Heroin-assisted treatment midway report from 2022-2023

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Abbreviations

GP	General practitioner
HABiB	Heroin-assisted treatment in Bergen
HABiO	Heroin-assisted treatment in Oslo
HAT	Heroin-assisted treatment
IM	Intramuscular
IV	Intravenous
NAV	Norwegian Labor and Welfare Administration
SROM	Slow-release oral morphine
OAT	Opioid agonist treatment
OUD	Opioid use disorder
OUS	Oslo University Hospital

Executive Summary

This midway report examines the first two years of Norway's first heroin-assisted treatment (HAT) program, planned to run through 2026, as a time-limited clinical pilot project. The pilot project HAT was established as part of opioid agonist treatment (OAT) in Oslo and Bergen. From January 1, 2022, until December 31, 2023, 92 of a total of 97 patients were included in the research project to evaluate the newly established HAT clinics. This report describes the establishment of the clinics, patient experiences, and patient-reported outcomes while in heroin-assisted treatment. This report provides a midway assessment, and a final and extended report will be provided during the first half of 2026.

Key findings against evaluation questions:

1. To what extent have the clinics been implemented as intended?

Broadly, the clinics have been implemented as intended in both Oslo and Bergen (open for twice-daily supervised heroin intake, injectable and tablet heroin is available, and additional psychosocial and healthcare services offered). Patients receive a standard OAT medication, usually methadone or long-acting morphine, for an overnight bridge medication. During this initial HAT pilot period, national guidelines for OAT were updated to include the use of 6-12-hour and 24-hour morphine tablets (SROM). These morphine-based medications have also been prescribed to HAT patients as an option for their overnight bridge medication. Although the use of 24-hour morphine is currently supported by the OAT guidelines, the international evidence base for HAT is derived from the use of methadone as an overnight bridge medication. The impact of using these morphine-based medications as the overnight bridge medication for HAT is unknown.

Additionally, the clinic's capacity is less than original estimates. The original heroin-assisted treatment patient project was estimated to attract up to 10% of people who inject opioid drugs in Oslo and Bergen, resulting in approximately 150-300 patients as the total treatment capacity when full capacity would be reached. At the midway point, approximately one-third of this estimate are currently enrolled.

The establishment of new treatment clinics was accompanied by many logistical and practical considerations. Establishing and optimizing clinical routines, staff recruitment and training,

access to the medication, and promoting buy-in among prospective patients and referring clinicians has been a process. These various considerations may collectively have contributed to the inclusion of patients taking longer, or starting later, than what was originally anticipated.

2. What were the referral, enrollment, and retention rates for the first two years?

From the opening of the clinics in the beginning of 2022 until the end of 2023, 167 referrals were received (56 in Bergen and 111 in Oslo). In total, 37% of referrals were refused (29% in Bergen and 41% in Oslo). The most common reason for refusal was "admission pause" at the HAT clinic, meaning that the clinic was at its maximum capacity, as decided by the clinic management. This was the reason for 28% of the refusals in total (6% in Bergen and 36% in Oslo).

There have been 97 patients enrolled in heroin-assisted treatment, and 92 consented to be followed up by the research study (65 in Oslo, 27 in Bergen). Since the opening of the clinics, there have been 27 patients (29%) that have left treatment (21 from Oslo, 6 from Bergen). Of these, over half of the patients were transferred to conventional OAT.

3. What were the main experiences of heroin-assisted treatment from the perspectives of patients, their relatives, and clinicians?

To date, 111 interviews have been conducted (61 with patients, 32 with clinicians, and 18 with patients' relatives). Overall, patients' satisfaction with heroin-assisted treatment was high. The program has low attrition rates, and patients adapted quickly to new routines. From the patients' perspectives, the three most common benefits of being in HAT were access to medical heroin, the positive patient-clinician relations, and the supportive environment of the clinic. The most challenging aspects were the intense treatment regimen, the strict clinic rules, as well as the increased downtime and concerns over the future of heroin-assisted treatment.

Relatives of patients had varied experiences of heroin-assisted treatment's impact on the patients and on their own caring tasks, but they were generally positive towards the treatment because of the structure of care and safety, including observed medication intake by health personnel and medicinal quality of the medication the program provided.

Clinicians reported aspects of treatment provision that were rewarding, which made them believe in the treatment's feasibility and utility for patients. Clinicians also reported challenges relating to dosing and rule enforcement.

4. What are the key characteristics of patients enrolling in heroin-assisted treatment?

At admission, patients had a mean age of 46 and the majority were male (80%). Most patients were born in Norway (87%). Patients reported multiple vulnerabilities when enrolling in treatment, as detailed below.

- **Housing**: Although no participants reported experiencing homelessness at the beginning of treatment, 17% reported their housing being unstable in the previous month.
- **Employment and education**: Almost all participants were unemployed at the start of treatment, with only four reporting part-time work. Approximately 47% of participants had not completed secondary school education, and 20% reported difficulties with reading and/or writing.
- **Food access**: In the month prior to treatment start, half of patients reported hunger and one-third reported limited food access.
- **Crime**: 11% of participants reported recent incarceration, and more than half of the patients (62%) report being a victim of a crime in the 3 months prior to starting heroin-assisted treatment.
- **Health**: Overall, participants' mental and physical health were poor at baseline: 20% rated their mental health as bad. The main physical complaints included sleep difficulties, oral health complaints, joint pain and reduced memory perceived as the most problematic.
- **Substance use:** the use of multiple substances was common for the group. Nearly all patients (90%) reported using illegal heroin during their lifetime, with high proportions also reporting lifetime use of cannabis, amphetamines and methamphetamines, and other illicit opioids Approximately 40% of patients had experienced an unplanned overdose in their lifetime, with 6% experiencing one in the month prior to treatment initiation.

The HAT population seems to be burdened across multiple domains, and at a higher level than what is seen with patients in conventional opioid agonist treatment in Norway. These initial findings indicate that HAT may reach a more severely burdened segment of those with opioid use disorder than conventional opioid agonist treatment.

5. What areas of patients' lives improve while in heroin-assisted treatment?

Trend and change analyses are ongoing and only preliminary findings are available to show the effects of treatment. Results will be available in the final report in 2026 in an extended format.

However, preliminary trends indicate a **reduction in criminality**. One year after treatment started, there was a 65% reduction in self-reported crimes committed for profit, and a 31% reduction in drug-related crimes.

Additionally, preliminary analyses show **improvements in self-reported mental and physical health**. At follow-up, the percentage of those that rated their mental health as good increased to nearly 50% at 12 months, a change of 52% from baseline. Over time, patients reporting severe physical symptoms progressively decreased at three months (43%), six months (38%) and 12 months (34%). These findings suggest a gradual improvement in the self-reported somatic symptom severity over the course of the treatment, but improvements that develop gradually over time following longer-term treatment adherence.

It is important to note that while the severity of symptoms is declining, most patients are still reporting either moderate or severe symptoms even after 12 months of treatment, which indicates that while there is an improvement, many patients continue to experience a significant burden of symptoms, again hinting towards long-term treatment needs.

6. What is the cost-benefit assessment of the intervention?

Funding for both clinics in Oslo and Bergen was approximately 155 million NOK combined for the period of 2020-2023 (Oslo 103 million, Bergen 52 million). The last two years (from 2022-2023) contain the period when patients were included. We are not aware of the clinics receiving any additional funding beyond what was granted by the Ministry of Health. The funding is intended to cover clinic facilities, staff, medications, and "other costs," of which the costs for 2023 in Oslo were distributed roughly as 60% staff, 28% medications, and 12% on

other costs (including rent for the clinic, etc.). Reports indicate that medication costs are increasing which was not taken into account in the allocated budget. The clinics report that the allocated funding limits treatment capacity, and at the same time, and that limited funding at least partially explains the “intake-stop” which occurred during 2023.

A formal cost-benefit analysis of the evaluation will be available in the final report in 2026.

7. Should heroin-assisted treatment continue? If so, what changes are needed?

At the midway point, heroin-assisted treatment appears to show initial indications of improvement for patients that remain in treatment over time. Clinic capacity and budget will need to be addressed to enable clinics to reach their full potential. A more complete description of patient progress and the impact of the intervention will be provided in the final report in 2026.

1. Introduction

1.1 Opioid agonist treatment and the need for heroin-assisted treatment

Opioid use disorder (OUD) is often understood as a chronic, recurrent condition associated with a range of physical, social, and psychological problems that place a significant burden on the individual in terms of morbidity and mortality. Due to the chronic course of OUD, people with the condition often require long-term involvement from the treatment system. Opioid agonist treatment (OAT) includes the use of opioid agonists, most often methadone and buprenorphine. In general, OAT is associated with a reduced risk of fatal overdoses, infections, and criminal behavior.

Although these forms of treatment have been successful, standard OAT does not result in satisfactory outcomes for about one in ten people with OUD, which can have fatal consequences. Heroin-assisted treatment (HAT) includes the supervised use of pharmaceutical heroin (diacetylmorphine) twice daily in a clinical setting. A long-acting opioid (traditionally methadone) is used for overnight treatment coverage. Most HAT programs use injectable or tablet diacetylmorphine, although other forms of use (inhalation and intranasal) are available in some countries, however for the latter, with less research-based documentation of effects and should therefore currently be considered experimental treatment approaches (**Table 1**).

Heroin-assisted treatment has been implemented in various countries for over 30 years (**see section 1.2**). Results from high-quality randomized controlled trials indicate that HAT can be effective in reducing crime and heroin use, and that patients in the target group remain in HAT longer than in methadone-only-based OAT [1, 2]. For retention in treatment and reduced illicit heroin use, the evidence from randomized controlled trials consistently supports the effectiveness of HAT over oral methadone for a subset of patients. [1].

Despite the international evidence supporting HAT, knowledge of how HAT functions and how it can be integrated into a national treatment system, such as the Norwegian health care system is lacking. In 2021, a government-supported five-year HAT pilot project was introduced in Oslo and Bergen. Guided by evidence provided from the existing evidence base of HAT in other countries, the Norwegian HAT program was designed for and utilizes injectable and tablet form diacetylmorphine. Funding for the Norwegian HAT program included not only

funding for the clinical program, but also included a comprehensive research evaluation component (2021-2026) (further described in **section 3**). The Norwegian Centre for Addiction Research (SERAF, UiO) leads the research team in collaboration with the Section for Clinical Addiction Research (RusForsk, Oslo University Hospital), Bergen Addiction Research (BAR, Haukeland University Hospital), Centre for Alcohol and Drug Research (CRF, Aarhus University), and the service-user organization, ProLARNett.

The primary aim of the research project is to examine the effects from implementing HAT in Norway for individual patients and for the Norwegian health care services. **This midway report aims to provide a preliminary evaluation of this time-limited pilot project for 2022-2023.**

Main point:

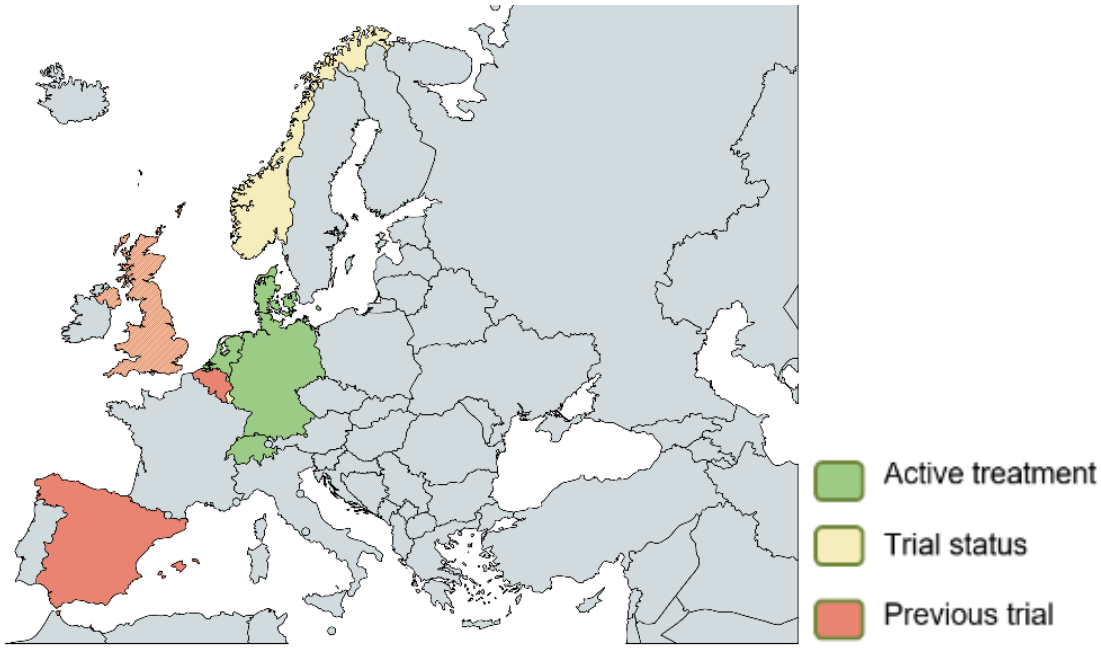
- Heroin-assisted treatment involves twice daily dosing of pharmaceutical heroin (diacetylmorphine) in a supervised setting.
- This midway report gives a preliminary evaluation of heroin-assisted treatment in Norway from 2022-2023, with a focus on patient reported characteristics and outcomes, as well as from qualitative interviews with patients, staff and relatives.

1.2 Heroin-assisted treatment internationally

Since its inception as supervised treatment in Switzerland in 1994, HAT has expanded to other countries including the Netherlands, Germany, Denmark, and Canada (**Figure 1**). Except for Denmark, all of these countries' HAT programs started as randomized controlled trials (RCTs)). The accompanying research studies supported positive short-term and to some extent longer-term outcomes, resulting in the extension of these HAT trials that were subsequently integrated into their national healthcare treatment systems. In recent years, Luxembourg and Scotland have also started offering HAT as pilot projects.

Currently, HAT is available in eight countries (**Table 1**). There is variation among the countries in number of clinics where HAT is available, medication route options (injectable, oral tablet, inhalation, and intranasal), and criteria for inclusion/exclusion from treatment.

Figure 1. Countries in Europe with heroin-assisted treatment



In addition to the existing HAT programs, research studies on HAT have been conducted in countries where HAT is no longer currently available. Research studies have been conducted in Spain (2003-2006) and Belgium (2011-2013), however the clinics closed after the research studies ended. The United Kingdom also carried out a research trial (RiOTT 2005-2009), which then continued as well as non-trial clinics from 2010-2015, until funding was withdrawn. This program is not currently in operation.

The current pharmaceutical product provided for most of the HAT clinics internationally stem from one company based in Switzerland, and with limited competition regarding price.

Overnight bridge medication

Since heroin is a short-acting opioid with a 4-8h duration, HAT programs utilize a long-acting opioid as an overnight bridge medication following their last clinic visit in the afternoon to the next morning. The principle for general OAT is to apply long-acting medications with a once-per-day administration, or longer dosing intervals, such as per oral methadone or buprenorphine. These medicines will result in stable blood concentrations of methadone if taken daily. The basis for long-acting opioid agonists in OAT has its rational in stable methadone blood concentrations, as well as safety considerations to reduce diversion and/or non-medical use. As the bridge medication in HAT programs, only full agonists such as methadone are relevant options. An alternative in OAT in some countries (primarily Austria)

has also been 24h morphine or slow-release oral morphine (SROM), which is another full agonist to the μ-opioid receptors. Medicinal alternatives such as morphine that must be administered more often than once per day (duration 6-12h), are generally considered less advantageous and thus less relevant for the OAT settings and therefore has very limited utility.

