

On the path towards universal coverage of hepatitis C treatment among people receiving opioid agonist therapy (OAT) in Norway: a prospective cohort study from 2013 to 2017

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Abstract

Background The development of new direct-acting antiviral (DAA) medications together with opioid agonist therapy (OAT) have been put forward as having an important role in the management and elimination of chronic hepatitis C (HCV) infection. Yet, HCV treatment uptake and coverage have remained low among OAT populations. We aimed to calculate cumulative HCV treatment coverage among individuals enrolled in OAT in Norway between 2013 and 2017, and to document the treatment transition to interferon-free regimens. Moreover, we aimed to describe adherence to DAAs in the same cohort.

Methods This observational study was based on data from The Norwegian Prescription Database (NorPD). We studied dispensed OAT and HCV treatment annually to calculate the cumulative frequency, and employed secondary sources to further calculate prevalence, incidence and HCV treatment coverage from 2013 to 2017, among the OAT population. Factors associated with adherence to DAAs were identified a priori and subject to logistic regression.

Results 10,371 individuals were identified with dispensed OAT, 1,475 individuals of these with dispensed HCV treatment. Annual HCV treatment coverage increased from 3.5% (95% CI: 3.2-4.4) in 2013 to 17% (95% CI: 17-20) in 2017, giving a cumulative HCV coverage among OAT patients in Norway of 38.5%. A complete shift to interferon-free treatment regimens occurred, where DAAs accounting for 32% of HCV treatments in 2013 and 99% in 2017. About two-thirds of OAT patients were considered adherent to their DAA regimens across all genotypes. High-level of OAT continuity was associated with improved adherence to DAAs ($aOR\ 1.4,\ 95\% CI:\ 1.2,\ p=0.035$).

Conclusions A large increase in HCV treatment coverage attributed by a complete shift to interferon-free regimens among the Norwegian OAT population has been demonstrated. However, a further substantial scale-up in HCV treatment is required to reach the universal targets of controlling and eradicating the HCV endemic.

Background

The large burden of chronic hepatitis C (HCV) among people who inject drugs (PWID) and recent developments in HCV medications creates an opportunity to eradicate HCV epidemics. Worldwide, about 71 million people are chronically infected with the virus and 399.000 died annually from HCV related complications like liver cirrhosis or hepatocellular carcinoma [1, 2]. Despite the low aggregated HCV prevalence in many countries (1.5-3.5% in Western Europe and <1.5% in North America), prevalence is much higher among PWID (50%, or more) [3-5]. The World Health Organization's Global Health Sector Strategy aims to eliminate viral hepatitis as a public health treat by 2030 [2]. The even bolder Norwegian HCV strategy aims to reduce national incidence by 90% by 2023 [6]. Eliminating chronic HCV requires a significant effort in terms of increasing uptake of testing, diagnosing, and linking to care. In addition, other strategies have been proposed alongside increasing antiviral treatment, such as opioid agonist therapy (OAT) scale-up, safe injection sites and sterile injection equipment to reach these objectives [2, 7].

Injecting drug use and needle sharing is the major driver of HCV incidence [8], however, the coverage of preventive interventions, such as needle and syringe programs, remains poor among PWIDs [9]. Number

of PWIDs in Norway is stable at around 9000 (2.6 per 1 000 inhabitants aged 15-64 years) [10, 11], and opioids and amphetamines are the main injected drugs [11, 12]. Modelling studies suggest that around 7000 former and current PWIDs are living with chronic HCV with an estimated 400 new cases annually [13, 14]. Both HCV-related liver morbidity and mortality are increasing among PWIDs and are likely to continue to increase until 2022 [14].

OAT has been put forward to play a vital role in the management of chronic HCV among people with opioid dependence and has been shown to reduce the risk of HCV acquisition [15]. For these reasons, OAT may be crucial intervention for achieving large reductions in HCV transmissions by reducing risk behaviors like injecting use, sharing of injecting equipment and number of sex partners [16]. HCV testing rates have been low in the national OAT program in Norway with great annual and regional variations [5, 17-20]. Only in parts of western Norway, as part of the multicenter INTRO-HCV study, all patients receiving OAT have been systematically tested and examined with elastography as part of an annual health assessment since 2017 [21]. Even if access to HCV treatment is improving, HCV treatment coverage remains low [8, 22-25]. Globally, the coverage of HCV curative treatment was 13% by 2016 [26]. In Norway, annual HCV treatment coverage among OAT patients was between 1.3% to 2.6% in the period from 2004 to 2013, giving a cumulative HCV coverage for the period of 14% [27].

