated treatment of hepatitis C virus infection among people who inject drugs: A multicenter randomized controlled trial (INTRO-HCV). *Plos Medicine, 18*(6), Article e1003653. 10.1371/journal.pmed.1003653.

Falade-Nwulia, O., Gicquelais, R. E., Astemborski, J., McCormick, S. D., Kirk, G., Sulkowski, M., Thomas, D. L., & Mehta, S. H. (2020). Hepatitis C treatment uptake among people who inject drugs in the oral direct-acting antiviral era. *Liver International, 40*(10), 2407–2416. 10.1111/liv.14634.

Ferraro, C. F., Stewart, D. E., Grebely, J., Tran, L. T., Zhou, S., Puca, C., Hajarizadeh, B., Larney, S., Santo Jr, T., & Higgins, J. P. (2021). Association between opioid agonist therapy use and HIV testing uptake among people who have recently injected drugs: A systematic review and meta-analysis. *Addiction, 116*(7), 1664–1676.

Fraser, H., Martin, N. K., Brummer-Korvenkontio, H., Carrieri, P., Dalgard, O., Dillon, J., Goldberg, D., Hutchinson, S., Jauffret-Roustide, M., & Kåberg, M. (2018). Model projections on the impact of HCV treatment in the prevention of HCV transmission among people who inject drugs in Europe. *Journal of Hepatology, 68*(3), 402–411.

Gotte, M., & Feld, J. J. (2016). Direct-acting antiviral agents for hepatitis C: Structural and mechanistic insights. *Nature reviews Gastroenterology & Hepatology, 13*(6), 338–351. 10.1038/nrgastro.2016.60.

Grebely, J., Bruneau, J., Lazarus, J. V., Dalgard, O., Bruggmann, P., Treloar, C., Hickman, M., Hellard, M., Roberts, T., Crooks, L., Midgard, H., Larney, S., Degenhardt, L., Alho, H., Byrne, J., Dillon, J. F., Feld, J. J., Foster, G., Goldberg, D., Lloyd, A. R., Reimer, J., Robaeys, G., Torrens, M., Wright, N., Maremmani, I., Norton, B. L., Litwin, A. H., & Dore, G. J.International Network on Hepatitis in Substance, U. (2017). Research priorities to achieve universal access to hepatitis C prevention, management and direct-acting antiviral treatment among people who inject drugs. *International Journal of Drug Policy, 47*, 51–60. 10.1016/j.drugpo.2017.05.019.

Grebely, J., Conway, B., Cunningham, E. B., Fraser, C., Moriggia, A., Gane, E., Stedman, C., Cooper, C., Castro, E., Schmid, P., Petoumenos, K., Hajarizadeh, B., Marks, P., Erratt, A., Dalgard, O., Lacombe, K., Feld, J. J., Bruneau, J., Daulouede, J. P., Powis, J., Bruggmann, P., Matthews, G. V., Kronborg, I., Shaw, D., Dunlop, A., Hellard, M., Applegate, T. L., Crawford, S., Dore, G. J., & Group, D. F. S. (2018). Paritaprevir, ritonavir, ombitasvir, and dasabuvir with and without ribavirin in people with HCV genotype 1 and recent injecting drug use or receiving opioid substitution therapy. *International Journal of Drug Policy, 62*, 94–103. 10.1016/j.drugpo.2018.10.004.

Grebely, J., Dalgard, O., Conway, B., Cunningham, E. B., Bruggmann, P., Hajarizadeh, B., Amin, J., Bruneau, J., Hellard, M., Litwin, A. H., Marks, P., Quiene, S., Siriragavan, S., Applegate, T. L., Swan, T., Byrne, J., Lacalamita, M., Dunlop, A., Matthews, G. V., Powis, J., Shaw, D., Thurnheer, M. C., Weltman, M., Kronborg, I., Cooper, C., Feld, J. J., Fraser, C., Dillon, J. F., Read, P., Gane, E., & Dore, G. J. (2018). Sofosbuvir and velpatasvir for hepatitis C virus infection in people with recent injection drug use (SIMPLIFY): An open-label, single-arm, phase 4, multicentre trial. *The Lancet Gastroenterology & Hepatology, 3*(3), 153–161. 10.1016/s2468-1253(17)30404-1.