The nine international clinical trials that primarily make up the evidence-base for supervised injectable heroin treatment have all used oral methadone as the standard bridge medication for overnight coverage [3]. When administered in HAT programs methadone is typically provided at the clinic as daily observed intake, and not as take-home medicine, as the timing of the intake during the day in stable methadone treatment has limited impact on its effect. As such, most HAT programs would provide all HAT medications provided as observed daily intakes, a benefit from the daily attendance and long opening hours at the clinics. However, some countries also use 24-hour morphine SROM for overnight coverage, particularly during the COVID-19 pandemic [4, 5] **(Table 1).**

In international literature, the term SROM (slow-release oral morphine) is used for both 6 to 12 hours and 24-hour duration and may therefore be unclear which option has been used. In those countries which offer SROM, it may also be unclear whether it is primarily administered at clinics or also as a take-home medication. In Canada, they offer both injectable diacetylmorphine and hydromorphone in their clinic. In their guidelines for the injection-based OAT program, they specify that SROM may be taken under supervision alongside the last heroin dose, which also implies that the morphine medications used would be a 24h type SROM. Application of both per oral morphine products with less than 24h duration or take-home bridge medications in HAT has weak scientific evidence and are thus experimental treatment practices.

In May 2022, new national Norwegian guidelines for OAT were issued, giving more medication options for conventional OAT. This included 6-12-hour morphine sulfate tablets (Dolcontin), as second line medication, if methadone or buprenorphine options did not yield sufficient results. From November 2023, 24-hour morphine (Contalgin) became available in Norway as an option in general OAT, as second line medication. Current guidelines (updated in April 2024) indicate that for OAT patients who have had insufficient treatment effect with buprenorphine or methadone, SROM (24-hour duration) can be considered, and that it should be taken with more frequent supervision than with for example buprenorphine, the regular

first line OAT medications. In the Norwegian HAT program, these morphine-based medications (both 6-12h duration and 24h duration) are also prescribed to HAT patients and are currently being used as the overnight bridge medication for some patients. However, since the most recent update of the OAT guideline the 24h duration SROM should be applied, and the shorter duration morphine options phased out. The implications of using this additional morphine-based medication in the HAT pilot is discussed more in **section 9.**

Take-home doses of heroin are not available in Norway.

Table 1. Countries currently offering heroin-assisted treatment.

Country	Start[1]	Clinics	Administration options				Overnight medication
			Injection	Tablet	Inhalation	Intranasal	
Switzerland[2]	1994	23	x	x		x	Methadone, SROM
Netherlands	1998	17	x		x		Methadone
Germany	2002	14	x				Methadone, Levomethadone
Denmark	2010	5	x	x			Methadone, SROM
Canada[3]	2005	2	x				Methadone, SROM*
Luxembourg	2017	2		x			Methadone
Scotland	2019	1	x				Missing data
Norway	2022	2	x	x			Methadone, SROM

[1]Either as a research study or within health system
[2]Also available in prisons; Intranasal administration is part of a multi-center clinical trial
[3]Experienced significant interruptions
SROM: slow-release morphine; 6-12 and 24-hour morphine
*within the injectable OAT provision

Heroin-assisted treatment in Denmark

Given the similarities between the Danish and Norwegian treatment systems, a comparison of HAT in Denmark and Norway has been incorporated into the research evaluation plan for the Norwegian program. Heroin-assisted treatment has been a standard type of care in Denmark since March 2010. Treatment is available in five clinics in Denmark, with two located in the Capital Region, two in the Region of Southern Denmark, and one in the Central Denmark Region. The government provides substantial financing for treatment through the national budget, but the municipalities provide additional funding. For this reason, service levels vary between clinics and over time. The Danish program has a current max capacity of up to 300 patients in treatment at the same time, a limit that has not been reached during the program's history.

According to a published report from the Danish Health Authority, a total of 573 patients were enrolled in treatment between 2010 and 2018 [3]. However, the most recent estimate is that about 240 patients are enrolled in total at any given date in the five Danish clinics combined. From 2010 to 2015, the Valmuen clinic in Copenhagen had the most patients, with the count exceeding 80 in the last year of this period, followed by a subsequent decrease to around 60 patients. From 2016 to 2020, the clinic in Odense, which previously held the second-highest patient count, recorded the highest numbers - consistently surpassing 80 and reaching about one hundred patients in the final 3 years. However, recent reports indicate that the Odense clinic has about 80 patients or less in HAT in April 2024.

Nevertheless, the clinic in Odense in Denmark has a proven capacity for 100 patients and served as a "model clinic" for the design suggested for the Norwegian clinics. The staff configuration for the clinic in Odense serving up to 100 enrolled patients were 18 nurses and health care assistants, 3 social workers, and 2 medical doctors. The Odense clinic has four injection sites and a total space of about 400m^2. In Odense, currently about 95% of the patients inject the heroin medication, and only a handful patients rely on tablets.

Patients are eligible for HAT in Denmark if they (1) are opioid dependent and (2) have failed to respond adequately to OAT with buprenorphine or methadone for at least 12 months. Patients are not eligible for HAT if they have (1) an ongoing, serious untreated mental health problem, (2) ongoing dependence on sedatives/hypnotics, or (3) ongoing dependence on alcohol. To monitor treatment at both the patient level and the general level, patients

complete a follow-up form at enrolment and regularly during enrolment. Overall, the trend for patient numbers in Denmark indicates a gradual increase in numbers in HAT treatment during the first 4-5 years of the program, thereafter a fairly stable patient volume around 240 patients at any given time, and possibly a slight decline in numbers in recent years.

2. Heroin-assisted treatment in Norway

2.1 The establishment of heroin-assisted treatment in Norway

The public and political debate about HAT first emerged in Norway around 2007. At that time, support for HAT was scarce among parliamentary parties and HAT was not a visible issue in public debate. This, however, changed markedly during the subsequent decade. When the government made its final decision to implement a time-limited trial HAT project in 2019, HAT had become a highly debated issue. At that time, a majority of parliamentary parties and a series of other actors with substantial public influence had then been arguing for HAT for several years [4].

The shift from a near absence of support for HAT in the mid-2000s to the establishment of the first HAT clinics in 2022 did not result from pressure or demands from

clinical addiction treatment researchers. Rather, it was driven by influential individual politicians, activists, user groups, and eventually also by representatives from the national news media and political parties in parliament. These actors described HAT as an important initiative for the most disadvantaged injecting drug users for which the existing OAT was not sufficient. However, HAT also seemed to play a broader symbolic role by posing a potential marker of change in the debate on drug policy reform that intensified during the decade leading up to the HAT project's enactment. During that decade the debate on drug policy reform, criticism of the negative costs of the “punitive” approach towards injecting drug users, and the demand for a more liberal drug policy had gained increased momentum in the political debate. This affected the Norwegian drug policy landscape and was likely a crucial prerequisite of the increased political support for HAT [4].

It is therefore also the case that the changes in policy approaches were driven more by opinion leaders and politicians, than by the scientific and locally relevant evidence base. In Norway, everyone with OUD has access to medical care and social services free of charge, and in recent years an almost immediate access to treatment (without waiting lists). In addition, between 70-80% of the target population for OAT are in treatment, they are retained for long-term treatment, and the majority are fairly satisfied with treatment [5-7]. Also, very few persons in Norway would be arrested or imprisoned due to minor drug crimes such as use and possession

of drugs. However, many with drug use disorders are imprisoned in Norway, though for offences other than drug use and possession. “The war on drugs” has not been a prominent feature of Norwegian drug policy or clinical practice in recent years. Conversely, according to the Global Drug Policy Index, Norway ranks on top when compared with other countries for having a balanced drug policy [8]. Therefore, the narrative of the “addicted” persons chased by the police and not receiving appropriate health and social services has not been rooted in formal data from Norway but has nevertheless been an important narrative for policy making.

Despite the increased political support for HAT, addiction treatment and addiction research communities, as well as certain user organizations among others, were critical of using limited economic resources for the establishment of HAT. Instead, they argued for using the resources to improve existing OAT services because that would be more cost effective and could benefit a higher number of patients. On the opposing side of the debate, some political parties and user organizations argued for the implementation of HAT because they saw it as a necessary addition and expansion of OAT to fit the needs and challenges of the most vulnerable group of OUD patients who did not benefit from OAT [4].

In the decade prior to the government’s enactment of the five-year HAT pilot project in 2019, there had been several assessments and scientific reviews initiated by the government health authorities that considered the potential for introducing HAT in Norway [9, 10]. Building on the assessment that there was not yet enough published scientific evidence to support HAT’s effectiveness for the subgroup of OUD patients to which this treatment option is intended, the conclusion was that it was too early for its introduction. The later political support for HAT was primarily for a time-limited HAT project, in order to gain knowledge to lay the foundation for a decision on whether HAT should be introduced permanently. This amended approach differs from other countries, such as Denmark, where HAT was introduced in 2010 as a permanent OAT service option without any preceding trial project, nor plans for formal research-based evaluations [11]. Since then, however, several new studies on HAT have been published, including randomized controlled trials, systematic reviews and other studies that support HAT’s positive effects for patients remaining in HAT and the wider society [2, 12]. However, the question on how to best utilize governmental funding to benefit the entire population with OUD in a country remains unanswered.

Main point:

- Parliament's political support for HAT changed from near absence in the mid-2000s to a sufficiently broad cross-party support by 2019.
- HAT has been a disputed issue in Norway among clinical and research milieus in the addiction field, as well as across political actors and user groups.
- The introduction of the clinical project together with a research evaluation aims to extend the evidence base of HAT's utility and potentially reduce an ideologically polarized debate, not founded with evidence.

Acquisition of diacetylmorphine

The acquisition of the heroin medication (diacetylmorphine) for the Norwegian HAT project relied largely on the established Danish experience and followed negotiations with the provider (Inphena) and the Norwegian Medicines Agency. The process took time and was primarily handled by the clinics. The medicinal product acquired is the same as the one used in Denmark and most other HAT projects globally. The Danish company, Inphena, handles the access. In Norway, the clinics are part of university hospitals, and delivery/access is through ordinary channels within the hospital system. The cost for the medication is high, not least for the tablets provided, and the unit price has increased during the project period. There are no real alternatives to the current company, which can be said to have a monopoly for delivery of the medications.

2.2 Heroin-assisted treatment clinics in Oslo and Bergen

The Government decided in 2018 to establish a time limited pilot project in Oslo and Bergen, with an initial expectation of clinics to open by January 2021. The Oslo HAT clinic (HABiO) opened in January 2022 and the Bergen HAT clinic (HABiB) opened in March 2022. The "delayed" start of patient inclusion with one year illustrates the inherent challenges there are to establish a new and highly specialized treatment, such as HAT, that requires trained staff, suitable localities, and access to new medicines. The currently operating clinics have several similarities and differences relating to the clinic location, routines, and staffing. These aspects are displayed below.

Location

HABiO is situated within the Oslo University Hospital (OUS), a large hospital complex. The clinic reports that the hospital campus location has provided several advantages related to drug delivery and cooperation with the adjacent Section for Addiction and Addiction Outpatient clinics, which also provides conventional OAT.

HABiB has operated from two temporary locations in succession and is planning to relocate to a more permanent site by the end of 2024. The first start-up location was not suitable for operation, which led to a delayed start-up and a reduced capacity for patients. After the first year of operation, HABiB moved to a second temporary location, which was more suitable, but still not optimal.

Both clinics report concerns from the neighboring buildings/community. At HABiO, OUS security services have reported an increase in unwanted activity in the hospital area after HABiO's establishment. There have also been some complaints from employees working in nearby buildings. The clinics report that this is continuously discussed with patients in treatment. In the event of excessive challenges related to undesirable behavior on the hospital grounds, HABiO reports that they would have to consider discharging the patient. Fortunately, this has not yet been necessary, but it has been considered in the case for some incidents. The unit manager at HABiO receives reports of all incidents noted by security services and experiences good cooperation with them.

At HABiB, the surrounding neighborhood association and residents were uncertain and concerned about what might happen to their neighborhood when HABiB was established. A neighborhood meeting was held to provide information and answer questions, and there have been several meetings with the neighborhood board afterwards. There have been no complaints from neighbors at the current premises, which the clinic interprets to mean that the neighbors are no longer concerned.

Planning and protocol

The planning for both clinics started in 2020, and it took about two years to be clinically operative with staff and all necessary procedures. Establishing clinical housing as well as

acquiring access to the medication took time. Both are explanations for the delay in patient inclusion which did not start before early in 2022.

The treatment protocols in the two clinics are based on the program description developed by a multidisciplinary team led by SERAF in 2019 and on subsequent locally developed clinical procedures at each clinic. SERAF's program description was based on international literature reviews of the evidence base, visits to the Danish clinics, dialogue with Norwegian clinicians, and input from researchers and service user organizations. There is no formal treatment protocol for HAT in Norway. Thus, the evidence-based program description (SERAF 2019) and the local clinical guidelines established today's guiding documents. The SERAF program description estimated that treatment need was for about 300 patients at any given time in Oslo and Bergen combined. In addition, with a suggestion that any clinic should not be designed for more than 100 patients enrolled at the time. (Hence, the estimated treatment need for Oslo would be 1-2 clinics of up to 100 patients each. While in Bergen the estimated need would be one clinic with a capacity of up to 100 patients).

Routines

The two clinics operate with two daily sessions when patients arrive: one in the morning (HABiO: 08:15 - 11:00, HABiB: 08:30- 11:00) and another in the afternoon (HABiO: 14:00 - 16:00, HABiB: 14:00 - 17:00). Patients receiving tablet-form heroin at HABiO can arrive until 17:00. From 12:00-14:00, the clinics are closed to patients and the time is used for individual follow-up of patients, documentation, meetings, staff development, and other work for staff.

During the opening hours for patients, individuals self-administer their prescribed injectable or tablet heroin. Patients receive a longer-acting opioid for coverage overnight, traditionally methadone (according to international treatment protocols) or SROM tablets.

The clinic premises have different rooms where patients progress through various steps in the treatment process, spending up to two hours at the clinic each day. After entering the waiting room, patients have a pre-screening conversation with a doctor or nurse, during which their medical condition and daily dosage are assessed. Based on a clinical assessment, breathalyzer tests are administered to avoid overdoses due to the interaction between alcohol and heroin. The individual heroin dosage is adjusted according to the clinical assessment of each patient's needs.