The introduction of direct-acting antiviral (DAAs) medications, with a curation rate of >90%, safer and better-tolerated than interferon-based therapy, has dramatically changed the treatment of chronic HCV infections [28, 29]. Even if currently expensive, they are considered cost effective from a societal perspective as universal coverage with antiretroviral treatment could prevent large expenses related to future complications [30-35]. Combining DAAs with the OAT delivery platform may thus prove critical for achieving reductions in HCV prevalence and incidence [22]. A number of treatment barriers exist, which should in turn be carefully addressed, nevertheless, treatment barriers should not exclude PWIDs from HCV treatment [8, 36, 37]. Both World Health Organization and Norwegian guidelines support DAA treatment among PWIDs and have also shown good outcomes in systematic reviews [24, 25, 38].

The pathway to universal HCV treatment coverage has not been well documented at country levels, hence, the primary aim of the study was to:

- Document HCV treatment uptake annually and cumulatively after the introduction of DAAs among patients receiving OAT in Norway from 2013-2017 and to calculate HCV treatment coverage, both annually and cumulatively.
- A secondary objective is to document whether there has been a shift or not to interferon-free treatment regimens.

- A third objective is to evaluate adherence to DAAs among OAT patients across all genotypes in Norway as there are limited studies among this marginalized group of patients.

Methods

2.1 Study design and data sources

This is an observational study among OAT patients from 2013 to 2017 in Norway. Data were extracted from The Norwegian Prescription Database (NorPD) from January 1, 2013 to March 31, 2018. The database covers the entire Norwegian population and records all drugs dispensed from pharmacies in Norway, hence leaving only over-the-counter drugs and drugs administered at hospitals and nursing homes. All drugs are classified according to The Anatomical Therapeutic Chemical (ATC) classification system [39]. Defined daily doses (DDDs) according to 2018 [40] were employed to quantify the dispensed OAT and HCV medications respectively. The DDDs are the assumed average maintenance dose per day for a drug used for its main indication [41].

Data from The Norwegian Centre for Addiction Research were used for estimating the prevalence of chronic HCV among OAT patients, whereas incidence data among Norwegian PWIDs was gathered from The Norwegian Institute of Public Health and Meijerink et al. [14] The former publish annual status reports on prevalence, whereas the latter have demonstrated the incidence in a compartmental model for HCV infections from 1973-2030 in Norway. These data were not linked on an individual level.

2.2 Study population and definitions

The study population included all individuals with at least one dispensed prescription of buprenorphine (ATC code N07BC01), methadone (N07BC02), buprenorphine-naloxone (N07BC51), and levomethadone (N07BC05). Other opioids are very rarely used for OAT in Norway and considered outside national guidelines [42]. Patients <18 years and with other indications than OAT were excluded from the study on the basis of formulation, chronic pain and palliative care reimbursement codes (Figure S1).

Exposure to HCV treatment was defined as being dispensed either pegylated interferon alpha (L03AB05 and L03AB11) and ribavirin (J05AP01) or DAAs (group J05AP) during the study period. Thus, definition of treatment uptake was any individual on OAT who has been dispensed HCV treatment. Any individual who died was censored in the calendar year they passed away. Rates were calculated by dividing number of individuals with dispensed HCV treatment by individuals on OAT, stratified by each calendar year. The cumulative frequency, which is the addition of successive years of treatment uptake, was then calculated.

HCV treatment was stratified as overall treatment with any chronic HCV medication and treatment with solely DAAs.