Grebely, J., Hajarizadeh, B., Lazarus, J. V., Bruneau, J., & Treloar, C.International Network on Hepatitis in Substance, U.. (2019). Elimination of hepatitis C virus infection among people who use drugs: Ensuring equitable access to prevention, treatment, and care for all. *International Journal of Drug Policy, 72*, 1–10. 10.1016/j.drugpo.2019.07.016.

Grebely, J., Larney, S., Peacock, A., Colledge, S., Leung, J., Hickman, M., Vickerman, P., Blach, S., Cunningham, E. B., & Dumchev, K. (2019). Global, regional, and country-level estimates of hepatitis C infection among people who have recently injected drugs. *Addiction, 114*(1), 150–166.

Hajarizadeh, B., Cunningham, E. B., Reid, H., Law, M., Dore, G. J., & Grebely, J. (2018). Direct-acting antiviral treatment for hepatitis C among people who use or inject drugs: A systematic review and meta-analysis. *The Lancet Gastroenterology & Hepatology, 3*(11), 754–767.

Iversen, J., Grebely, J., Topp, L., Wand, H., Dore, G., & Maher, L. (2014). Uptake of hepatitis C treatment among people who inject drugs attending Needle and Syringe Programs in Australia, 1999-2011. *Journal of Viral Hepatitis, 21*(3), 198–207. 10.1111/jvh.12129.

Kaló, Z. (2020). Women who use drugs and mental health. *The impact of global drug policy on women: Shifting the needle*. Emerald Publishing Limited.

Karlsson, N., Santacatterina, M., Käll, K., Hägerstrand, M., Wallin, S., Berglund, T., & Ekström, A. M. (2017). Risk behaviour determinants among people who inject drugs in Stockholm, Sweden over a 10-year period, from 2002 to 2012. *Harm Reduction Journal, 14*(1), 1–11.

Kielland, K. B., Amundsen, E. J., & Dalgard, O. (2014). HCV treatment uptake in people who have injected drugs—Observations in a large cohort that received addiction treatment 1970–1984. *Scandinavian journal of Gastroenterology, 49*(12), 1465–1472.

Kåberg, M., Navér, G., Hammarberg, A., & Weiland, O. (2018). Incidence and spontaneous clearance of hepatitis C virus (HCV) in people who inject drugs at the Stockholm Needle Exchange—Importance for HCV elimination. *Journal of Viral Hepatitis, 25*(12), 1452–1461.

Micallef, J., Kaldor, J., & Dore, G. (2006). Spontaneous viral clearance following acute hepatitis C infection: A systematic review of longitudinal studies. *Journal of Viral Hepatitis, 13*(1), 34–41.

Midgard, H., Bramness, J. G., Skurtveit, S., Haukeland, J. W., & Dalgard, O. (2016). Hepatitis C treatment uptake among patients who have received opioid substitution treatment: A population-based study. *PLoS ONE, 11*(11), Article e0166451. 10.1371/journal.pone.0166451.

Midgard, H., Ulstein, K., Backe, Ø., Foshaug, T., Sørli, H., Vennesland, K., Nilssen, D., Dahl, E. H., Finbråten, A.-K., & Wüsthoff, L. (2021). Hepatitis C treatment and reinfection surveillance among people who inject drugs in a low-threshold program in Oslo, Norway. *International Journal of Drug Policy*, Article 103165.

Page, K., Evans, J. L., Hahn, J. A., Vickerman, P., Shiboski, S., & Morris, M. D. (2019). HCV incidence is associated with injecting partner age and HCV serostatus mixing in young adults who inject drugs in San Francisco. *PLoS ONE, 14*(12), Article e0226166. 10.1371/journal.pone.0226166.

Piazza, N. J., Vrbka, J. L., & Yeager, R. D. (1989). Telescoping of alcoholism in women alcoholics. *International Journal of the Addictions, 24*(1), 19–28. 10.3109/10826088909047272.

Platt, L., Minozzi, S., Reed, J., Vickerman, P., Hagan, H., French, C., Jordan, A., Degenhardt, L., Hope, V., & Hutchinson, S. (2017). Needle syringe programmes and opioid substitution therapy for preventing hepatitis C transmission in people who inject drugs. *Cochrane Database of Systematic Reviews*, (9).

Prussing, C., Bornschlegel, K., & Balter, S. (2015). Hepatitis C surveillance among youth and young adults in New York City, 2009-2013. *Journal of Urban Health, 92*(2), 387–399. 10.1007/s11524-014-9920-5.