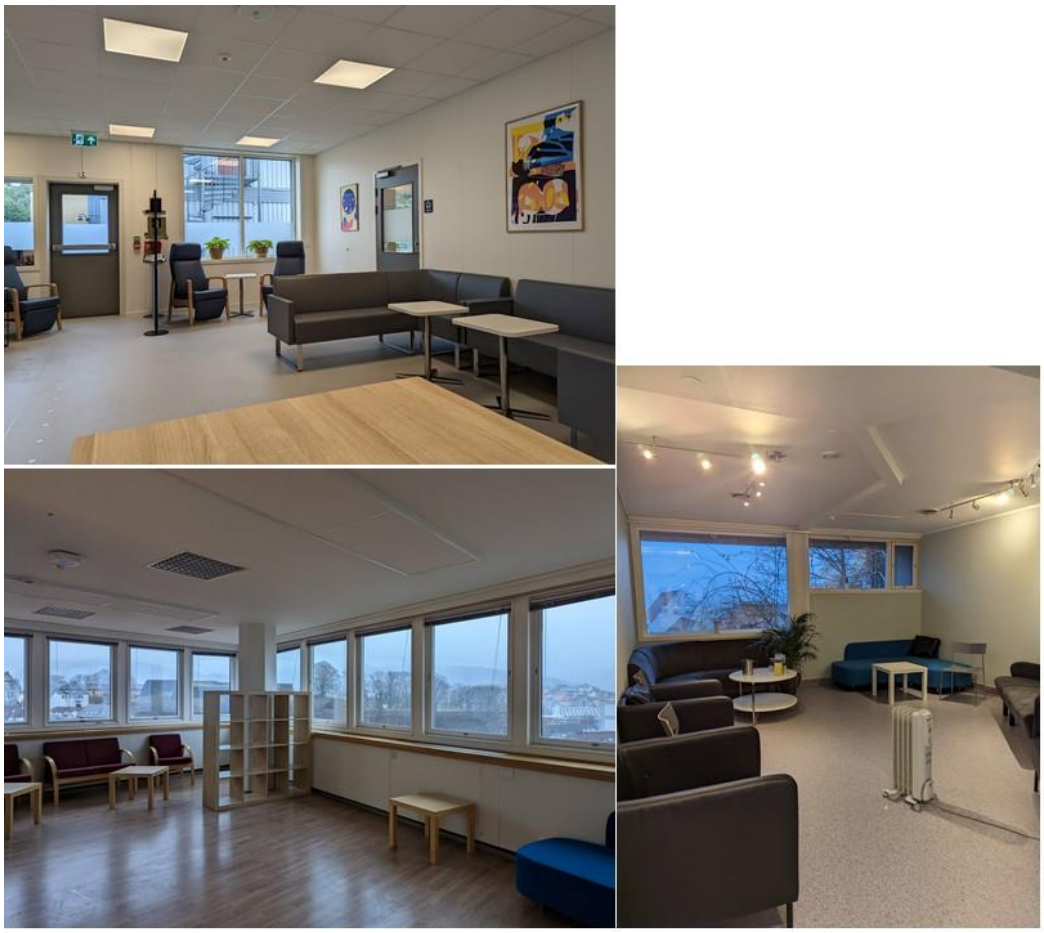
After the initial assessment, patients move to supervised injection booths (**Figure 2**) where specific guidelines for safe injection are provided. This includes hygiene rules and avoiding injecting in risky areas like the groin and neck area, as well as instructions for safe intramuscular injection. There are five injection booths in operation at HABiO.

Figure 2. Injection booths

Left, HABiO; Right, HABiB. Image: Ann Oldervoll

Following self-administration of the medication, patients proceed to the observation room (**Figure 3**), where they are required to stay for observation for at least 20 minutes after intake of the medication. During this time, any severe events or breathing difficulties are closely monitored by a staff member. Observation duration and other safety measures may differ between HABiO and HABiB, based on clinical judgment.

Figure 3. Observation rooms



Left top Oslo; Bottom left Bergen; Bottom right waiting and observation room in previous Bergen location
Images: Ann Oldervoll

Staffing

The clinic staff at each site includes at least one medical doctor specializing in addiction medicine, specialist nurses, nurses, social workers, and cleaning staff. The nurses perform pre-assessments, dispensing of medication, post-assessments, and additional healthcare services such as health check-ups and wound care. There are minimum staffing requirements needed for the clinics to run safely. Patients are also given the option to access voluntary counseling and psychosocial support, including assistance with housing, finances, and employment, which is provided by social workers.

Within five months of its inception in January 2022, the number of patients at HABiO increased to 30. At that point, additional personnel resources were needed before the clinic could enroll more patients. At present, both clinics have 18.5 fulltime equivalent position, with the majority being nurses. At HABiO, two senior consultant positions have been budgeted, but the

clinic has been unable to fill these positions (currently running with one full-time doctor). HABiB has one full-time doctor position, which is shared between two doctors.

Medications and dosing

Patients receive heroin in injectable or tablet form, in two doses per day. Dosages are different for each patient and are adjusted for intravenous (IV), intramuscular (IM), and oral use. For injectable heroin, at HABiO the average dose per visit is 266 mg (median 270mg; range 150mg-420mg day) and at HABiB the average dose per visit is 320 mg IV/331mg IM (median 360mg; range 140-460 mg IV; median 320mg; range 140-500mg IM). For oral heroin (tablets), the average dose in HABiO per dose is 589 mg (median 600mg; range 200 mg- 900 mg).

At HABiO, most patients use injection as their only route of use (55%), with the remaining 21% using oral tablets and 24% using a combination of oral and injection.

At both clinics, overnight coverage given is either methadone, 6-12-hour morphine sulfate (Dolcontin), or 24-hour morphine (Contalgin). At HABiB, all but one patient have recently been converted to 24-hour morphine for their overnight coverage.

Implementation differences between the clinics

After nearly two years of operation, the clinics have many commonalities, but it is also evident that the two clinics have developed slightly different clinical routines and operations. These differences may yield valuable insights and practical experience regarding unique organization methods of clinic operations, as well as varying approaches to solving similar (and sometimes differing) practical and professional challenges across the clinics. However, should HAT become a permanent treatment option, practicing a different organization of the treatment provision across clinics could be problematic and undesired. Below, are some of the differences in the clinics' organization and provision of HAT:

- **Difference in practices regarding prescription of medications beyond the standard treatment medication offered in HAT.**
    - HABiB prescribes benzodiazepines to some of their patients, which has led the clinic to introduce drug screenings for these patients by occasionally collecting urine samples. HABiO has a more restrictive practice concerning prescription of medications beyond the standard opioid agonist medication offered in HAT and has primarily left the prescription of benzodiazepines to prescribers external to

HAT (typically the GP). This difference is seemingly also a reflection of different procedures and practices of conventional OAT in Bergen and Oslo.

  - HABiO occasionally provides additional medications, such as blood thinners, hepatitis C medication, antibiotics, vitamin D, and iron supplements to patients as needed.
  - HABiO and HABiB report that the two clinics are in close dialogue about prescribing practices beyond the standard medication offered in HAT.

- **Different responses to the risk of diversion**.
  - At HABiO, unstable patients are given methadone or 24-hour SROM for their overnight bridge medication, which they are given as direct observed treatment at the clinic. Since 2022, stable patients were given the option of 6-12-hour SROM, also for take-home. Some patients living in institutions were given their 6-12-hour SROM by heath personnel at the facilities.
  - At both clinics, the administration and choice of overnight bridge medication is assessed on an individual basis.
- **Differences in meals provided.**
  - The clinics differ in whether they offer food to patients in the clinic's observation room. HABiO serves a meal every morning, while HABiB offers no meals. Both clinics offer coffee and other warm beverages.
- **Differences in staff.**
  - Both clinics have a comprehensive, multi-disciplinary staffing model, yet there are some differences.
  - HABiB has employed one social worker and one psychologist in addition to nurses, social workers, and medical doctors. In Bergen, there are two medical doctors working part-time in HAT and with additional responsibilities in other OAT clinics.
  - HABiB must follow hiring practices from Haukeland University Hospital, which require all staff to have full-time positions. The clinic reports that this is a challenge for staffing ratios, and it results in overstaffing in order to ensure weekend coverage.

- HABiO has prioritized two social workers over a psychologist. HABiO has budgeted for two full-time medical doctors to work solely with HAT; however, only one position is currently filled due to recruitment challenges.

- **Difference in opening and working hours**.
  - The clinics' opening hours are nearly identical, although HABiB is open one hour later for injection in the afternoon.
  - Staff at HABiB are allowed 10-hour shifts by the hospital. However, HABiO shifts are capped at 7.5 hours, resulting in fewer staff at the times of day when need is greatest. Differing hospital rules in Oslo and Bergen thus impact both opening hours and clinicians' working hours (shift length).

The above differences should be seen in relation to the fact that Oslo and Bergen are cities of dissimilar size and with a different number of people with OUD, and thus different numbers of potential patients who might fit HAT's target group. Other local contextual differences are also likely to impact the implementation of HAT in the two cities. In addition, HABiO has an annual budget about double the size of the budget of HABiB. Currently, the number of patients in HAT are reflected in this, with about 1/3 of the HAT patients in Bergen and 2/3 in Oslo.

Main point:

- The opening of the HAT clinics was delayed by challenges with obtaining and preparing clinic facilities.
- Implementation of HAT after clinics opened has been impacted and restricted particularly by limited access to staffing, clinic facilities (primarily in Bergen), and limited budget which is still limiting the HAT clinics.

2.3 Referrals to heroin-assisted treatment

The clinics have registered all referrals to HAT, with information on referral source and whether it was primary or secondary. A primary referral means that it has come from an external source, while secondary means that the referral came from within the same department at the hospital (typically regular OAT).

During the period from the opening of the clinics in the beginning of 2022 until the end of 2023, 167 referrals were received by the clinics (56 at HABiB and 111 at HABiO). Most patients

referred were male (79%; 75% at HABiB and 81% at HABiO). The mean age of the referred patients was 45 years (43 at HABiB and 46 at HABiO).

Of the referrals, 63% were categorized as secondary, i.e., referred from the specialized addiction treatment services at the same hospital (79% in HABiB and 61% in HABiO). In total, 37% of referrals were declined (29% in HABiB and 41% in HABiO), and among these most patients were offered alternative treatment options.

Overall, half of the referrals (52%) came from the conventional OAT service at the same hospital (77% in Bergen and 39% in Oslo). The second most common referral was from the Norwegian Labor and Welfare Administration (NAV) (13% of total referrals; 11% in Bergen and 14% in Oslo). The third most common source of referrals were from general practitioners (GPs) with 12% of referrals in total (7% in Bergen and 14% in Oslo).

Three-fourths of the referrals were received during 2022, the first year of the clinics' opening. That same year also had the largest amount of refused referrals, with 74% of referrals that were declined were during 2022. The clinics registered whether the referrals were accepted or refused, along with the accompanying reason for refusal (**Table 3**). The most common reason for refusal was "admission pause," meaning that the clinic was at its maximum capacity, as set by the clinic managers. This was the reason for 28% of the refusals in total (6% at HABiB and 36% at HABiO). These periods of "admission pause" have probably also had an impact on the number of referrals sent to the clinics. Referrers would be less likely to refer patients during these periods, which sometimes were of several weeks duration and informally announced in the local network. The second most common reason for refusal was a patient's history of violence, with 17% of refusals in total (6% at HABiB and 20% at HABiO). "Medication in OAT", which means they continued or started medications in OAT instead of HAT, was a common reason for refusal, either suggested by the clinicians or initiated by the patients themselves in 16% of refusals in total (31% at HABiB and 11% at HABiO). This may be explained by the update to the national guidelines for OAT that came in May 2022 and presented an opportunity for more medication options in conventional OAT, including a somewhat higher access/use of tablet-based morphine sulfate of 6–12-hour duration.

Table 3. Reasons for refusal of heroin-assisted treatment in Bergen and Oslo clinics

Total no of referrals: 167 Total no of refusals: 61	HAT-Total Refusals: 61/167		HABiB Refusals: 16/56		HABiO Refusals: 45/111	
	n	Valid %	n	Valid %	n	Valid %
Other treatment more suitable (OAT)	4	6.6			4	8.9
Severe mental disorder	3	4.9			3	6.7
Risk of violence	10	16.4	1	6.3	9	**20.0**
Severe somatic disorder	1	1.6			1	2.2
Not in the target group[1]	8	13.1	4	6.3	4	8.9
Medicinal Reason -> New medications in OAT	10	16.4	5	**31.3**	5	11.1
Other	1	1.6			1	2.2
Did not meet up for intake interview	1	1.6	1	6.3		
Reduced cognitive function	1	1.6	1	6.3		
Patient's own request (OAT, other addiction treatment)	3	4.9	3	**18.8**		
Admission pause	17	27.9	1	6.3	16	**35.6**
Risk of violence and Severe mental disorder	2	3.3			2	4.4
TOTAL	61	100.0	16	100.0	45	100.0

[1]Low heroin use, inhalation, young age, pain management, another health trust

Main points:

- 167 referrals were received during the first two years of the clinics' operation.
- Most referrals came from OAT, followed by NAV and GPs.
- Three-quarters of referrals and refusals came during the first year.
- The most common reason for refusal was "admission pause", followed by "new medications in OAT" and "history of violence."
- Lack of capacity at the clinics likely resulted in fewer new patients entering HAT, particularly during 2023.

2.4 Enrollment and retention

Enrollment

The original estimate for the number of patients who would need HAT was up to 300 patients at any given time in Oslo and Bergen combined. Currently, after two years of operation, there are 97 patients that have ever been enrolled in HAT during the first two years. This is approximately one-third of the original estimate of treatment need. The clinics report various reasons for why intake is lower than expected, and are described in **section 2.5.**

Retention in treatment

From the start of treatment in January 2022 (HABiO) and March 2022 (HABiB) there have been 27 patients (29%) that have left treatment (21 from HABiO, 6 from HABiB). Of these, over half of the patients were transferred to conventional OAT, which means they ended HAT, but not OAT.

The 92 patients included in the research at the clinics during this observation period from January 2022 through 2023 have "produced" 95 treatment years in total (one treatment year is equal to one patient in treatment for 365 days). The mean duration of treatment among those included was between 14-15 months. Among those 27 patients that left treatment only two left treatment during the first month (among those registered in the research), and the mean duration of treatment among these was about 6 months before they left HAT.

Main point:

- Over the first two years, there have been 97 participants that have started in HAT, and 92 consented to take part in the research project.
- Of the 27 participants that left treatment, half were transferred to conventional OAT.
- In total the clinics have produced 95 treatment years of HAT provision, and among those that left treatment, the mean treatment duration was 6 months.

2.5 Implementation progress

Overall, the clinics were designed based on the project description developed by SERAF in 2019 and following discussions with clinicians from Denmark's HAT clinics and from Norwegian clinicians from addiction services.

The implementation of HAT within the hospital systems has been examined using qualitative data gathered primarily from interviews with clinicians and unit leaders. Participant observation in the clinics, also involving participation in staff meetings, provided additional insight into the HAT implementation process. To capture the preparation process, interviews with unit leaders started about a year before the clinics opened. In this midway report, we focus primarily on the experiences of clinic leaders and staff regarding the implementation process after the HAT clinics were established.

Factors impacting the implementation and enrollment

Clinic leaders mentioned several factors that facilitated the implementation of HAT into the clinics. They included adequate time for preparation and training of staff prior to clinic opening (partially due to delays in the opening of clinics), the valuable support from other parts of the hospital organizations, including assistance from the leadership above the clinic level, and dialogue on professional and practical matters with leaders in the already established HAT clinics in Denmark. The leaders report that recruitment and enrollment of patients must be done with close consideration for staff well-being, patient safety, and with concern for the treatment environment.