HCV treatment coverage was defined as individuals on OAT identified in NorPD annually, adjusted for death, HCV prevalence, and new cases of chronic HCV each year, which had received treatment for chronic HCV during the study period. Mean prevalence during the study period among patients enrolled in OAT ranged from 51% in 2013 to 43% in 2017 [5, 17-20] and proportional prevalence among OAT individuals were calculated per calendar year. Incidence was around 400 per year for PWIDs during the study period [14]. It proved methodologically challenging to estimate the HCV incidence among OAT individuals from PWIDs due to lack of reliable evidence from the literature, and for this reason expert opinion were obtained from clinicians in addiction medicine and set to 0.70 (70%). We developed the following basic model for our coverage calculation:

$$HCV_{cov} = \frac{t_{HCV}}{p_{HCV} + i_{HCV}} * 100$$

where HCV cov is HCV coverage, t_HCV = number of OAT patients with dispensed HCV treatment, p_HCV = number of OAT patients with chronic HCV and i_HCV = number of new cases of chronic HCV among OAT patients. Coverage was calculated annually for Norway and by Health County, and as cumulative frequencies.

We defined adherence to DAA as having collected prescriptions equivalent to three months of treatment or more. DAAs for adults, which in Norway is prescribed only by specialists in either infectious medicine or gastroenterology, are collected for one-month-at-a-time basis where a typical DAA treatment course is 12 weeks, i.e. three dispensed prescriptions and ≥ 84 DDDs. The exception is the drug combination ledipasvir/sofosbuvir, which may be prescribed for eight weeks (two collections and ≥ 54 DDD) for cases of previously untreated genotype 1 infections. This allowed us to examine adherence based on number of dispensed prescriptions and DDDs. Impending factors associated with treatment adherence to DAAs were identified a priori and included gender, age, and OAT continuity, and subject to multivariate analyzes in a step-by-step model.

Finally, OAT continuity was defined according to dispensed DDDs and stratified into three categories, ranging from a high level of OAT continuity in category I (>2 DDD), medium in category II (2-1 DDD), and to a low level of OAT continuity in category III (<12 DDD). One DDD for methadone and buprenorphine is 25mg and 8mg respectively.

2.3 Statistical analyzes and strategy

Descriptive data are presented as frequencies, percentages, means, and with corresponding 95% confidence intervals where appropriate. Logistic regression on factors associated with adherence are presented as adjusted odds ratio (aOR) when adjusted for age, gender and OAT continuity.

The initial processing of the received encrypted file from NorPD was completed in SPSS version 24. Secondly, the file was converted and subsequently analyzed in Stata SE version 15 (StataCorp, TX, USA). Map figures were made in R.

2.4 Data handling and ethical considerations

Since all data was analyzed anonymously no written consent was obtained from any of the individuals in the study. This study was approved by the regional committee for ethics in medical research (no. 2018/939/REK Vest). It was conducted in accordance with the Helsinki Declaration and as an observational study in accordance with international accepted STROBE guidelines [43].

Results

3.1 Basic characteristics of study population

A total of 10,371 individuals were identified in NorPD having received ≥ 1 OAT prescriptions during the study period from 2013 to 2017 (Table 1). Almost 70% were male, mean age of 43 years and 45 years in 2013 and 2017, respectively. The majority of the OAT patients were treated with buprenorphine-based OAT medication (55% in 2013, 60% in 2017). Over 50% of individuals on OAT had a high level of continuity. Altogether 692 individuals died during the study period.

(insert Table 1)

3.2 HCV treatment uptake and coverage

3.2.1 HCV and DAA treatment uptake

All individuals were stratified according to the year in which they received OAT and HCV treatment. Excluding deaths, this gave a fairly stable OAT population just in excess of 7500 annually. In 2013, 146 OAT patients received HCV treatment. Treatment uptake increased over time with 597 patients receiving HCV treatment in 2017. Overall 1475 patients on OAT received HCV treatment during the study period, with an annual HCV treatment uptake increasing from 1.9% (95% CI: 1.6-2.3%) of OAT patients in 2013, to 7.9% (95% CI: 7.3-8.5%) in 2017 (Table S1). By 2017, the cumulative frequency of HCV treatment reached 19% among patients on OAT.