Roberts, A., Mathers, B., & Degenhardt, L., on behalf of the Reference Group to the United Nations on HIV and Injecting Drug Use. (2010). Women who inject drugs: A review of their risks, experiences, and needs. http://www.ewna.org/wp-content/uploads/2017/09/Women-who-inject-drugs.pdf.

Rojas, T. R., Di Beo, V., Delorme, J., Barre, T., Mathurin, P., Protopopescu, C., Bailly, F., Coste, M., Authier, N., & Carrieri, M. P. (2019). Lower HCV treatment uptake in women who have received opioid agonist therapy before and during the DAA era: The ANRS FANTASIO project. *International Journal of Drug Policy, 72*, 61–68.

Roy, E., Boudreau, J. F., & Boivin, J. F. (2009). Hepatitis C virus incidence among young street-involved IDUs in relation to injection experience. *Drug and Alcohol Dependence, 102*(1-3), 158–161. 10.1016/j.drugalcdep.2009.01.006.

SAMHSA. (2017). *Substance abuse treatment: Addressing the specific needs of women* Treatment Improvement Protocol (TIP) Series, No. 51 https://store.samhsa.gov/sites/default/files/d7/priv/sma15-4426.pdf .

Smith, D. J., Jordan, A. E., Frank, M., & Hagan, H. (2016). Spontaneous viral clearance of hepatitis C virus (HCV) infection among people who inject drugs (PWID) and HIV–positive men who have sex with men (HIV+ MSM): A systematic review and meta–analysis. *BMC Infectious Diseases, 16*(1), 1–13.

Socías, M. E., Ti, L., Wood, E., Nosova, E., Hull, M., Hayashi, K., Debeck, K., & Milloy, M. J. (2019). Disparities in uptake of direct-acting antiviral therapy for hepatitis C among people who inject drugs in a Canadian setting. *Liver International, 39*(8), 1400–1407. 10.1111/liv.14043.

Sundsbø, S. M. (2013). *Unge voksne, en kartlegging av aldersgruppen 18-25 år i et åpent rusmiljø i Oslo sentrum* https://www.oslo.kommune.no/getfile.php/13122990-1461762385/Tjenester%20og%20tilbud/Helse%20og%20omsorg/Rusomsorg/Fag%20og%20kompetanse%20-%20Rusomsorg/Unge%20voksne%20i%20åpne%20rusmiljø.pdf.

Temple-Smith, M., Stoové, M., Smith, A., O'Brien, M., Mitchell, D., Banwell, C., Bammer, G., Jolley, D., & Gifford, S. (2007). Gender differences in seeking care for hepatitis C in Australia. *Journal of Substance Use, 12*(1), 59–70. 10.1080/14659890601010373.

The Norwegian Directorate of Health. (2018). *Hepatitt C skal elimineres som folkehelseproblem* https://www.helsedirektoratet.no/faglige-rad/hepatitt-c/hepatitt-c-skal-elimineres-som-folkehelseproblem-i-norge.

Valerio, H., Alavi, M., Law, M., Tillakeratne, S., Amin, J., Janjua, N. Z., Krajden, M., George, J., Matthews, G. V., & Hajarizadeh, B. (2020). High hepatitis C treatment uptake among people with recent drug dependence in New South Wales, Australia. *Journal of Hepatology*.

Valerio, H., Alavi, M., Silk, D., Treloar, C., Martinello, M., Milat, A., Dunlop, A., Holden, J., Henderson, C., Amin, J., Read, P., Marks, P., Degenhardt, L., Hayllar, J., Reid, D., Gorton, C., Lam, T., Dore, G. J., & Grebely, J. (2020). Progress towards elimination of hepatitis C infection among people who inject drugs in Australia: The ETHOS Engage Study. *Clinical Infectious Diseases*. 10.1093/cid/ciaa571.

WHO. (2016). Global health sector strategy on viral hepatitis 2016-2021. *Towards ending viral hepatitis* https://www.who.int/hepatitis/strategy2016-2021/ghss-hep/en/.

WHO. (2021). *Global progress report on HIV, viral hepatitis and sexually transmitted infections, 2021: Accountability for the global health sector strategies 2016–2021: Actions for impact: Web annex 2: Data methods.*

WHO. (2022). *Global health sector strategies on, respectively, HIV, viral hepatitis and sexually transmitted infections for the period 2022-2030.*

WHOCC. (2020). *International language for drug utilization research ATC/DDD* Retrieved 24.01.2020 from https://www.whocc.no.