Looking at longitudinal data, several themes emerged relating to the process of implementing HAT. After the clinics opened, challenges surfaced particularly in relation to 1) development of clinical procedures and routines, 2) clinic facilities, 3) staffing, 4) finances/budget, and 5) integration of research in the clinic. These challenges are further described below:

1) The development of clinical procedures and routines:

Introducing a new medication for a group of patients known for poly-substance use was challenging. It demanded constant considerations, evaluation, and subsequent revision of procedures, as well as continuous dialogue among the clinical staff about how to best assess and solve matters related to practical, medical, and interpersonal aspects of treatment delivery and organization. This process of development was most intense in the first phase after clinic opening. The clinics have been operational for over two years, and routines and procedures are currently more well-established. However, discussions about reorganization of HAT practical procedures and service provision are still ongoing. This was similarly described by clinicians in both clinics.

2) Clinic facilities:

Prior to opening, staff in both clinics experienced uncertainty and delays in establishing a suitable clinic facility as a major challenge. HABiO was eventually located in a facility that was designed and built for the purpose of housing a HAT clinic, although in a temporary module-based building. The current space, staffing and number of injection sites at HABiO would be quite like the “model clinic in Odense” as has shown capacity for up to 100 patients at any time. HABiB faced greater challenges and has been housed in two subsequently temporary

facilities in a building previously used for treatment and follow-up of people with substance use. The clinic in Bergen is still anticipating a final move to their permanent facility, which is still under construction. The first temporary facility of the Bergen clinic had a maximum capacity of 10-15 patients because of space restrictions and a layout that was not well-suited for a HAT clinic. The second temporary facility (the current) of Bergen's clinic was larger and partially rebuilt to better fit the needs of a HAT clinic, this time with a capacity of 40 patients. The challenges with facilities in Bergen also affected the working conditions of staff in undesirable ways, which caused some unrest – particularly during the period in the clinic's first temporary location.

3) Staffing:

Challenges in hiring staff for HAT affected both clinics, particularly in the first year of their operation. There were challenges in acquiring enough nurses, which is reflective of an overall shortage in nurses in the Norwegian healthcare system. The same challenge was experienced at times for medical doctors. Both clinics still managed to fulfill the necessary professional staff needs, but with occasional limitations, leading to restrictions in intake capacity for patient enrollment (such as during holidays). Another staffing challenge was related to overtime payment, regulations about working hours, and the length of shifts allowed in the hospitals. This affected the staffing situation and caused some discontent among staff because of a perceived lack of overtime payment and shortage of staff during the weekends. HABiO eventually hired security guards for the weekends to compensate for the reduced number of clinical staff at work on these days. Bergen has been able to extend their staff over time to better meet these challenges.

4) Finances and budget limitations:

The financing of the two clinics is another factor that has influenced the implementation of HAT. Funded through the government's state budget, the clinics have experienced a marked increase in operational costs since 2022, primarily due to inflation. Staffing costs, including higher salaries, along with the rising price of diacetylmorphine, represent the primary expenditures for the HAT clinics. Despite increased costs, the latest annual budget allocated to HAT did not reflect this increase in costs. Consequently, at the time of this writing, the budgetary constraints have imposed limitations on patient intake, capping the number at

approximately 35 in Bergen and 50 to 60 in Oslo. Therefore, the clinics' actual patient capacities are currently significantly lower than originally projected. [13].

5) Integration of research into the clinic:

The HAT evaluation project involves integration of research and data collection into the clinics and additional tasks for clinical staff, while clinicians also collaborate with external researchers for various types of data gathering. Unit leaders and staff have expressed enthusiasm and gratitude for this cooperation and the feedback from researchers about preliminary findings, but it is not without challenges. For example, staff must expend time and effort on the task of involving the patients in study participation. Data collection is primarily completed by a small number of staff, which may leave the evaluation vulnerable.

These challenges were less important to clinicians than what was described in the first four points above. This point is still included because clinicians' experience with the integration of research into the HAT project is relevant to the research-based evaluation of HAT itself. At the starting point and onwards, staff that were recruited to the HAT clinics have been made aware that data collection and research is an integral part of their duty.

At HABiO, a select number of nurses are designated to have the main responsibilities for research follow-up. HABiO reports that this organization creates an internal system and organization for ensuring data is collected in a timely manner. The baseline forms are primarily collected by social workers, and subsequent follow-up questionnaires are collected by nurses, as part of their everyday tasks.

3. Research team and aims

3.1 Research team and collaboration

The research team for the evaluation of the HAT pilot project is a collaboration of five entities. These organizations offer a diverse, mixed methods approach that utilizes various specialties and backgrounds. Each component of the research team is external to the HAT clinics. The Norwegian Centre for Addiction Research (SERAF) at the University of Oslo leads the research team in collaboration with the Unit for Clinical Research on Addictions (RusForsk) at Oslo University Hospital, Bergen Addiction Research (BAR) at Haukeland University Hospital, Centre for Alcohol and Drug Research at Aarhus University (CRF), and the user organization ProLARNett. Each group is primarily responsible for different thematic areas, yet collaboration occurs among all groups**.** Collectively, this approach offers a comprehensive method evaluating HAT, and importantly from research actors external to the clinics and their management lines.

The research team includes contributions from 14 researchers, 2 PhD students, 3 master's students, a project coordinator, and service-user representatives. The research group meets monthly to share updates and foster active collaborations. Researchers and the research project coordinator are in frequent contact with the clinic staff and leadership.

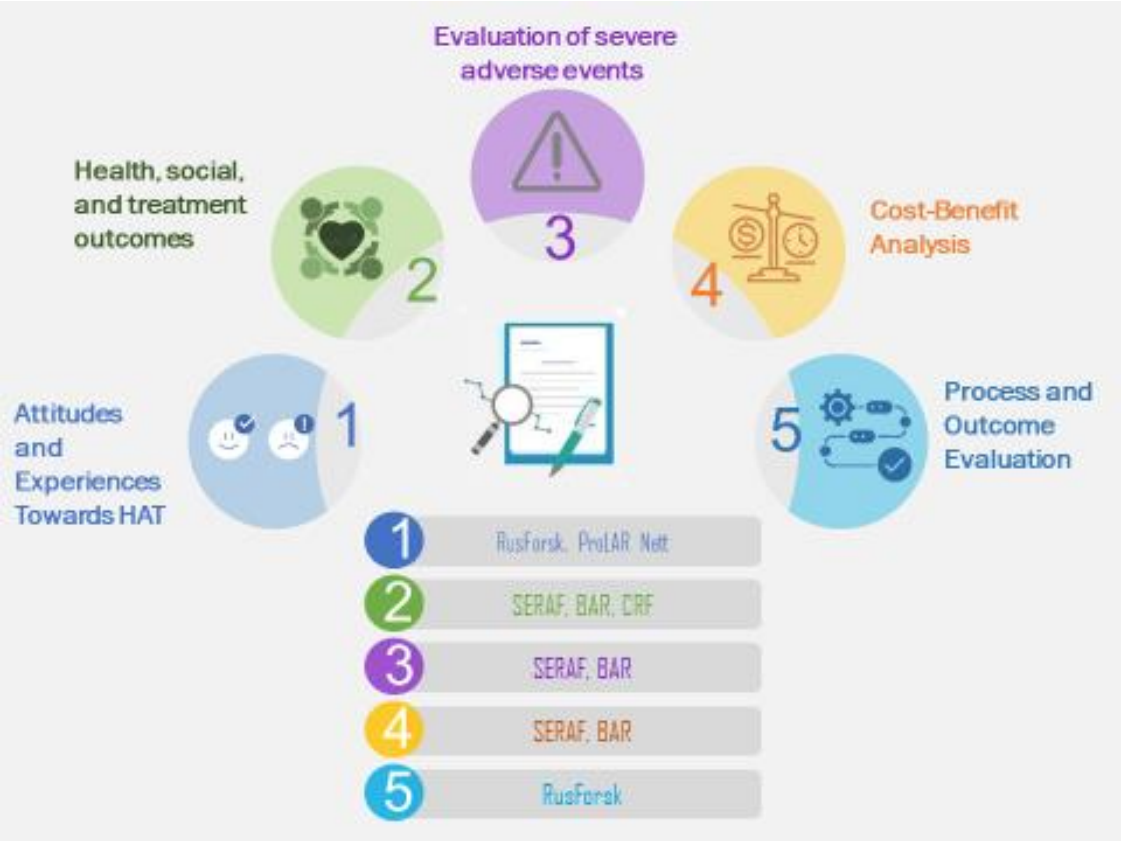
In addition, there has been national and international scientific collaboration on research-related projects with:

- Department of Physiology and Pharmacology “V. Erspamer", Sapienza University, Rome, Italy
- Section of Experimental Drug Abuse Research, Department of Forensic Science, Oslo University Hospital, Oslo, Norway
- Oslo Centre for Biostatistics and Epidemiology, OCBE, Faculty of Medicine, University of Oslo

3.2 Research structure and aims

Based on the Norwegian Directorate of Health’s specifications in the project proposal, the research covers the multiple thematic areas listed with different responsible research teams **(Figure 4).**

Figure 4. Thematic research areas and main responsible research group



This study utilizes qualitative, quantitative, and registry-based methods. Each of the thematic areas incorporates data from multiple sources, including in-depth and semi-structured interviews, questionnaires, clinical records, registries, and account information (**Table 2**). The main aims for the thematic areas are outlined in **Table 2** and further specified in **sections 4 and 5**.

Table 2. Thematic areas, data sources, and main aims.

	Thematic area	Data source	Main aim
1	**Attitudes and experiences of HAT**	In-depth and semi-structured interviews with patients, family members and staff	Capture the experiences with HAT as seen from differing perspectives, concerning the benefits and challenges experienced by those who receive HAT, the rewards and challenges experienced by those providing HAT, and the potential indirect impacts of HAT for the caring tasks of patients' relatives.
2	**Health, social, and treatment outcomes**	Questionnaires Clinical records Registries	Describe changes in mental and physical health among patients receiving HAT, and in what way it is associated with outcomes such as quality of life, utilization of health- and social services, social reintegration, criminal behavior and use of illicit drugs.
3	**Serious adverse events**	Clinical records	Report any serious adverse events and incidents at treatment initiation, during treatment, and after discharge from HAT.
4	**Cost-benefit analysis**	Clinical records Registries Key-account figures	Perform an economic evaluation of the program with associated clinical benefits and societal costs.
5	**Process evaluation**	Interviews and questionnaires with patients, staff, and administrators	Evaluate the organizational processes involved in the implementation of HAT in Norwegian specialist healthcare services, and the eventual impact from HAT on OUD patients' utilization of conventional OAT.
6	**Additional**	Additional data specified in further protocols	

Source: Myklebust et al., 2024.

The use of data from clinical records is included in three of the five main thematic areas. While ethical approval has been granted to access this data, there are logistic barriers to receiving this data. Therefore, it was not possible to include information concerning serious adverse events in this midway report. This information will be included in the final report.

Research project development and implementation

During the period from autumn 2020 to spring 2021, there was a concerted effort by the researcher group to establish close collaboration between the medical advisory team and the clinical project managers at both HAT clinics. The aim was to optimize the clinical relevance of the questionnaires and establish effective procedures for integrating research protocols and

planned data collections into clinical routines. By spring 2021, protocols had been established for recording patient flow, processing applications, and handling acceptances and rejections.

Progressing into autumn 2021, the research group conducted two working group meetings involving the medical advisory team, clinical project managers, and key personnel from both clinics, with the objective of collectively ensuring successful implementation of the research component at the clinics. Additionally, two training seminars were conducted for staff members of the HAT clinics in Oslo and Bergen, respectively.

In the transition from autumn 2021 to spring 2022, efforts culminated in the development of a Handbook for the Implementation of Research Protocols into Clinical Routines, authored by the research group.

After the initiation of clinic operations, ongoing procedures for follow-up of the research were established. These included monthly status meetings in the research group concerning project progress within subproject groups in Oslo, as well as biweekly clinic follow-ups by the project coordinator focusing on recruitment and data collection in both clinics.

Main points:

- The research group collaborated closely with key personnel in both clinics to ensure clinically relevant research questions and implementation of research procedures before the opening of the clinics.
- The research group has ongoing regular contact with project coordinators in both clinics to ensure data quality.

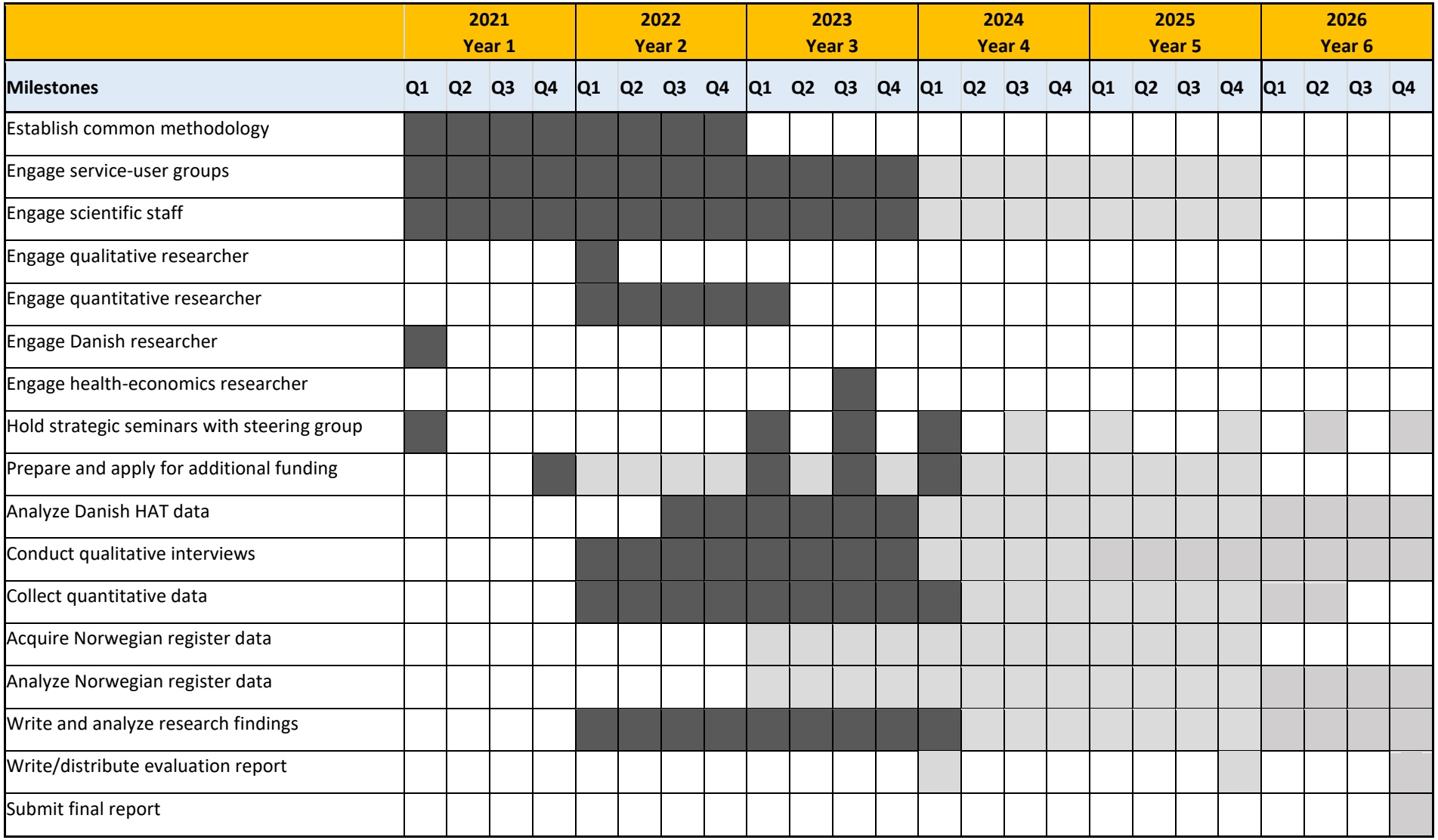
3.3 Timeline

The clinics opened in early 2022, but the research aspect began prior to that with meetings to develop assessment materials and collaboration on study design (**see 4.1 Development and implementation**). An evidence summary was produced by SERAF in 2019, which provided a basis for the future HAT clinics in Norway [13]. The first qualitative interviews were conducted in November 2020 with clinic project leaders (who later became unit leaders). Research plans and questionnaire development began in 2020.

