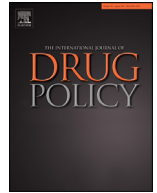




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Commentary

Experiences with take-home dosing in heroin-assisted treatment in Switzerland during the COVID-19 pandemic—Is an update of legal restrictions warranted?

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ABSTRACT

Heroin-assisted treatment comprises the use of diacetylmorphine (pharmaceutical heroin) for individuals with severe opioid use disorder. In Switzerland, take-home doses in heroin-assisted treatment are more strictly regulated as compared to conventional opioid agonist treatment. In light of the COVID-19 pandemic, the Swiss Federal Council provisionally adapted its policy, allowing for longer prescriptions of take-home diacetylmorphine. Before the beginning of the pandemic, take-home doses only occurred in exceptional circumstances and under strict criteria for patient eligibility. Following the legislative adaptations, we critically revised our internal centre policies as well. We report our experiences with oral take-home diacetylmorphine from a Swiss outpatient university centre specialising in heroin-assisted treatment. An additional 45 patients received take-home doses following the first lockdown. While some patients wished to return to their previous treatment regimen, most patients managed their medication well and showed good adherence. We also noticed an increase of treatment admissions that are likely related to the relaxed regulations. Previously, the strict therapeutic framework of visiting a HAT centre twice a day for supervised dispensing seemed to have discouraged these individuals from seeking medical treatment. From a medical point of view, the politically driven restrictions on take-home doses in heroin-assisted treatment are questionable and do not support the goal of harm reduction.

Introduction

Opioid agonist treatment (OAT) is the gold standard treatment for individuals suffering from opioid use disorder and has been implemented with success in many countries worldwide (Degehardt et al., 2019). Long-acting opioids such as methadone, buprenorphine and slow-release morphine sulfate are used in OAT, with methadone maintenance treatment being the most widely used treatment approach (Jegu, Gallini, Soler, Montastruc, & Lapeyre-Mestre, 2011; Kreek, Reed, & Butelman, 2019). However, some patients respond poorly to OAT and continue to use illicit heroin or drop out of treatment, because of the lack of euphoric effects (“high”) of heroin use (Dürsteler, 2015). Methadone also has a negative reputation among some prospective patients, and others reject the idea of taking medication since they prefer to only use substances with which they are familiar (Goldsmith, Hunt, Lipton, & Strug, 1984; Hunt, Lipton, Goldsmith, Strug, & Spunt, 1985). Heroin-assisted treatment (HAT) was introduced in Switzerland in 1994 for this patient

population (Güttinger, Gschwend, Schulte, Rehm, & Uchtenhagen, 2003). HAT comprises the prescription of pharmaceutical heroin (diacetylmorphine, DAM) either as an injectable liquid or in form of orally administered tablets. The pharmacokinetics of DAM differ by route of administration, with the intravenous injection reaching significantly higher peak plasma concentrations and a faster onset of action when compared to oral use (Rook, Huitema, Brink, Ree, & Beijnen, 2006). There is no discernible difference in pharmacokinetics of oral morphine and oral DAM. However, inconclusive findings regarding differences in the subjective effects have been reported. One study found that patients experienced a mild rush following the use of oral DAM, whereas other studies found that patients were not able to distinguish oral DAM from oral morphine or methadone (Margarida et al., 2021). In Switzerland, participation in HAT is strictly regulated by the Federal Office of Public Health and requires federal treatment approval for each individual patient (Swiss Federal Council, 2020a). To qualify for treatment, patients need to be at least 18 years old, suffer from severe

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opioid dependence for two years or more, need to have failed at least two prior conventional treatment attempts and present psychological, physical, or social impairments. HAT is offered in specialised outpatient treatment centres in which patients usually attend daily for supervised dispensing and administration (Perneger, Giner, Del Rio, & Mino, 1998). In Switzerland, there are many treatment centres and treatment slots available for opioid-dependent individuals when compared to other developed countries (Nordt & Stohler, 2006). Fatal overdose events in connection with OAT are extremely rare, heroin-related mortality has declined significantly in the past 20 years and fatal events that are taking place are in many cases attributable to polysubstance use (Suchtmonitoring Schweiz, 2017). The good accessibility of treatment services and the comparatively low mortality also reflect in the fact that the opioid dependent cohort is ageing (Dürsteler-MacFarland, Vogel, Wiesbeck, & Petitjean, 2011). Since the introduction of HAT, numerous studies have demonstrated the effectiveness of this approach in order to improve health, reduce risky and delinquent behaviours, and retain patients in treatment (Strang et al., 2015).