Of the 1475 individuals that received HCV treatment during the study period, 1235 were treated with DAA medications. The annual DAA treatment uptake ranged from 0.6% (95% CI: 0.4-0.8%) in 2013, to 7.8 (95% CI: 7.2-8.4%) in 2017. The proportion of treated individuals receiving DAAs increased over time from 32% of HCV treated OAT patients in 2013 to 99% in 2017.

3.2.2 HCV treatment: coverage

We calculated annual HCV coverage among the estimated number of OAT patients that are HCV infected, which ranged from 3.5% (95% CI: 3.2-4.4%) in 2013 to 17% (95% CI: 16.9-19.6%) in 2017. This gave a cumulative frequency that reached 38.5% in 2017 (Table 2). Figure 1 shows cumulative HCV coverage from 2013 to 2017 by the four health counties in Norway (HCV_{cov} and data from Table S2 were used for these calculations). There is little variation in treatment coverage across the four health counties.

(insert Figure 1 + Table 2)

3.3 Adherence to DAAs

Overall, almost 70% of the OAT patients were adherent to their DAA regimen and thought to have finished their DAA treatment course (Table 3). There was no major differences by gender or OAT drug. However, for age, patients in the age group 18-35 were less adherent (42%) compared with older age groups. The

drug combination of elbasvir/grazoprevir, commonly used for treatment of genotype 1 infections, had by far the utmost adherence (93%) compared to treatment combinations of sofosbuvir/velpatasvir, and ledipasvir/sofosbuvir, which both were around 70%. However, sometimes ledipasvir/sofosbuvir is prescribed for eight weeks, in which case yields an overall adherence of 78%.

In multivariate analyzes, only adherence to DAAs was associated with OAT continuity (adjusted OR 1.4, 95% CI: 1.0-1.8 p=0.035).

(insert Table 3)

Discussion

The HCV treatment coverage has increased substantially, yet it seems to low if the ambitious targets of ending the endemic are to be met. Annual treatment uptake increased from 1.9% of all OAT patients in Norway in 2013 to 7.9% in 2017, which gives a cumulative frequency of around 19% over the study period. However, cumulative HCV treatment coverage among OAT patients with assumed chronic HCV in Norway was just above 38%, with annual treatment rates that ranged from 3.5% in 2013 to 17% in 2017. Secondly, we observed a complete shift in the HCV treatment among OAT patients in Norway during the study period, from two-thirds treated with DAAs in 2013, to nearly all in 2017 (99%). Finally, about two-thirds of all OAT patients with chronic HCV were considered adherent to their DAAs regimen, which improved with level of OAT continuity.

Immense advances have been made in chronic HCV treatment since the introduction of DAAs in recent years, however multiple studies have demonstrated continued low treatment uptake among PWIDs and OAT patients midst this marginalized group of patients [23, 27, 44]. The marked scale-up and complete shift to DAAs among OAT patients in Norway during the study period is in line with both international recommendations set out by the WHO and national guidelines to offer HCV treatment to both PWIDs and OAT patients [2, 45]. Prior to the introduction of DAAs, Midgard et al (2016) showed an annual treatment coverage of 1.3% to 2.6% between 2004 and 2013 among Norwegian OAT patients, giving a cumulative treatment coverage of 14% during the entire study period. Considering there is not in place a national and systematic program for testing and linking to HCV care among PWIDs, nor has the full effectiveness of integrated treatment combining OAT and HCV treatment been fully demonstrated [46], HCV coverage would probably be substantially higher with a comprehensive model of integrative care where both testing and treatment were provided in OAT outpatient clinics.