Figure 5 below outlines the research milestones and progress during the 5-year study period. The year prior to the opening of the HAT clinics (2021) primarily focused on the establishment of the research methods and engagement with service-user groups, the research team and

key clinical personnel. Because Danish HAT data and qualitative data were already available, research activity in 2021 focused on these areas. In the following years (2022-2023), the focus was on data collection for both the quantitative and qualitative studies. Future research in 2024 and 2025 will utilize additional data sources (patient journals, clinic data, registry data, cost-effectiveness evaluations, and overall implementation and process evaluations).

Figure 5. Timeline and milestones for the research project on heroin-assisted treatment (2021-2026)



4. Heroin-assisted treatment research progress

4.1 Experiences in HAT: qualitative research progress

The qualitative data gathering is aimed at capturing the experiences with HAT as seen from different perspectives of groups involved with this treatment. Data collection was done using different methods and with different data sources. At the time of writing, this has encompassed participant observation in the HAT clinics, as well as longitudinal in-depth, semi-structured interviews with patients, their relatives, and clinical staff, including the clinic leaders. A total of 111 interviews have been conducted so far:

- 61 individual interviews with patients (1-2, 6-8 and 12-14 months after their enrollment in treatment). These research participants were between 31 and 68 years of age.
- 32 individual and group interviews with clinicians (3-4 and 12-13 months after clinic opening), including clinic leaders (twice yearly, starting one year prior to opening). These research participants were of different professions, and include nurses, medical doctors, social workers, a psychologist, and unit leaders with varied competencies. Most interviewees were nurses, who also make up the largest professional group of HAT staff.
- 18 interviews with patients' relatives: relatives of nine patients were interviewed two times (4 and 14 months after patients' enrollment in treatment). These research participants differed largely in their relationships with and closeness to the patients, as well as in their knowledge of HAT's operation.

The main planned qualitative data collection is now completed, as described above. Data collection covering the patients' ensuing experiences will, however, continue until the end of 2024 through patient interviews and participant observation in the clinics, as well as with workshops and collaboration with user representatives to capture experience gained after several years of operation. Clinic leaders will be interviewed twice yearly until the end of 2026.

Participant observation has been conducted inside the clinics before and during the process of qualitative interviewing of patients and clinicians. The aim of observation was three-fold: to become familiar with the everyday operations of HAT; to prepare for and guide ensuing

interviews; and to collect data and obtain insights on HAT that could not be gained through qualitative interviews. This involves observing naturally occurring interactions as they unfold without interference from research, and also gaining insights through informal conversations with both patients and clinicians. Data from participant observation also added another source of data which can be triangulated with the interview data to validate findings, when several data sources, for example, confirm the same findings.

Being present inside the clinics over time was important to gain better insight into HAT's operations and to resolve queries that could more easily be answered through direct observation than through interviews. Observation also involved getting to know and interact with both the patients and clinicians, which was crucial in being able to build relations and rapport. This was particularly important to make it more likely that patients would consent to take part in the in-depth interviews.

No participants were offered compensation for taking part in the qualitative data gathering. All interviewees were asked for written consent to take part in the interviews. Interviewing patients was challenging in numerous ways. Since most interviews were conducted after medication intake, we used the same opioid intoxication scoring tool as used in the HAT clinics to make sure researchers never asked for consent or conducted interviews if patients were too affected by the medication and/or other substances. The tool is a translated version of the one previously developed and used in Danish HAT clinics [14]. Recruiting participants for the interviews was challenging in terms of being able to meet users at a time when they were both willing and not too affected by the medications to participate. A seven-person research team has carried out the interviews with patients: five researchers from RusForsk and two peer researchers with lived experience of OUD from ProLARNett. The researchers had no previous relation with the recruited patients.

Main point:

- 111 interviews have been conducted, primarily with patients and clinicians, as well as close relatives of HAT patients.
- Interview data provides knowledge about the early experiences with and views of HAT among these different groups.

4.2 Patient-reported outcomes: quantitative research

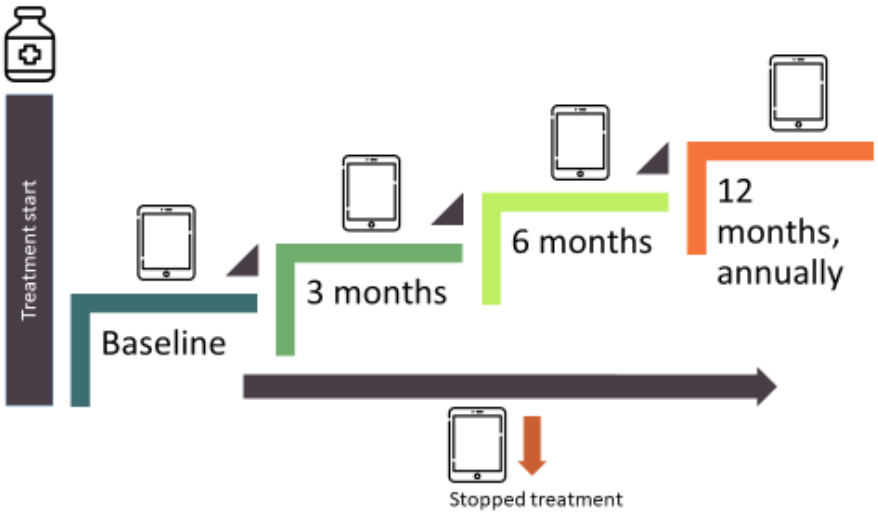
From January 15, 2022, to December 31, 2023, 92 participants have consented to be part of the quantitative research study (65 in HABiO, 27 in HABiB). According to clinic staff, there have only been five patients that have not wished to sign the consent form upon entering treatment. Some of these patients had been in treatment for such a short period of time that they had left treatment before they were informed of the research project. Patients receive treatment regardless of their participation in the research study.

Research participation in the clinics is high. All patients that consent to participate in research are asked to complete questionnaires at various time points and provide their national identity number for registry-based research.

The quantitative studies utilize questionnaire data collected from patients at the clinics at repeated time-points (**Figure 6**). This includes once at baseline (ideally within two weeks of treatment start). Subsequently, patients are asked to complete identical follow-up questionnaires at scheduled intervals during treatment: 3, 6, 12, 24, 36, and 48 months. Additionally, in cases where a patient discontinues the treatment, both the patient and the relevant staff are also asked to complete a separate questionnaire that aims to identify the reasons for the termination of the treatment.

This design with repeated measures allows for the monitoring of changes across different domains and multiple variables. All data are collected electronically using tablets. Each form takes approximately one hour to complete. Participants are given the opportunity to complete the questionnaire in parts during multiple visits.

Figure 6. Questionnaire-based study design.



As described earlier, 92 participants have consented to be part of the quantitative research study. The aim is to include all patients who start treatment. To date, nearly all HAT patients have consented to participate in the research. While this represents the majority of HAT patients, it is a smaller number than the projected 150-300 patients described in the initial HAT evidence summary [13].

Patients are not offered compensation for participation in the study, and the forms are completed with assistance from clinic staff. The project coordinator at SERAF provides ongoing support to clinic staff regarding the timeline for questionnaire completion. Based on the cohort of patients that have consented to be part of the research study, future registry-based studies are also planned with central registries in Norway and Denmark. Due to the relatively short duration of the treatment program and the small number of individuals enrolled, registry linkage has not yet been conducted in Norway. However, these linkages will be completed prior to the drafting of the final report and will be included as part of the final evaluation.

Main point:

- Nearly all HAT patients have consented to be part of the quantitative research study.
- The repeated measure design will allow for the ability to monitor changes over time while in treatment.
- Registry data will be accessed at a later stage, due to currently too low number of patients included.

5. Research Findings

5.1 Experiences in heroin-assisted treatment

Analysis of qualitative data is ongoing, but the planned data collection is mostly completed and includes data covering the experiences of HAT as seen from the perspective of patients, their relatives and clinicians working in HAT. Below follows a description of some preliminary and published results about the experiences and views of 1) patients in HAT, 2) HAT clinicians, and 3) relatives of HAT patients.

Patients:

A study based on qualitative data investigating patients' satisfaction one to two months after enrollment in treatment has been published [15]. This study outlined the three most prevalent benefits and challenges of being in HAT from the patients' perspective. Access to medical heroin, the positive patient–clinician relations, and the supportive environment of the clinic and overall treatment were experienced as main benefits. The most challenging aspects were the intense treatment scheme and limitation in the medications provided, the strict clinic rules, as well as the increased downtime and concerns over HAT's longevity. One to two months after their enrollment, the interviewed participants were more satisfied than dissatisfied with entering and being in treatment. From what participants described as changes in their everyday life after entering treatment, it is also clear that their quality of life has improved in certain areas. Being in HAT helped make their everyday lives safer, more predictable, stable, and with less pressure to commit crime or obtain money in undesirable ways (**Table 4**.). These benefits are likely also to contribute positively to treatment retention [15].

As these are early results from the early phase when HAT was newly established and not yet in normal operation with the full number of patients, an important topic for further analysis will be the patients' satisfaction in the longer-term and what potential changes they experience with respect to the benefits and challenges.

Table 4: Patients' experienced benefits and challenges of being in heroin assisted treatment - one to two months after enrollment in treatment

BENEFITS	CHALLENGES
Access to medical heroin (medical) - Reduced stress and financial pressure - New routines and hope	**Treatment scheme (configurational)** - Lack of medications - Too intense
Patient–clinician relations (relational) - Respectful relations - Being heard	**Clinic rules (configurational)** - Unfounded rules - Negative influence on relation with clinicians
Supporting environment (configurational) - Opportunities for psychosocial assistance - Safer user setting	**Downtime and uncertainties (configurational and relational)** - Too much free time - Uncertainties about project's future

Source: Ellefsen et al. 2023

Another ongoing study investigates the patients' experiences of receiving medical grade heroin (diacetylmorphine) and the transitions of administration routes (intravenous, intramuscular, and oral) during the HAT program (De Pirro et al. *In preparation*). This study investigates how different routes impact the subjective perceptions of the patients and the treatment trajectories. Preliminary findings show that HAT participants tend to remain in the program, even after switching administration routes that may lead to different subjective effects. Participants reported enhanced functionality and gratitude for the HAT program 8-18 months into treatment. These preliminary findings fill a gap in the literature [16], and enhance our understanding of the subjective effects of diacetylmorphine and how it is influenced by different administration routes. Importantly, the HAT program has low attrition rates, and patients adapt quickly to new routes and subjective effects, although they may not initially find all aspects ideal. It seems the attraction of the medication in the HAT program remains across administrative routes and that patients quite quickly adapt to new routines and experienced effects, resulting in long-term retention for most.

HAT clinicians

Preliminary analysis of interviews with clinicians shows there are three areas of HAT they experience as particularly rewarding and three that are the most challenging. These will be outlined in a publication. The preliminary results show that clinicians, quite unequivocally, think the treatment is positive for patients and thus should continue beyond the trial period. The rewarding aspects of the treatment were what led clinicians to perceive HAT as a feasible and valuable treatment. This assured them of the treatment's utility, which was important for them because the treatment was new.

However, they thought certain challenges could have been better resolved, and that there is a small subgroup of the most unstable patients for whom they are uncertain about the treatment's utility. There were many challenges linked to implementing a new treatment without established clinical procedures and routines, and much effort was made to adjust and develop routines and protocols from the initial opening of the clinics to a state where the clinics were becoming more streamlined with established routines. However, changes in treatment procedures are still ongoing, and new challenges emerge along with influential changes in national conventional OAT guidelines. However, the national OAT clinical guidelines, are not in principle guidelines for HAT, although the guidelines also likely influence HAT as both the staff and the patients may be transferring between different entities in addiction treatment.

Relatives of HAT patients

Analysis of data from interviews with relatives of HAT patients is ongoing, but data already shows highly diverse experiences with changes in their own caretaking responsibilities after their relative entered HAT. They were also diverse in their level and type of contact and relationship with their relative in HAT, which meant they had different insights into HAT's operation and impact on their relative. Overall, relatives expressed being pleased with their relatives entering HAT, as it was a clear improvement compared to their situation before entering HAT. Many relatives emphasized that they felt less anxious and insecure after their relatives had entered HAT because the patient thus had gotten structured care and assistance in place around them. Some relatives described being initially skeptical of HAT, but they changed their view after having time to reflect, to assess the available treatment alternatives and to see changes in the patients. Some were critical of the treatment being too medically

oriented and not involving enough psychosocial assistance, such as initiatives to get their relative into some form of education or job training.

Main point:

- Patients' satisfaction with HAT was high one to two months after enrollment in treatment.
- The program has relatively low attrition rates, and patients adapt quickly to new routes of administration and subjective effects of the medicines, although they may not initially find all aspects of HAT ideal.
- Clinicians described different aspects of treatment provision that were rewarding and which made them believe in the treatment's feasibility and utility for patients.
- Relatives of patients had varied experiences of HAT's impact on the patients and on their own caretaking responsibilities, but they were generally positive to HAT because of the structure of care and safety it provided to patients.

5.2 Peer experiences in drug treatment research

ProLARNett is a national service user association for people in OAT in Norway. ProLARNett works with user participation at system, service, and individual levels. In addition, the organization hosts various projects each year, with a focus on harm reduction, family work, and activities.

ProLARNett has been involved in the HAT research group since 2019, with participation in project design and questionnaire development from the start. ProLARNett sought to use the "peer-to-peer" method to gather information from patients. In collaboration with researchers at RusForsk, they developed a semi-structured interview guide with up to 20 questions. The questions were largely about how satisfied the patients were with the treatment at the start and after 6 months.

The plan was for ProLARNett to interview approximately 10 people at HABiO and 10 people at HABiB. This got off to a slow start, but eventually eight patients were interviewed at HABiO at the start of treatment (within the first month of entering HAT) and two patients after six months. In Bergen, only one interview was conducted at baseline.

The interviews were recorded and entered into the original research database. The plans for conducting further interviews were changed for 2024, and ProLARNett now plans more

informal conversations from which short notes will be written. These will be sent to RusForsk and used for analytical purposes.

ProLARNett and RusForsk are planning to hold several workshops in both Oslo and Bergen in 2024. Patients in HAT will be invited to these workshops. The first workshop of this kind was organized in Oslo, April 2024. The aims of these workshops are to discuss diverse ways and methods to include differing patient perspectives in the ongoing research.