Adaptations in OAT policies during the COVID-19 pandemic

Following the outbreak of the COVID-19 pandemic, international policies regarding the supervision of opioid administration have been adapted to account for patient safety and ensure continued treatment access: in the USA, the Substance Abuse and Mental Health Services Administration (SAMHSA) permitted an expansion of the use of take-home doses of methadone (Figgatt, Salazar, Day, Vincent, & Dasgupta, 2021). Equally, Canadian guidelines were adapted to promote remote assessments as opposed to in-person clinic visits and take-home dosing regulations for buprenorphine and methadone were relaxed (Lam, Sankey, Wyman, & Zhang, 2020). On April 2nd, 2020, the Swiss Society of Addiction Medicine (SSAM) published their recommendations for handling the pandemic. They proposed extended utilisation of take-home doses in OAT, a simplified treatment admission process for HAT and medication deliveries for particularly vulnerable patients (SSAM, 2020). Under usual circumstances, almost all Swiss outpatients in OAT receive take-home oral doses of methadone or slow-release morphine for 7 to 14 days, depending on cantonal regulations. Whereas no criteria for take-home doses are defined in our area of service, the canton of Zürich recommends take-home prescriptions for all “adequately stabilised” patients (Department of Health Canton Zürich, 2017). Take-home doses in HAT are rare in comparison, only provided in tablet formulation for oral use, and only occur in exceptional circumstances and under strict criteria for patient eligibility.

The need for policy adaptations is further demonstrated by a recent study that found a marked impact of the COVID-19 pandemic on patients receiving OAT (Russell et al., 2021). According to these authors, affected individuals experienced treatment disruptions and had reduced access to OAT, harm reduction services, withdrawal management and mental health counselling. This is in accordance with the findings of Galarneau et al. (2021) who also noted that opioid-dependent individuals experienced decreased access to harm reduction and medical care services. However, in OAT take-home doses and prescription deliveries were found to have had a positive impact: patients reported to feel relieved as they gained more control over their medication and felt more stable (Russell et al., 2021). Therefore, the overall increase of treatment disruptions and the reduced access to treatment facilities suggest that even though the need for policy changes was recognised early on and subsequently accounted for, the extent to which take-home dosing expansions were implemented might have been insufficient in North America. The COVID-19 pandemic aggravated the incidence of opioid overdose events, and it has been found that individuals with opioid dependence require higher levels of care in case of infection (Centers for Disease Control & Prevention, 2020; Henderson et al., 2021; Qeadan et al., 2021). Therefore, effective policies and sustained

access to OAT are paramount to maintain the continuum of care for these highly marginalised patients (Dunlop et al., 2020).

Expanding the policy for take-home DAM

HAT is currently offered in few European countries and in Canada (Smart & Reuter, 2021). In Switzerland, take-home doses in HAT are more strictly regulated compared to conventional OAT (Swiss Federal Council, 2019). DAM must be administered under professional supervision and oral DAM take-home doses are only allowed in well-justified exceptional cases for socially and medically stable patients and for a maximum of two days. Four conditions are defined in the regulations, all of which must be met by the patient to qualify for take-home doses (Swiss Federal Council, 2020b). Patients must have received uninterrupted HAT for at least 6 months and need to be in stable health and social condition. Additionally, the two most recent urine screenings must test negative for any drugs except for DAM and the risk of misuse must be estimated as low. In light of the challenges posed by the COVID-19 pandemic the Swiss Federal Council provisionally adapted its policy, allowing clinicians to extend take-home doses of DAM for up to seven days (Swiss Federal Council, 2020b). However, the aforementioned criteria for take-home doses still apply. With the prescription of four daily doses or more for take-home, the treating physician is also required to contact the patient twice a week to ensure adherence (i.e. whether DAM is used as prescribed).