Treatment with DAAs in Norway was until February 1, 2018, limited by strict eligibility criteria based on stage of liver fibrosis. Since then, DAA treatment has been offered to all regardless of genotype and level of liver fibrosis. As a result, treatment demand increased and coverage of curative HCV treatment has amplified, especially among former PWIDs and immigrants [13] being infected prior to the arrival in Norway. Nonetheless, despite high availability of new treatment, access remains low to current PWIDs [13]. The Norwegian Hepatitis C policy identifies improved access to treatment, prevention, and surveillance of the endemic as crucial to succeed with HCV eradication [42]. Arguably, even with DAA treatment for all, low threshold OAT, needle and syringe programs in place, it is hard to see how this can be achieved unless testing and linkage to care is provided where PWIDs and OAT patients actually are. This opts for decentralized testing and treatment and probably a change in how the specialist health care delivers treatment for current PWIDs. In terms of surveillance, chronic HCV prevalence and incidence data are not readily available for Norway. The infection is regarded as a Group A infectious disease and it has been mandatory to notify The Norwegian Surveillance System for Communicable Diseases (MSIS) since 1990. However, only cases of acute HCV was notifiable initially. Since January 1, 2016 it was changed to merely include HCV RNA and HCV core antigen [13]. Thus, it is impossible to tell whether cases before 2016 were acute or chronic, or whether patients achieved sustained virological response (SVR) on their own, or how many cases were actually notified [27].

About two-thirds of all patients were considered adherent to DAAs according to recommendations from the prescribing specialist, across all genotypes. Adherence can be a key predictor for response to DAAs [47]. Elbasvir/grazoprevir (93%), clinically associated with genotype 1 and 4, came across as the most adherent drug combination, while the other most encountered combinations of DAAs were around 70%. Our intention was to evaluate to what extent patients initiated and complied to treatment, rather than drawing a comparison between individual DAAs. The main reason for this is varying adherence to drug protocol and guidelines for DAAs during the study period from a prescriber's perspective. A Swedish study found that adherence to drug recommendations varied considerably between genotypes and was only moderate after introduction of DAAs, although it increased markedly after 2015 [48]. Adherence to DAAs was associated with OAT continuity, and as such, predicted a higher adherence compared to lower level of OAT continuity in our model. Studies have shown that patients receiving higher doses of OAT, e.g. methadone, above 60mg/day, have better treatment outcomes compared to lower doses [42, 49] and for this reason we set high level of continuity above two DDD. This is in line with previous studies demonstrating that OAT continuity is a factor for HCV treatment [27]. Age was not considered statistical significant, however, considerable less adherence was noted in the younger age groups. Although there are few real-life studies measuring adherence among this marginalized group of patients, some studies, for example the SIMPLIFY study, have shown a much higher level of adherence among recent PWIDs [50]. Similarly, a Canadian study demonstrated that strong adherence to DAAs is achievable with appropriate support [47]. Dissimilarities in methodology and study settings, however, prevent for precise comparisons. Linking these data, on an individual level, to biomarkers of SVR12 was, however, beyond the scope of this

paper. In addition, we had no system in place to control whether these patients actually swallowed and metabolized these drugs and as such cannot comment to the extent the medications were actually taken.

Strengths And Limitations

All dispensed drugs in Norway are registered in NorPD. This provide researchers and other stakeholders alike with sound, precise and a near complete database. The main strength of the study is thus it provides a large sample of OAT individuals being treated for chronic HCV, and as such can serve as baseline data for further research, especially decision-modelling for eradicating chronic HCV in Norway.

However, as with all observational studies there are several limitations, which should be considered when interpreting both results and conclusions. First, treatment with OAT in Norway is not uniform. Some individuals collect the drugs at pharmacies as dispensed prescriptions while others receive the drugs at OAT outpatient clinics. Drugs administered in outpatient clinics are not necessarily captured by the prescription database (NorPD). Secondly, OAT and HCV treatment administered to hospitalized and institutionalized patients are not recorded in NorPD. Nonetheless, it should be stated that almost all HCV treatment is initiated in outpatient clinics in Norway and hence included in NorPD [27, 51]. In addition, some dispensed prescriptions may lack reimbursement codes and medical indication for use, and DDDs does not necessarily reflect the Prescribed Daily Dose (PDD).

Furthermore, data was not linked on an individual level to diagnosis codes of chronic HCV. This is due to the quality of MSIS prior to 2016 is poor and the authors had to employ other data sources when estimating HCV prevalence and incidence rates from a number of different sources, including modelling and expert opinion. For example, when calculating the HCV prevalence, mean population data for Norway was used, rather than more accurate regional data as the latter was not readily available.