It is desirable to have more perspectives from the patients in HAT themselves, including what they think about their own treatment in HAT. Due to the small number of patients, and the delay in startup, ProLARNett reports that it is difficult to collect data on how the clinic affects the patients currently. In the current population and the interview data collected, most patients in HAT express satisfaction with the treatment they receive. In addition, they experience an improvement in their life situation. However, if the clinic had been fully occupied with many patients, as intended, patient satisfaction may have differed.

Main point:

- User representatives have been involved from the development of the research plan as part of the research group.
- Involving people with lived experience of the topic in research is important.
- HAT patients will be involved during workshops and with interviews.

5.3 Patient-reported outcomes

The quantitative data is derived from a comprehensive questionnaire which covers multiple domains. This includes information regarding the patients' living situation, income sources, crimes committed and experienced, various aspects relating to their mental and physical health, substance use, and overdoses **(Figure 7).**

Figure 7. Domains included in the quantitative questionnaires used to examine changes while in heroin-assisted treatment.

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From January 2022 to December 31, 2023, of the 92 research participants, 86 patients completed at least one section of the baseline questionnaire (see **Figure 6** for study design). The reported information in this section pertains to this group, with the majority (71%, n=61) enrolled in HABiO and the remaining 29% (n=25) in HABiB.

Demographics, economy, and income

At admission to treatment, patients had a mean age of 46, which is several years older than the general first time OAT entrants. The majority were male (80%), with HABiB having a slightly higher proportion of female patients than HABiO. Most patients were born in Norway (87%), and 20% reported that at least one parent was born in a different country. Half of the participants (51%) lived in rented housing or own their own housing, and more than one third lived in temporary or municipal institutional housing for people who use substances (34%). No participants reported experiencing homelessness at the beginning of treatment, however 17% reported their housing being unstable in the previous month. Almost all participants were unemployed at the start of treatment, with only four reporting part-time work. Approximately

47% of participants had not completed secondary school education, and 20% reported difficulties with reading or writing.

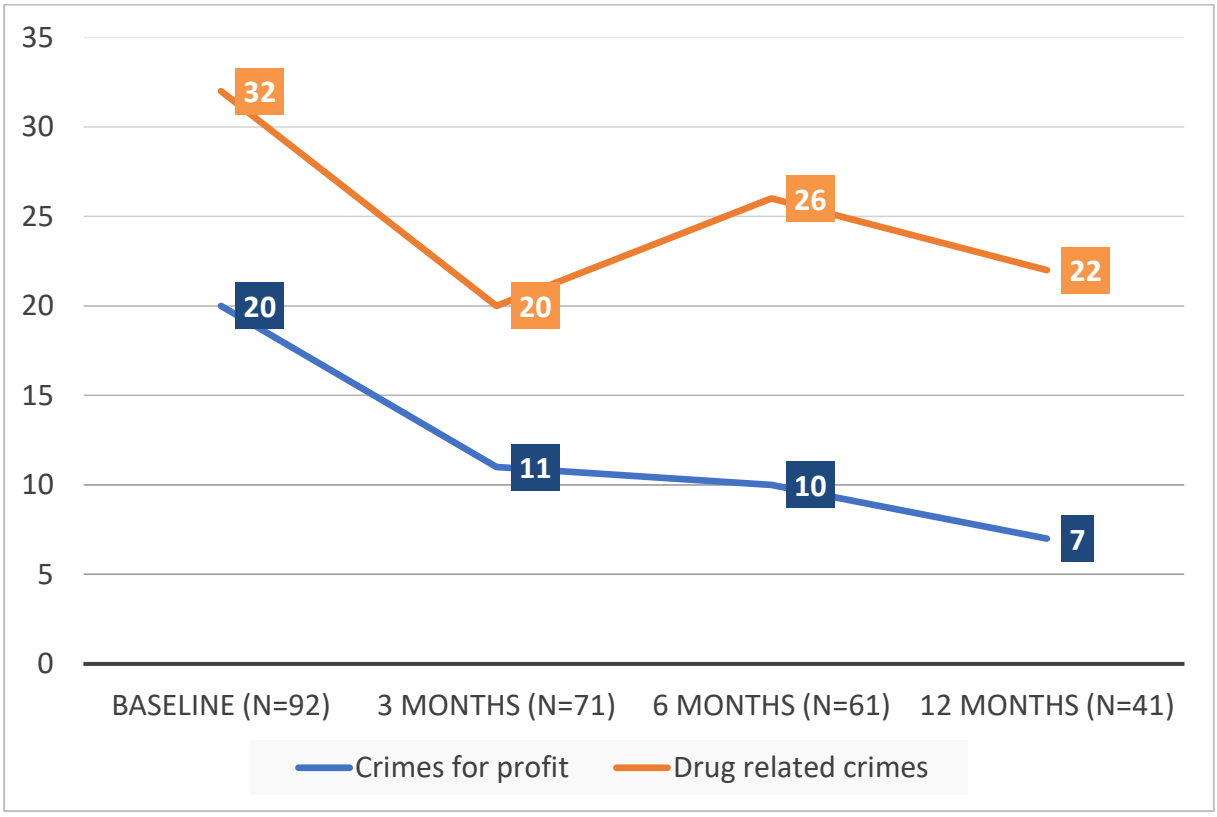
Limited food access in the past 30 days was reported by 32%, and hunger by 44%. Higher hunger rates were noted in males (51% vs. 13% in females) and those with unstable housing (79% vs. 36%). Although not significant, limited food access was higher in those with unstable housing (54% vs. 28%). Generally, those with higher education had lower hunger and limited food accessibility, however, this finding was not significant. No significant links were found between other factors and food access or hunger.

When compared with patients in conventional OAT in Norway, a larger proportion of HAT patients were without work and reported regular drug use [6].

Crime

Participants were asked about recent incarceration in the three months prior to starting in HAT. Of respondents, 11% reported recent incarceration. Participants were also asked about recent crimes committed at baseline, 3, 6, and 12 months after treatment start. Trends indicate a reduction in criminality (**Figure 8**), which is similar to a previous Norwegian study on conventional OAT patients [17]. Among HAT patients, at 12 months after treatment start there was a 65% reduction in crimes committed for profit and a 31% reduction in drug-related crimes. However, preliminary findings may indicate that ongoing crime is higher among HAT patients than previously found for conventional OAT patients [17]. The study found that 18% of conventional OAT patients reported ongoing crime at follow-up, whereas 46% of HAT patients report ongoing crime at 3-month follow-up. More than half of the patients (62%) reported being a victim of a crime in the 3 months prior to starting HAT.

Figure 8. Self-reported recent crime for HAT patients in Norway, 0-12 months from treatment start (%)

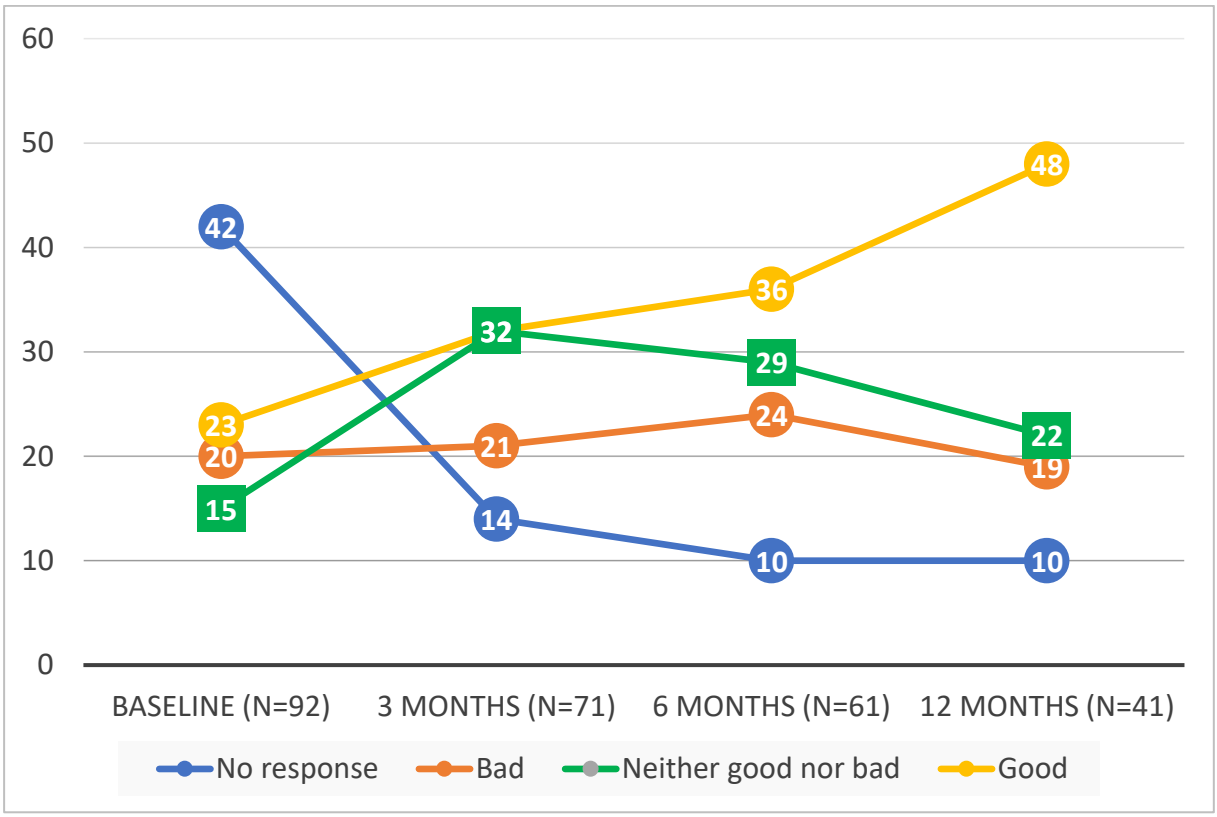


Mental health

Mental health is a central theme among people with illegal drug-use. It may affect the level and type of use, retention in and outcome for treatment programs. In this research project, mental health is initially assessed by two questions: "How do you rate your own mental health?" (1= "extremely bad" to 5= "extremely good" with 3 as a neutral median), and "to what extent do you experience depression and anxiety" (with similar ratings).

Preliminary analysis reveals that there appears to be a trend of improved mental health while in treatment during their first year. Of the respondents, at baseline 20% rated their mental health as bad and 23% as good or above (**Figure 9**). At follow-up, the percentage of those that rated their mental health as good increased to nearly 50% at 12 months, a change of 52% from baseline.

Figure 9. Self-rated mental health for HAT patients in Norway, 0-12 months from treatment start (%)



The preliminary results suggest that the effects of HAT on mental health take some time to manifest. The initial rate of "no response" (those who did not answer the question) at baseline (42%) drops to a consistent 10% from the third time point (6 months). Further monitoring and inclusion of patients will likely give a clearer picture of how HAT might affect mental health and well-being among patients.

Previous treatment

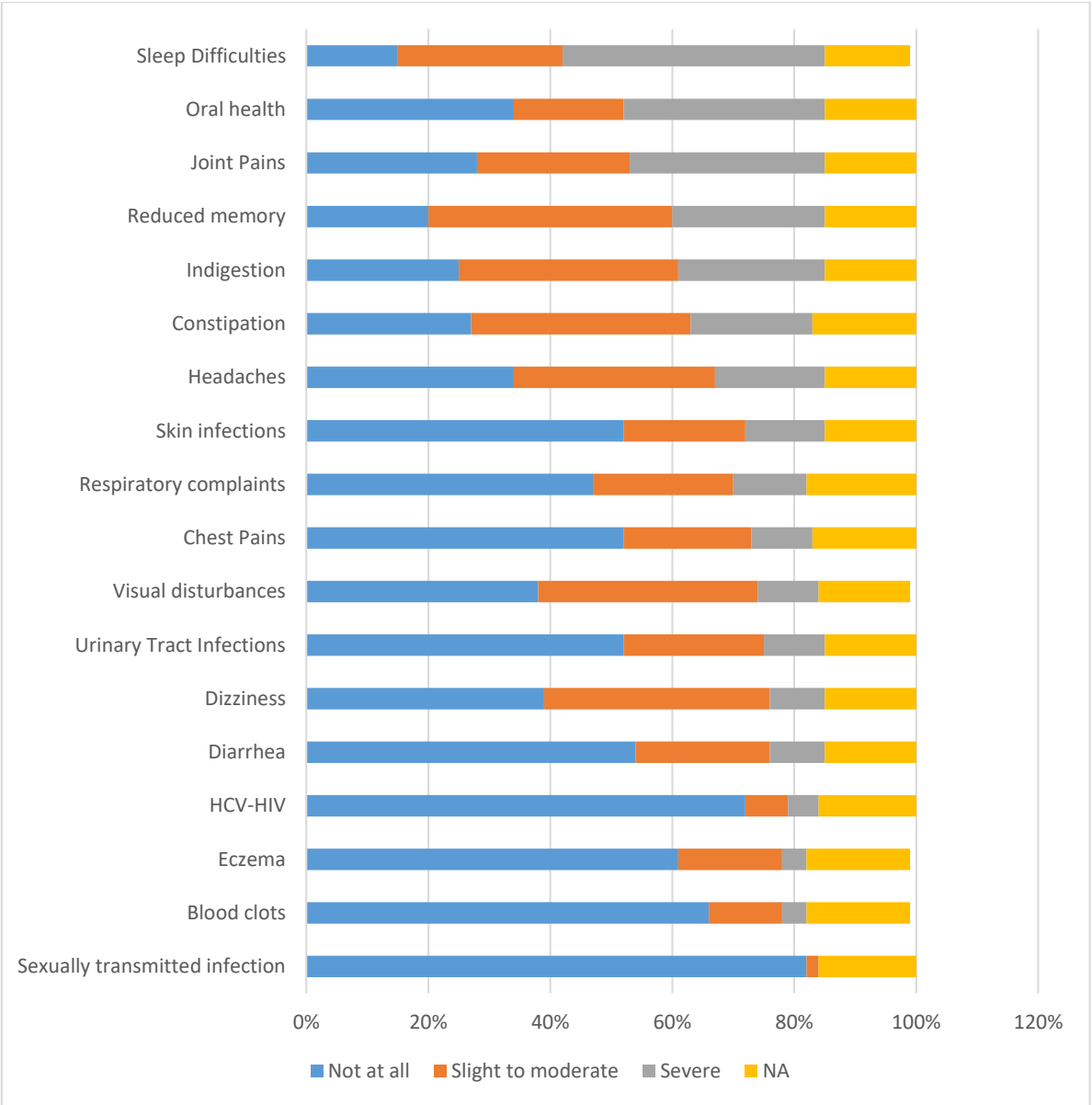
Almost all patients (95%) had previous experiences with OAT for substance use, with the most common medical options in use being methadone (73%) and buprenorphine (51%). Most patients (72%) described previous treatment discontinuation from OAT as voluntary.

Physical health

Patients undergoing treatment for OUD frequently exhibit a high rate of somatic comorbidity [18]. Somatic complaints, including pain, discomfort, or reduced functioning, are among the most common issues in healthcare services, and are associated with poor quality of life and substantial functional impairment. Heroin-assisted treatment patients were asked to indicate

the extent to which they had been troubled in the past three months by different somatic symptoms (**Figure 10**). The intensity of these symptoms varied across a wide spectrum, with sleep difficulties, oral health complaints, joint pain and reduced memory perceived as the most problematic at baseline.