Take-home dosing experiences falling into three groups

We report our experiences with take-home doses of DAM tablets for oral administration from an outpatient university treatment centre in Switzerland during the COVID-19 pandemic. In late 2019, 149 patients with severe opioid use disorder regularly received DAM, either orally, for intravenous injection or both. The Federal Office of Public Health announced its preventive measures to mitigate the spread of the infection on March 16, 2020, closing bars, restaurants, and recreational facilities (Federal Office of Public Health, 2020). In an effort to reduce the risk of infection for our patients, we aimed at decreasing the number of visits to our treatment centre by asking our patients to limit their visits to a maximum of one per day and offering take-home doses of oral DAM instead. Patients deemed suitable (i.e., patients that showed good treatment adherence and had no severe psychiatric or physical conditions) were given the option to show up for dispensing three times a week, while some patients were given take-home doses for the maximum of seven days. To include as many patients as possible in this preventive measure, we critically reflected our internal centre policy as well. The criterion of “social stability” is not precisely defined in the regulation (Swiss Federal Council, 2020b) and allows for certain clinical flexibility. Before the beginning of the pandemic, we interpreted this criterion more conservatively, with the legislative changes of extended take-home doses leading us to revise this interpretation. Whereas we deemed permanent employment the strongest indicator of social stability before, we began to carefully evaluate the daily activities of non-employed patients and also considered their social environment and their engagement in family life.

Patients with unstable conditions such as severe psychiatric or physical comorbidities continued to attend daily. The rationale for this was that some of these conditions necessitated daily medical checks while others affected the patients’ ability to store or take medication as prescribed and without professional assistance.

Before the beginning of the pandemic 19 patients had already received take-home doses. We evaluated suitable patients and individually spoke to every patient who regularly visited for dispensing (approximately 140 with the remaining patients receiving their medication in care homes). As a result, an additional 45 patients received take-home doses of oral DAM who had not received take-homes before the beginning of the pandemic. Take-home doses ranged from 200 or 400 mg for

half a day up to 4000 mg of DAM for the use across several days. In 15 patients pre-existing take-home prescriptions were expanded in accordance with the new policy. The majority of these patients (52 out of 60) adapted quickly, were satisfied with their new treatment modalities, and did not report any negative outcome. For the remaining minority patients ($n = 8$), who were dissatisfied, they fell into two additional groups. The first group consisted of six patients who had previously injected liquid DAM twice a day and were subsequently only allowed to visit once a day. They reported severe cravings, lack of motivation and difficulties in concentrating even though they received take-home doses of DAM tablets for oral administration. Those patients stated that orally administered DAM did not produce the desired “high” and repeatedly asked for permission to return to their former schedule of two daily visits. To cope with the new situation, some of these patients reported to again engage in high-risk behaviours like using of illicit street heroin or dissolving of DAM tablets for intravenous injection at home. The second group consisted of two patients who now received take-home doses due to the exceptional state of the pandemic but would not have qualified otherwise. They continued to ask for an increase of their daily dose and further prolongation of their take-home DAM prescriptions. They reported distress caused by the need to regularly visit our treatment centre, wished to attend less frequently for dispensing, and repeatedly stated that their opioid dose was too low. Tackling the latter, we offered additional take-home medication with long-acting opioids or more frequent visits at our treatment centre for oral or injectable DAM dispensing.

Advantages and disadvantages of take-home DAM

The vast majority of the 60 patients who newly or additionally received take-home DAM managed their medication well. Patients received take-home doses for several days but were obliged to take half of their daily oral DAM dose under supervision during the days of dispensing. This policy was well accepted and ensured regular therapeutic contact with our staff. Thereby we ensured that patients still had the ability to address personal problems or emergencies, even though they now visited the centre less often.

Out of 60 patients, 52 were satisfied with their new prescription. Many reported an improvement in their quality of life. Particularly those employed in professions with changing work hours stated that they felt relieved to make room for clinic visits less often. Other patients stated that it was now much easier for them to pursue recreational activities, conduct daytrips or visit their families. No increase in emergency hospitalisations of our patients due to either psychiatric conditions or physical illnesses was observed during this period. Most importantly, no overdose events occurred. Some of our patients had already qualified for take-home DAM before the beginning of the pandemic but had never chosen to use them. After being urged to take the take-home doses, they benefitted from the relaxed setting with increased freedom and responsibility.

However, in three of 60 cases we noticed behaviours that forced us to stop prescribing take-home DAM doses. These signs included the attempt to smuggle tablets out of the treatment centre when attending for supervised oral administration and leaving bags with medication behind by accident (e.g., due to lack of concentration). Two of these three patients came forward and asked for a replacement of their take-home medication because they had lost or were “unable to find” it. In these cases, we stopped take-home DAM prescriptions and replaced these with slow-release morphine when patients did not attend the treatment centre.