When measuring adherence among different age groups we should be careful when interpreting results. Older patients are more likely to have cirrhosis and longer HCV treatment courses compared to younger patients. Finally, PWIDs are a heterogenic group of individuals, and one should be careful not to generalize OAT patients to include all PWIDs.

Conclusions

This is the first population-based study documenting the transition to DAA treatment regimens among Norwegian OAT patients. A marked scale-up in HCV treatment attributed by a complete shift to interferon-free regimens among Norwegian OAT patients has been demonstrated. Adherence to DAAs across all

genotypes remained sound, especially for genotype 1 and for high level of OAT continuity. Annual HCV treatment coverage ranged from 3.5% in 2013 to 17% in 2017, giving a cumulative HCV coverage among OAT patients for the study period just above 38%. However, Norway is far from universal coverage of HCV treatment. There is a need to establish more accurate monitoring system and more precision in prevalence and incidence rates of chronic HCV among PWID to get more precise coverage data. Efficacy of health system strategies is needed in order to further scale-up of the most effective HCV policies to this group and for countries to be able to control and eliminate HCV.

Abbreviations

OAT	Opioid agonist therapy
DAA	Direct-acting antivirals
HCV	Hepatitis C virus
PWID	People who inject drugs
NorPD	The Norwegian Prescription Database
ATC	Anatomical Therapeutic Chemical classification system
DDD	Defined daily dose
PPP	Prescribed daily dose
NIPH	The Norwegian Institute for Public Health
SERAFF	The Norwegian Centre for Addiction Research
MSIS	The Norwegian Surveillance System for Communicable Diseases
Anti-HCV	Antibodies to the Hepatitis C virus
SVR	Sustained virological response
INTRO-HCV	Integrated treatment of hepatitis C virus infection

Declarations

Ethical approval and consent to participate

The study was approved by the Regional Ethical Committee (REK Vest), Norway, on June 19, 2018. No informed consent from the participants was necessary.

Consent for publication

Not applicable.

Availability of data and material

Supplemental tables, figure and data sources in this observational study are available in this published article and its additional files.

Competing interests

I.O. is employed at the Centre for Pharmacoepidemiology, Karolinska Institutet, which receives grants from several entities (pharmaceutical companies, regulatory authorities, and contract research organizations) for performance of drug safety and drug utilization studies, unrelated to this work. None of the other authors have competing interests.

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Authors' contributions

This observational study was led by CFA in terms of study design, analyzes, drafting and writing the article. SS and JHV was particularly involved with acquisition of data, analyzes and interpretation. Maps were made by JMØ and KAJ. All authors contributed to the conception, writing, and revising the draft(s) critically. All authors have read and approved the version to be published.

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Tables

Table 1: Basic characteristics of patients receiving OAT from 2013 to 2017 in Norway

Basic characteristics	Total	2013	2014	2015	2016	2017
Individuals >1 OAT	10371	7709	7914	7958	7804	7709
Deaths	692	165	151	138	114	124
<hr/>						
Gender, n (%)						
Male	7135 (69)	5221 (69)	5390 (69)	5430 (69)	5354 (70)	5254 (69)
Female	3236 (31)	2323 (31)	2373 (31)	2390 (31)	2336 (30)	2340 (31)
<hr/>						
Age, n (%)						
<25		211 (3)	185 (2)	171 (3)	135 (2)	120 (2)
26-40		2813 (37)	2797 (36)	2718 (40)	2574 (33)	2432 (32)
41-60		4289 (57)	4537 (58)	3644 (53)	4627 (60)	4613 (61)
>60		231 (3)	244 (3)	287 (4)	354 (5)	420 (6)
<hr/>						
OAT medication, n (%)						
Methadone/Levomethadone		3406 (45)	3264 (42)	3216 (41)	3066 (40)	2981 (39)
Buprenorphine based*		4138 (55)	4499 (58)	4604 (59)	4624 (60)	4604 (61)
<hr/>						
Dispensations of HCV drugs**	1475	146	167	243	322	597
<hr/>						
OAT continuity category, n (%)						
I: ≥2 DDD		5310 (51)				
II: 1- <2 DDD		3078 (30)				

III: <1 DDD

1983
(19)