Figure 10: Baseline overview of symptom severity among heroin-assisted treatment patients



The data regarding the severity of somatic symptoms were further categorized as 'Low-Moderate' and 'Severe,' as illustrated in **Figure 11**. Initially, at baseline, nearly half of the cohort reported experiencing severe symptoms, showing a substantial initial somatic symptom burden. Over time, the percentage of patients with Low-Moderate symptom severity gradually increased, rising to 57% at 3 months, 62% at 6 months, and reaching 66% by the 12-month

follow-up. Conversely, the proportion of patients experiencing severe symptoms showed a declining trend, decreasing to 34% at the end of the 12-month period.

In comparison, a recent study using a similar scale indicated that the incidence of severe somatic symptoms was lower among patients beginning conventional OAT in Norway [14]. At the onset of OAT, less than 25% of the participants experienced severe symptoms, with the percentage declining to under 20% after the first year of treatment. Among patients in HAT, nearly half of patients reported severe somatic symptoms at the outset of the treatment, which is higher compared to conventional OAT where less than 1 in 4 patients reported such symptoms initially.

These preliminary findings suggest a gradual improvement in the self-reported somatic symptom severity over the course of HAT. The largest change was seen in the severe category, showing a 15% reduction over 12 months. Interestingly, the moderate-low category showed a gradual increase in patient numbers, indicating a possible shift from severe to moderate-low symptomatology burden as the treatment progressed. This indicates improvements, and reduced symptom burden, but not necessarily a “cure” or a return to a symptom free state as the general pattern of development.

Nonetheless, it is important to recognize that after 12 months, a majority continue to report moderate to severe symptoms, indicating persistent symptom burden in this cohort despite noted improvements. This indicates a continued need for resources in the HAB clinic to follow up on somatic complaints. Further statistical analyses are in progress to evaluate the symptom trajectories and specific shifts during the first year of HAT. The outcomes of these analyses will provide deeper insight into the patient experience and the effects of the treatment program for the final report.

Figure 11. Physical symptom burden for heroin-assisted treatment patients during the first year in treatment

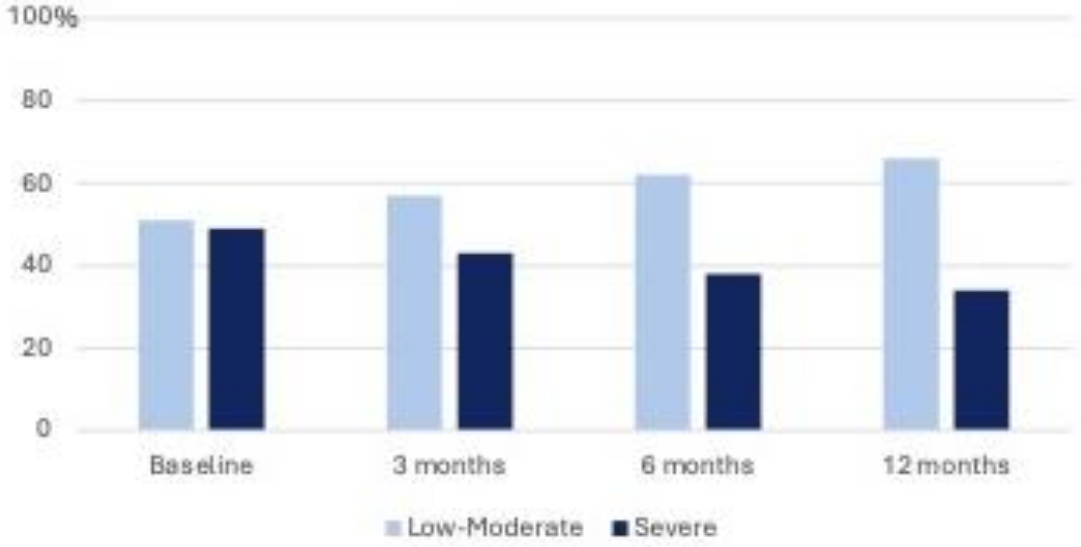
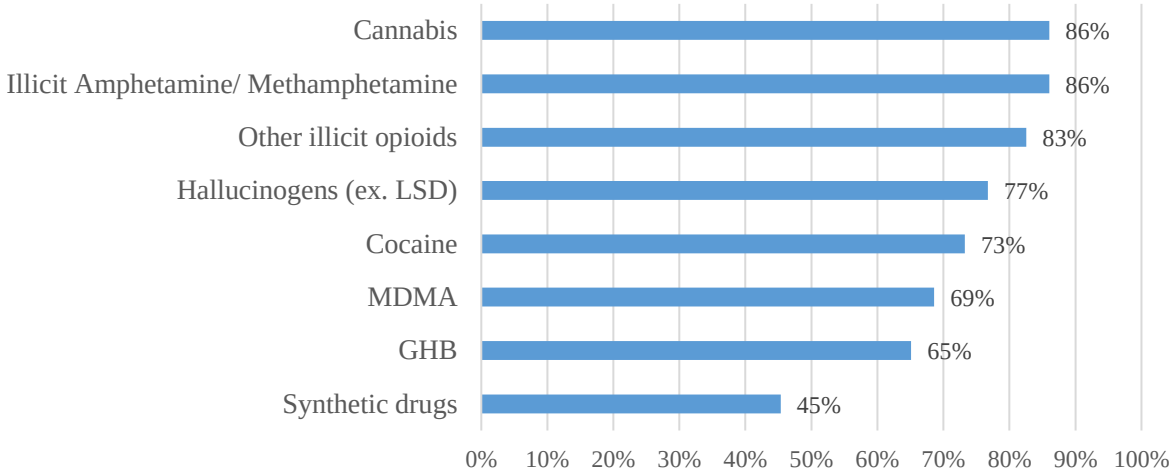


Figure 11 illustrates the progressive change in the total score of somatic symptoms from baseline (N=77), to follow up at 3 months (N=44), 6 months (N=52) and 12 months (N=32). The data for low-moderate symptom severities have been aggregated to depict a combined percentage, offering a view of the overall decrease in severe symptoms burden and corresponding increase in less severe symptomatology reported by the patients over time.

Drug use

The use of multiple substances was common for the group. At baseline, patients reported high proportions of cannabis, amphetamine, and illicit opioids use **(Figure 12).**

Figure 12. Self-reported lifetime substance use, percentage upon entry into heroin-assisted treatment



Approximately 40% of patients had experienced an unplanned overdose in their lifetime, with 6% experiencing one in the month prior to treatment initiation.

Motivations and expectations

Patients were asked about their motivations and expectations for HAT, with the most cited reasons being:

- "I need heroin, and want to get it in a legal, controlled and safe manner."
- "I expect to satisfy my opioid addiction."
- "I expect to have a better quality of life."

Upcoming studies will examine how many of these characteristics have changed during treatment.

Main point:

- The patient group experiences burdens and challenges, including housing instability, and history of overdoses.
- The patients reported a high level of somatic symptom burden when entering HAT and the severity seems to reduce gradually during the first year of treatment.
- Rates of self-reported crime appear to be reducing while in treatment.
- The number of patients reporting their mental health as 'good' have increased during the first year in treatment.
- The group displays strong motivation and high expectations from their participation in treatment.

5.4 Heroin assisted treatment patients in Denmark

Danish HAT data is available for 545 HAT patients who enrolled between 2010 and 2018. This includes both questionnaires and registry data.

A recently published study used national registry data to assess HAT patients in comparison with other patients enrolled in conventional OAT during the same period [19]. Compared with patients who were enrolled in treatment with methadone or buprenorphine, patients entering HAT were more likely to have a history of non-fatal overdoses, chronic hepatitis, and criminal convictions, indicating a more severe symptom burden and characteristics among HAT patients. Nearly half (48%) of HAT patients had a history of residential rehabilitation. Patients receiving buprenorphine as part of OAT were younger and more likely to be studying or working than patients receiving other forms of OAT. At the same time, patients who

received HAT were less likely to have had a history of treatment for psychiatric diagnoses when compared to OAT patients in general.

We have also analyzed factors associated with retention in HAT in Denmark (article has been submitted for publication). Analyses showed that the annual dropout from treatment was quite low. Retention rate at 12 months was 70%, and the median time to dropout was 2.5 years. Predictors of retention in HAT in this naturalistic setting were generally similar to what others have found. Cocaine use, benzodiazepine use, poor mental health, criminal behavior, and young age were associated with poorer retention in HAT.

In addition, we have analyzed the psychometric properties of the Short-Form 36 questionnaire among people receiving HAT (article under revision).

Main point:

- Based on the 545 patients enrolled in HAT in Denmark between 2010 and 2018, it was shown that HAT attracts a group of patients who have considerably more difficulties than patients who receive methadone or buprenorphine treatment in conventional OAT.
- Attrition is low in HAT in Denmark, with a 70% retention rate at 12 months.

5.6 Publications, presentations, and media

The research group collaborates on all writing and publications. **Table 5** below lists currently published and submitted papers to peer-reviewed journals. Additional publications are currently in progress. The researchers have also been active in research dissemination sharing initial findings during the period of 2021-2023. This includes via conferences, presentations, and meetings.

Table 5. Publications from 2021-2023.

Published
1. Milella, M. S., D'Ottavio, G., De Pirro, S., Barra, M., Caprioli, D., & Badiani, A. (2023). Heroin and its metabolites: relevance to heroin use disorder. Transl Psychiatry, 13(1), 120. https://doi.org/10.1038/s41398-023-02406-5
2. Ellefsen, R., Wüsthoff, L. E. C., & Arnevik, E. A. (2023). Patients' satisfaction with heroin-assisted treatment: a qualitative study. Harm Reduction Journal, 20(1), 73. https://doi.org/10.1186/s12954-023-00808-8

3. Ellefsen, R. (2023). Narkotikapolitikk i endring: Heroinklinikkenes oppkomst i Norge. Nordic Studies on Alcohol and Drugs, 0(0), 14550725231207251. https://doi.org/10.1177/14550725231207251
4. Melis, F., Hesse, M., Eide, D., Thylstrup, B., Tjagvad, C., Brummer, J. E., & Clausen, T. (2024). Who receives heroin-assisted treatment? A comparison of patients receiving opioid maintenance treatment in Denmark. Drug and Alcohol Dependence, 254, 111051. https://doi.org/10.1016/j.drugalcdep.2023.111051
5. Myklebust, L. H., Eide, D., Arnevik, E. A., Dadras, O., De Pirro, S., Ellefsen, R., Fadnes, L. T., Hesse, M., Kvamme, T. L., Melis, F., Oldervoll, A., Thylstrup, B., Wusthoff, L. E. C., & Clausen, T. (2024). Evaluation of heroin-assisted treatment in Norway: Protocol for a mixed methods study. BMC health services research.

Submitted and under peer-review

6. Kyrkjebø, T., Dahl, C., & Ellefsen, R. (n.d.) Er utdeling av medisinsk heroin tilstrekkelig for å bedre livskvaliteten til personer med opioidavhengighet? - En kvalitativ studie om heroinassistert behandling. Manuscript submitted to publication, Sykepleien Forskning (status: revision submitted after being accepted with minor revisions).
7. Brummer, J., Thylstrup, B., Melis, F., & Hesse, M. (n.d.). Predictors of retention in heroin-assisted treatment in Denmark 2010-2018 – a record-linkage study. Manuscript submitted for publication, Journal of Substance Abuse and Addiction Treatment (status: revision).
8. Melis, F., Clausen T., Castel C., Dadras O., De Pirro, S., Myklebust, L.H., Oldervoll, A., Wüsthoff, L.E., Eide, D. (n.d.). Patient characteristics from Norway's first heroin-assisted treatment clinics. Manuscript submitted for publication, Substance Use & Addiction Journal
9. Ellefsen, R., De Pirro, S., Wüsthoff, L. E. C., Haukland, V., Arnevik, E. A. (n.d). «We became their anchor point in life»: Clinicians' experience of providing heroin-assisted treatment.

6. Evaluation measures

Key evaluation measures are currently being assessed and will continue to be evaluated until the final report. As **Table 6** shows, most of the assessment for key measures is ongoing. To more fully evaluate the outcomes associated with HAT, more time and patients are needed. The final evaluation of the HAT program will be completed in 2026.

Key evaluation measures include:

- Implementation
- Patient, staff, and relatives' experiences
- Clinical outcomes (ex. serious adverse events)
- Patient-reported outcomes (ex. physical health, quality of life)
- Behavioral outcomes (ex. crime, drug use)
- Psychosocial outcomes (ex. mental health)
- Healthcare utilization
- Retention in treatment
- Cost-benefit
- Research dissemination outcomes (publications, presentations)

Table 6. Selection of evaluation measures for the heroin-assisted treatment pilot project

	Evaluation measures	Assessed	Ongoing	Unable to assess
1	Determine benefits of HAT from staff perspectives	x		
2	Determine benefits of HAT from patients' perspectives	x		
3	Determine benefits of HAT from relatives' perspectives	x		
4	Determine challenges of HAT from staff perspectives	x		
5	Determine challenges of HAT from patients' perspectives	x		
6	Determine challenges of HAT from relative' perspectives	x		
7	Describe factors facilitating implementation of HAT	x		
8	Describe barriers to implementing HAT	x		
9	Number of patients enrolled in treatment		x	
10	Number of serious adverse events		x	
11	Circumstances surrounding serious adverse events		x	
12	Changes in healthcare utilization while in HAT		x	
13	Number of patients transferred from HAT to OMT		x	
14	Attrition rates for HAT patients		x	
15	Changes in physical health while in HAT		x	
16	Changes in mental health while in HAT		x	
17	Changes in quality of life while in HAT		x	
18	Changes in high-risk behaviors while in HAT		x	
19	Changes in crimes committed while in HAT		x	
20	Changes in crimes experienced while in HAT		x	
21	Changes in illicit drug use while in HAT		x	
22	Changes in employment or education while in HAT		x	
23	Access to stable housing while in HAT		x	
24	Changes in social relationships while in HAT		x	
25	Cost-benefit of HAT		x	
26	Describe options for integration of HAT into OMT system		x	
27	Dissemination of research findings		x	

7. Clinical perspectives

Leaders from the clinics were asked to provide a short description of their overall impressions at this midway point of the HAT pilot project. Their summaries are below:

Clinic perspective from HABiO:

"The patient group we work with is very vulnerable, and often presents with complex conditions and high rates of comorbidity. The clinic's goal is to reach patients for whom conventional OAT has not provided a sufficient stabilizing effect, the so-called «hard-to-reach» and «hard-to-treat» group of patients. To achieve treatment retention, close follow-up is required from both the social worker and the patient's nurse who work to coordinate services outside the clinic as well.

The clinic is at the intersection of harm reduction and substance use treatment. Ethical assessments regarding the effects of treatment and discussions about treatment goals for the individual patient are an integral part of everyday life in the clinic. While patients are in treatment, we generally see good results, including a reduction in the use of illicit drugs, completed dental treatment, establishment of somatic healthcare follow-up, improved housing, and financial stability, as well as greater contact with relatives.