Unexpected effects of the enhanced take-home dose regulations

The increase of take-home prescriptions led to consequences beyond our centre that we had not anticipated. Safe injection facilities called “contact points” in Switzerland are offered by cantonal harm reduction programmes to provide safe spaces for the safe and hygienic use of illicit

substances. The service includes measures like needle dispensing and consultation from social workers. The head of the cantonal contact point service informed us that he had noticed a change in his clientele. First, he reported that some of our patients that he had not seen since they started HAT were now visiting contact points again. Second, he noticed an increase of visits from persons who were not regulars at the contact points and suspected that these persons visited to buy DAM tablets from our patients. However, he stressed that this was purely speculative, and he did not find any direct evidence for it.

Interestingly and probably interrelated, we noticed an increase of treatment admissions. From the end of 2019 to mid-2021 an additional 15 patients received HAT at our treatment centre. At first contact, these new patients reported that they encountered some of our patients and had learned about HAT. Traditional OAT with methadone or slow-release morphine had previously not helped them in ceasing their illicit heroin use leading to many of them not receiving treatment at the time of their presentation to the HAT centre. They stated that they had heard of our treatment centre before but did not think that the treatment we provided would in fact be able to help them due to the strict therapeutic framework and rigorous treatment conditions. Take-home doses seemed to have had an unintentional “advertising effect”. We therefore managed to induct new patients to HAT for whom no suitable treatment had existed before.

Safety concerns

While we are not aware of any overdose events that were caused by take-home doses from our treatment centre, oral DAM is potentially lethal to opioid naïve users. We did not find any evidence of an increase of this phenomenon, however the potential diversion of take-home doses (i.e. the selling of DAM tablets on the black market by dissatisfied patients) could be harmful. DAM tablets for oral use in Switzerland are only available in fairly strong doses of 200 mg (Diaphin IR® 200 mg). This is dangerous for opioid naïve individuals who want to experiment with drugs and who are under the misapprehension that taking a single tablet is unlikely to lead to an overdose. However, these are theoretical considerations, as we did not observe an increase of diversion. Interestingly, the Annual Crime Report of the Swiss Federal Statistical Office indicates the opposite: the canton in which our centre provides HAT saw a total decline of 17% in crime related to the Narcotics Act in 2020 when compared to the previous year ([Federal Statistical Office, 2021](#)). This is also supported by a personal communication with the cantonal department of public prosecution (Staatsanwaltschaft Basel-Stadt), which reported no increase in narcotic confiscations during the time of our policy adaptations. It is therefore unlikely that diversion of DAM to the black market increased due to our enhanced take-home regulations.

Discussion, outlook, and future development

On January 1st, 2022, the Swiss Federal Council plans to reverse the policy adjustments which allow the extended prescriptions of take-home doses ([Swiss Federal Council, 2021](#)). Additionally, since most of our patients received COVID-19 vaccines, we decided to lift the preventive measures of our treatment centre in mid-2021. However, the exceptional state of the pandemic allowed us to gather experiences with take-home doses that would not have been possible without the adapted regulations. We reviewed the 45 patients who newly received take-home doses due to the pandemic and found that about half qualified for continuation of the prescription according to our pre-pandemic internal policies. These patients can basically be categorised in two groups. Patients who recognised the advantages of take-home doses without ever reflecting on them before, even though they would have qualified for them. And patients who would not have qualified before but proved to fulfil legislative criteria after careful evaluation, showed good adherence and complied with the rules of take-home doses. Also, we did not stop

the expanded prescription of take-home DAM for patients who had benefitted from weekly dispensing, as these prescriptions are legislatively permitted up until 31st of December 2021.

We also found that the legal requirements for take-home doses are insufficient and do not reach their supposed goals of enabling more autonomy while at the same time achieving harm reduction. Some patients who would otherwise not have met the requirements to receive take-home DAM proved to handle their medication well and adhered to the treatment regimen. Few patients who newly received take-home DAM or had already received take-home medication but got their take-home doses expanded due to the pandemic showed poor adherence, lost their medication, or showed otherwise conspicuous behaviour. Most likely, this was a direct consequence of the restrictions that were still in place, even after relaxing take-home regulations. Due to these restrictions, we did not provide patients with the individually required DAM formulation (i.e., liquid DAM) which led to these signs of poor adherence. We emphasise that in the vast majority of our patients, good adherence without problematic behaviour was observed and no medical emergencies that were attributable to take-home doses emerged. This is in line with the findings of an American study, which found that the selling of take-home methadone is relatively uncommon (Figgatt et al., 2021). In practice, returning to the pre-pandemic treatment regimen posed a challenge for us since explanations on why take-home doses were not further prescribed were often not easy to accept for the individual patient. However, some patients stated great relief that they were allowed to return to two daily injections of liquid DAM.