OAT = opioid agonist therapy; DDD = Daily defined Doses

Source: NorPD = Norwegian Prescription Database

* Buprenorphine and buprenorphine/naloxone

** HCV drugs: interferon-based and direct-acting antivirals (DAAs)

Table 2: Annual and cumulative chronic HCV treatment coverage among OAT patients in Norway between 2013 and 2017

	Source	2013	2014	2015	2016	2017	Total
Chronic HCV treatment n (overall)	NorPD	146	167	243	322	597	1475
DAAs, n	NorPD	46	95	212	290	592	1235
DAAs % of HCV		32	57	87	90	99	84
Study population n, yearly incl. deaths	NorPD	7709	7914	7958	7804	7709	10371
Deaths	NorPD	165	151	138	114	124	692
Study population n, yearly, excl. deaths	NorPD	7544	7763	7820	7690	7585	9679
Prevalence chronic HCV, mean %	SERAFF	51	52	52	46	43	
Prevalence chronic HCV, n	SERAFF	3847	4037	4066	3537	3262	
Incidence chronic HCV among PWIDs n	NIPH, Meijerink et al.	396	388	381	374	366	
Incidence chronic HCV OAT from PWIDs n	Expert opinion	277	272	267	262	256	
Treatment coverage chronic HCV %		3.5	3.9	5.6	8.5	17.0	
Cumulative frequency chronic HCV		3.5	7.4	13.0	21.5	38.5	
95% Confidence intervall treatment coverage chronic HCV		3.2-4.4	3.5-4.8	5.3-6.7	8.2-10.1	16.9-19.6	

OAT = opioid agonist therapy, PWID = people who inject drugs, HCV = hepatitis C virus, DAA = direct-acting antivirals,

Sources: NorPD = Norwegian Prescription Database, SERAFF = The Norwegian Centre for Addiction Research, NIPH = Norwegian Institute for Public Health, Meijerink et al. (2017): Modelling the burden of hepatitis C infection among people who inject drugs in Norway, 1973-2030

Table 3: Adherence* to DAAs among OAT patients in Norway between 2013 and 2017

	Adherent	Non-Adherent	Total:
Adherence by gender, n (%):			
Male	551 (67)	191 (67)	742 (67)
Female	277 (33)	92 (33)	369 (33)
Total	828	283	1111
Adherence by age, n (%):			
18-35	119 (58)	85 (42)	204
36-45	259 (68)	122 (32)	381
46-55	302 (70)	128 (30)	430
>56	62 (65)	34 (35)	95
Total	742 (67)	369 (33)	1111
Adherence by OAT medication, n (%):			
Methadone	298 (65)	157 (35)	455
Buprenorphine based	444 (68)	212 (32)	656
Total	742 (67)	369 (33)	1111

Logistic regression on factors associated with adherence*

	aOR (CI 95%)	p-value
Age	0.98 (0.97-1.00)	0.17
Gender		
Male	1.00	
Female	0.92 (0.69-1.23)	0.57
OAT continuity		
Category I: >2 DDD	1.00	
Category II: <2-1 DDD	1.36 (1.02-1.82)	0.035
Category III: <1 DDD	1.36 (0.93-1.99)	0.11

OAT = opioid agonist therapy, DAA = direct-acting antivirals, aOR = adjusted odds ratio, CI = confidence interval, DDD = daily defined doses

Source: NorPD = Norwegian Prescription Database

*Adherence defined as collected \geq three prescriptions and > 84 DDDs (unless ledipasvir and sofosbuvir which also calculated as \geq two prescriptions and > 54 DDDs)