In the start-up phase, it has been necessary to adhere to the HAT model, while learning from our own experiences along the way to ensure proper operation, safety, and adequate patient-oriented treatment. Medication management requires continuous cross-checking by two nurses, drug intoxication assessment is staff intensive, and emergency situations require attention. It takes time to stabilize each patient, and sufficient medical resources are needed to both provide individual patient care and adjust doses appropriately. The pilot project's target group requires good staffing to safeguard the HAT model.

Since the establishment of HABiO, there have been reports of an increase in undesirable events in clinic vicinity. We continuously collaborate with security and our patients to minimize incidents. When assessing how many patients can be treated at

the same clinic, we must consider staff working conditions, patient care and treatment, the target group's comorbidity, and the location of the project.

We are constantly working to improve cooperation with conventional OAT when it comes to patient flow. We accept referrals to the clinic, but the influx varies. Our experience is that it takes quite some time for patients to attend the intake interview and start treatment after a referral has been assessed. In the case of many patients, this is most like related to their unstable living situation."

Clinic perspective and impressions from HABiB

"After two years of operation with HAT, the focus is now largely on optimizing routines and structure. We continue to spend time developing routines to optimize treatment provision at HABiB. Medication management is resource-intensive in terms of staffing. Assessments of patients and dose adjustments according to established routines require experienced nurses and social workers who know both the patient and the drug, which makes HAT extra vulnerable in the event of absence of staff.

Ethical discussions and assessments of what constitutes appropriate and good health care is a recurring issue. Assessment of discharge due to unwanted incidents, inadequate cooperation, and reduced functioning after starting in HAT are difficult professional and ethical discussions. For some patients, HAT offers harm reduction and stabilization, while for others it has contributed to changing their life. We have seen improvements in patients' housing situation and finances, participation in activities, and work. We have also seen the assessment and treatment of psychiatric and somatic issues, and transitions into conventional OAT since the start of HAT. We have established a good cooperation with the detoxification and the stabilization ward, where patients can be admitted while coming to HAT.

The patient group needs comprehensive follow-up and complex services that require close cooperation with municipal services, GPs, NAV, other parts of the primary health services, the correctional services, etc. For the therapist/contact nurse/social worker, this is an important task, but it is also challenging in individual cases to connect to services we believe the patients need.

At HABIB, we are still operating at a temporary location, as it has taken significantly longer to establish permanent location than planned. The location at start-up was not suitable for the operation of the HAT clinic, which led to a delayed start-up and reduced intake of patients. After one year of operation, HABiB moved to new temporary location that is more suitable for operations, but not optimal. We have experienced this as a challenge.

It is assumed that the number of referrals to HAT is influenced by knowledge of the treatment options. Therefore, it is crucial that the offer is made known to everyone who works with HAT's target group. This takes time and requires repetition to ensure correct information is shared. One patient put this into words when she said that "[she was] discouraged from applying to HAT, as it would be a setback for [her]." The patient herself describes that HAT was life changing for her, and after some time in HAT, she transferred to conventional OAT. Statements from other patients have also shown that there has been skepticism among patients to apply to HAT before they have become better acquainted with and heard others' experiences with HAT."

8. Financing and funding

Overall, the Ministry of Health has provided the HAT pilot project with 155 million NOK from 2020-2023. This funding is the sole source of funding for the two clinics currently operating in Oslo and Bergen. Roughly, the budget at HABiO is spent 60% on staff, 28% on medications, and 12% on other costs.

Since patient inclusion in treatment began in January 2022, the clinics have produced 95 treatment years of HAT, distributed across the 92 patients included in the current evaluation (midway report). Although this report is based on the first two years, which is typically a high-cost period for a clinic, and includes establishment of the clinic premises, the overall cost so far is above 1.5 million NOK per person-year of HAT treatment. However, this number is a crude total estimate and not a formal cost-benefit analysis, which is to be developed and presented in the final evaluation report anticipated during the first half of 2026.

If cost per patient-years is to come down, either costs for medications should be reduced, which seems unlikely with the current monopoly among medicinal providers for HAT in Europe, or the number of patients should increase while keeping the same number of staff. However, the latter approach will necessarily be a balancing maneuver in combining effective use of resources and keeping sufficient clinical quality.

Overall, the observation is that with the current funding the clinics have stated they are near maximum capacity for patient enrollment in treatment. Hence, if numbers are to reach those estimated at the outset, that is, up to 300 patients simultaneously enrolled, the overall funding seems inadequate. Additionally, it is still uncertain if the treatment need in the two catchment areas will result in as many as 300 patients in HAT at the same time, and it may well be that the current need for HAT is lower than estimated. The recent expansion of available medications in conventional OAT (including depot buprenorphine and 24h SROM) may have reduced the clinical attraction to and utility for a large HAT capacity and treatment need.

9. Challenges and limitations for the research project

The small patient group (numerically) at both HABiO and HABiB is the primary challenge to evaluating HAT at this stage. Reaching the threshold for sufficient sample and hence statistical power in the quantitative analyses may take longer than initially planned. A cohort of 150-300 patients may not be achieved until a slightly later stage than initially anticipated, with implications for the retrieval from central registry-data. The limited cohort size may have implications for the quantitative analyses and will affect modeling and a possible prediction value of results. For the more societal effects of HAT, a sufficient level of explained variance is often conditional on a wider set of predictors than in other studies. A low level of patients may limit the number of variables that may be included in such analyses due to statistical power.

However, the planned use of statistical methods such as linear- and generalized mixed-models are suited for the repeated analysis of patients throughout the observational period, as has been planned for in the study design. Also, with a continuous inclusion of patients the cohort will hopefully reach sufficient size to ensure statistical power in line with the study protocol, and for further such analyses to be included in the final report.

Certain missing areas of routine data collection will limit the final evaluation. For instance, currently there are no 'waiting lists' which could have given information on the degree of unmet need for patients who are eligible to enter into HAT.

To avoid overlapping tasks for clinicians, the research group chose not to include the validated questionnaires that were said to be already part of the clinical routine assessments into the research portfolio. However, due to clinic workload, some of these routine assessments do not appear to be included. As a result, certain assessment tools are not available for research. Further, relevant data from electronic patient files are not systematically collected and will need to be collected manually during the second phase of the evaluation.

Finally, the addition of morphine-based medications might have been attractive for some patients in HAT, as they provide alternatives beyond conventional OAT medications. We are uncertain how this influences the need for or attraction to HAT, and how it will affect the number of patients seeking HAT as more options for individual tailored treatment now exist in conventional OAT. In addition, the international evidence base does not include information

on the impact of using SROM (both 6-12- and 24- hour duration) as the overnight bridge medication for HAT. Although the use of morphine-based medications is included in the national OAT guidelines, from an evaluation standpoint, the use of these medications in HAT may make it difficult to discern if changes that occur while in HAT were due to heroin or to the use of morphine-based bridge medications.

Other than the use of new morphine-based medications, there is hitherto no evidence for large and considerable biases between the cohort in the two HAT clinics. The impact on the use of different overnight bridge medications will be explored further in the final report. Lastly, one of the strengths of the study lies in its design as a longitudinal evaluation of a new clinical practice, not as a randomized clinical trial. The evaluation is based on the total clinical population (of which nearly all are included), and not a selection of the population. That the evaluation of the HAT clinics is conducted by an external evaluation team outside of the clinics is considered an important strength to the project's evaluation plan and utility.

10. Next Steps

In addition to the ongoing analyses outlined in this report, the project has several planned studies which are outlined below.

Registry data analyses:

The study's ethical approval grants access to the use of registry data in Norway but requires separate applications to each registry. The application process will start in the spring of 2024 based on the present cohort, and possibly repeat at a later stage with the additional recruited patients and larger cohort.

In Denmark, similar registry data is accessible through the general approval of the project's researchers at CRF.

Cost-benefit analyses:

Health economics and cost-effectiveness analysis can guide decision makers. In general, the cost effectiveness of a treatment is intended to reflect the difference between the remedy's opportunity costs (pharmaceutical heroin) and those of the foregone or conventional alternative to capture a broader set of values beyond the scope of mere financial costs.

Initially, for assessing operating costs, a three-step, top-down methodology used and refined by a former healthcare services project will be applied. For subsequent cost-effectiveness analyses, outcome is often measured in quality-adjusted life years (QALYs) for individual patients, in number of accidents or fatal incidents, or as societal costs associated with patients' level of functioning and societal (criminal) behavior. These analyses are planned for the last stage of the study.

Toxicology sub-study:

Given the relative novelty of HAT, very few studies have explored the pharmacokinetics of pharmaceutical heroin in a clinical setting. The approval of diacetylmorphine in the context of Norway's HAT gives us the opportunity to conduct studies on heroin's effects in humans in a controlled and safe setting.

To advance our knowledge in this area, a pharmacokinetic pilot study was established in collaboration with expert toxicologists at OUS, researchers at SERAF and staff at HABiO. This

study will examine the pharmacokinetics and subjective effects of pharmaceutical heroin in patients receiving HAT. The primary aim of this study is to explore the association between the concentrations of the active heroin metabolites in the peripheral venous blood and simultaneously report on the subjective effects following heroin administration. A deeper understanding of the time course and the relationship between metabolite concentrations and subjective effects post-heroin administration can help to significantly refine treatment modalities through evidence-based adaptations. Such insights could facilitate the customization of existing therapeutic approaches and help to identify novel targets for pharmacological intervention. This study has received ethics approval and is currently in the planning-implementation phase.

11. Summary

Heroin-assisted treatment has been available in two clinics in Oslo and Bergen since 2022. This five-year research project is examining the effects of implementing HAT in Norway for individual patients and for the health care services. This report summarized preliminary findings at the midway point of a five-year pilot project, with a descriptive focus on the establishment and initial findings from the clinics. The final report will aim to include the treatments impact for patients, the cost-effectiveness of the treatment and the overall assessment of how this treatment compares to conventional OAT.

In the first two years of operation, there were 92 research participants that started at the HAT clinics. Attrition is relatively low, given the burdened patient population it is serving. Of the 27 patients that left treatment, half transferred to conventional opioid agonist treatment, which should be viewed as a positive outcome and development for the patient. Hence “drop-out” from treatment seems to be low.

Patients’ satisfaction with HAT was high one to two months after enrollment in treatment. Additionally, patients reported strong motivation and high expectations with their treatment. At the start of treatment, HAT patients reported multiple vulnerabilities, including indicators of food insecurity, recent incarceration, housing instability, and a history of overdoses. In addition, patients reported a high level of physical health symptom burden when entering in HAT. However, the severity seems to reduce while in treatment. Further, the number of patients reporting their mental health as ‘good’ increased during the first year in treatment. Additionally, there appears to be a trend in reductions of self-reported crime, though further analysis is necessary.

The expected enrollment is approximately one-third of what was originally projected as maximum capacity. The clinics report that this is due to multiple challenges, including inadequate staffing, limitations of the clinic facilities (primarily in Bergen), and an insufficient budget which is currently restricting the HAT clinics' capacity. Although this is less than original estimates, it should be kept in mind that the clinics have only been operating for two years. In addition, HABiB reports that informing and attracting patients into a new treatment takes time, and it is likely that attitudes from prospective patients and the referring clinicians will evolve during this pilot period.

In addition, the introduction and use of long-acting morphine-based medications in HAT during the pilot period may create evaluation challenges. An examination into this aspect will plan to be included in the final report. The clinics report evolving clinical practices, as they continue to develop and optimize routines. The final report will also aim to explore the need for developing future formal guidelines for HAT in Norway, as has been implemented for Denmark's HAT program.

Overall observations:

Implementation and enrollment in treatment

- Patient enrollment was initially delayed, but both clinics are now fully operating with what is generally considered high quality treatment.
- Patient numbers are currently one-third of initial projected estimates.
- Despite the intensive treatment requirements of twice daily dosing, the treatment seems to be sufficiently attractive.
- The lack of clinic waiting lists make it difficult to determine actual treatment need in relation to clinic capacity.
- The external evaluation of the HAT program has been well integrated into clinical practice.

Patient experiences and outcomes

- As with the Danish HAT, the Norwegian HAT pilot attracts a severely burdened population. Initial findings point towards HAT patients being more vulnerable than those receiving conventional OAT.
- Initial assessments show patients and staff are satisfied with treatment.
- Several patients have transitioned to tablet-based heroin, which is a safer and less intense mode of use.
- In accordance with the evidence base from international studies, it currently appears that HAT contributes to improvements in multiple domains for patients (such as physical and mental health and quality of life).
- Attrition rates are low and initial findings indicate that patients are staying in treatment. Most patients that leave HAT continue on to conventional OAT or other types of substance use treatment, which is considered an important benefit and outcome from the treatment.

Considerations

- Pharmaceutical heroin costs are increasingly expensive, and the clinics would have difficulty significantly expanding patient enrollment with the current allocated budget without reducing quality and safety. The current funding from the Ministry of Health is not sufficient to increase capacity to the planned capacity of 300 patients at the same time.
- The introduction of new morphine-based medications into the national OAT guidelines will need to be considered when evaluating the impact of HAT.
- The provision of 24h SROM with direct observed intake at the clinics daily could be considered evidence-based clinical practice, in line with what has been proven with methadone as bridge medication, but the scientific knowledge base is still weak.
- The provision of 6-12h morphine as part of HAT, (including as a take-home overnight bridge medication) is not established firmly in the scientific evidence base. It would therefore be considered more of an experimental clinical practice.
- The numerical low number of HAT patients has limited the application of statistical analyses as well as the retrieval of registry data for the mid-term report.

12. Conclusion

The implementation of a new treatment option was accompanied by many logistical and practical considerations and challenges. Establishing and optimizing clinical routines, staff recruitment and training, access to the medication, and promoting buy-in among prospective patients and referring clinicians is a process. The first two-years of this pilot project required much focus towards these considerations, which can explain why patient enrollment numbers are not at maximum capacity immediately after the clinics opened. It is expected that for any HAT patient the most "labor intensive" part of the treatment is the first year. Hence, in a more mature HAT program, more patients will have been in treatment longer and be stabilized, while relatively fewer will be new patients at any given time. Therefore, we expect the clinics to have somewhat higher capacity during the second half of the HAT period**. Increased patient capacity and time in treatment will contribute to the ability to analyze long-term treatment outcomes, which will be a priority during the second period of the pilot project.**

During the first two years, differences in clinical practices between HABiO and HABiB have emerged. Heroin dosages, overnight bridge medication, and co-prescribing of benzodiazepines may have an overall impact on outcomes for HAT patients. It is not unnatural that minor differences will develop; **the main importance is whether there are differences that affect access to and outcomes from treatment. This will be monitored more closely during the second half of the pilot project.**

Regarding treatment need, the actual number of patients in need is unclear, given the lack of waiting lists and potentially disrupted referrals during admission pauses. It may be that the estimates made back in 2019 were too high, and for example that the range of new medications and treatment climate in conventional OAT has resulted in less need for HAT than initially planned. **We suggest waiting lists are established to get a better overview of the treatment need, and thus anticipated capacity for the second half of the pilot project period.**

Overall, for the research part of the project, the second half will focus on maintaining good quality in data collection with regular quality checks, and to acquire registry-based data, as soon as the total patient population that has been in HAT exceeds 150-200 persons. More patients and time are needed to conduct a comprehensive evaluation, including cost-benefit analyses.

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