Increased visits of our patients in contact points provide a strong hint that the alteration of their treatment regimen was troubling for some individuals, as they returned to engage in high-risk behaviour. This might have been prevented with take-home prescriptions of liquid DAM, as orally administered DAM does not reach comparable peak plasma concentrations and does therefore not produce the same subjective effect. However, it could also be argued that oral DAM is more suited to achieve the goal of harm reduction when compared to liquid DAM. It is the safer route of administration in regard to overdose events and injecting-related injuries and diseases. Less injections would therefore be desirable to reduce these risks. However, the provision of the medication in a formulation suitable for each patient is equally important to avoid reengagement in high-risk behaviour such as illicit heroin use. Our system did not meet those patients' needs and some of them explicitly stated that their oral DAM take-home doses did not provide the required effect. Still, we did not feel comfortable with liquid take-home DAM, as it is not available in pre-packaged dosages but prepared by our staff individually for each patient in unlabelled syringes. Additionally, managing liquid DAM is more demanding and requires patients to ensure proper storage and cooling.

There was also hearsay about diversion, but we found no direct evidence that this had increased during the pandemic. Even though increasing availability on the black market is also to be expected with the increasing prescription of narcotics in general (Bell, 2010), narcotic act-related crimes decreased during the pandemic in our area of service (Federal Statistical Office, 2021). However, some individuals who we were previously unable to attract applied for HAT at our treatment centre and indicated that they had gotten to know DAM tablets from the black market. They were familiar with the substance and had heard about the adapted treatment regulations. Whereas the strict therapeutic framework had previously discouraged them from applying for HAT, they now thought that they might benefit from medical treatment. The availability of pharmaceutical DAM on the black market can be regarded as a double-edged sword, as it bears the risk of inexperienced users buying these tablets. Since the tablets arrive in blister packaging and look like a regular medical product, one could be led to believe that 200 mg is the "recommended" dose, which could in the worst-case lead to fatal outcomes. The fear that inexperienced users might get their hands on the substance is also the reason we refrained from prescribing additional liquid DAM as take-home medication due to the pandemic. Whereas DAM

tablets at least come in proper packaging with clear labelling of the exact content, an unlabelled syringe filled with a clear liquid was considered to be too unsafe. It has been shown however, that with regard to the individual patients' needs, liquid take-home DAM is in principle feasible (Oviedo-Joekes, MacDonald, Boissonneault, & Harper, 2021).

Conclusion

Most patients benefitted from the policy adaptations necessitated by the COVID-19 pandemic. Patients felt that they had gained more freedom in organising their everyday life and that take-home doses relieved them from the strain of making room for clinic visits in-between their work schedule. At the same time, we did not observe any overdose events or an increase in emergency hospitalisations due to psychiatric or somatic illnesses, which suggests that relaxed take-home regulations are feasible and safe. In our opinion, this is an impressive example of how impactful a change in policy can be on patients' lives. Patients and clinicians alike can benefit from working in a less controlled context, by exploring the individual patients' need and being able to discuss a broader range of treatment options.

The link between increase in treatment admission and relaxation of HAT regimen suggests that the requirement of visiting a clinic twice a day discourages some individuals from seeking medical treatment. This issue does not arise in the same way with traditional OAT where take-home doses can be prescribed for much longer periods of time and dispensing in pharmacies is available for stable patients. Take-home prescriptions in HAT are further complicated by the fact that DAM tablets are available in the dosage of 200 mg only. Although they can be halved by removing them from the blister, adjusting DAM doses to the individual patients' needs is unnecessarily difficult. The availability of different doses would also improve safety aspects, as loose tablets are more likely to be lost. Additionally, tablet splitting bears the possibility of contamination and dosage variation (Freeman, White, & Iranikhah, 2012).

Our clinical experience showed that the application of legislative requirements sometimes failed to include patients whose medical condition would have allowed for take-home doses. Vice versa, in other patients who met the legislative requirements we had to stop the take-home prescriptions due to poor adherence. From a medical point of view, the political restrictions on take-home doses in HAT result from unjustified prejudice and are not useful concerning the medical goal of harm reduction. Therefore, loosening the defined criteria for take-home doses to make more room for clinical evaluation in the deciding process would benefit clinicians and patients alike.

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Ethics approval

The authors declare that the work reported herein did not require ethics approval because it did not involve animal or human participation.

Declarations of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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