Figures

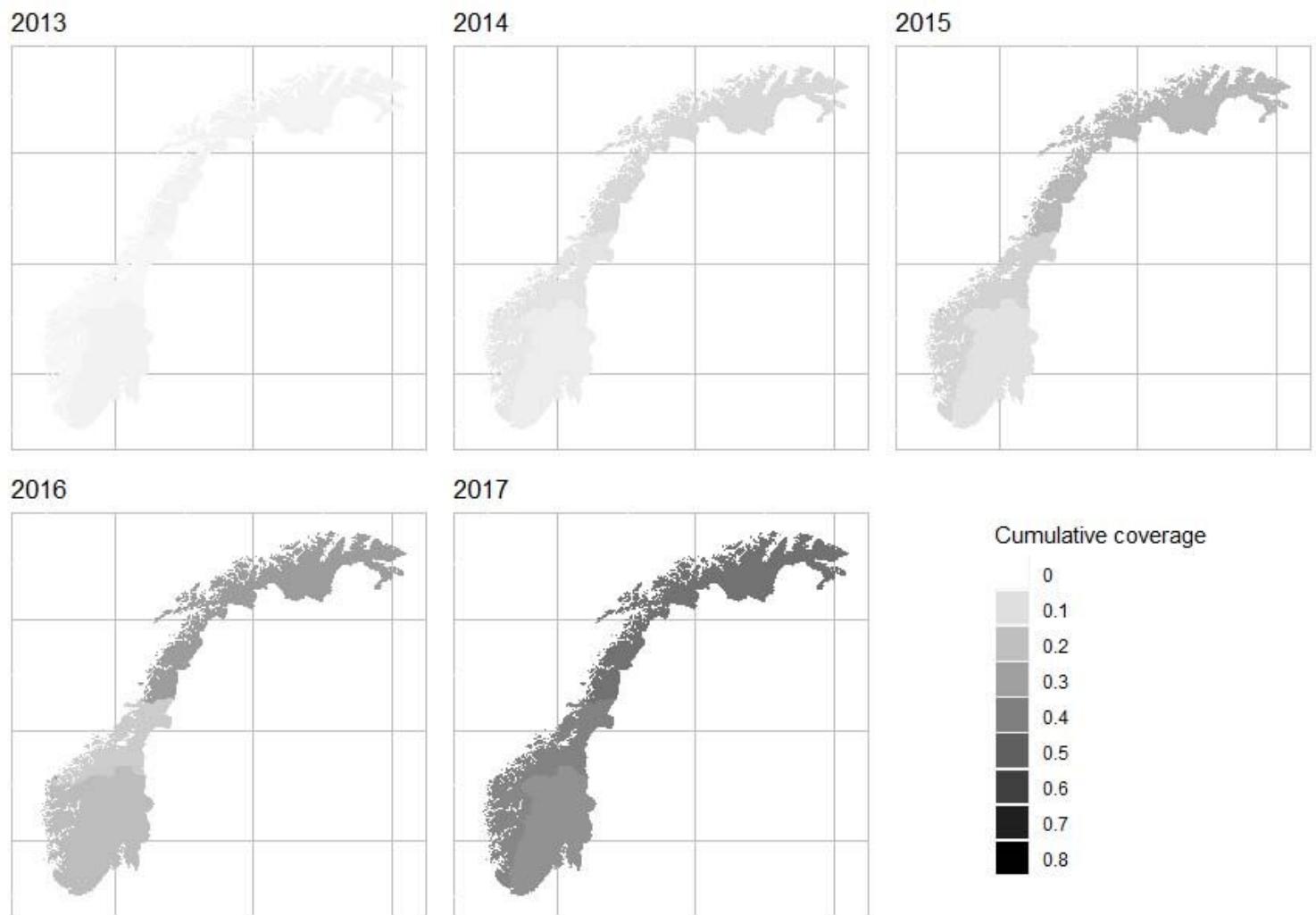


Figure 1

Cumulative HCV treatment coverage among OAT patients
Caption: OAT = opioid agonist therapy, HCV = hepatitis C virus. The figure displays the cumulative chronic HCV treatment coverage among OAT patients in Norway between 2013 and 2017. Cumulative HCV coverage is given in % according to Norway's four health regions. Sources: NorPD = Norwegian Prescription Database, SERAF = The Norwegian Centre for Addiction Research, NIPH = Norwegian Institute for Public Health, Meijerink et al. (2017): Modelling the burden of hepatitis C infection among people who inject drugs in Norway, 1973–2030, calculations are provided in Table S2

Supplementary Files

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- [Additionalfile1STROBEStatement.pdf](#)
- [Additionalfile2Flowchartofstudypopulation.tif](#)
- [Additionalfile4TableS2.xlsx](#)
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