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Increased flexibility in methadone take-home scheduling during the COVID-19 pandemic: Should this practice be incorporated into routine clinical care?

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ABSTRACT

In the context of the COVID-19 pandemic and the state of emergency that the government of Spain declared, the rapid adaptation of health services is of paramount importance to preserve access to and continuity of service delivery. This research note underscores the importance of ensuring a sufficient quantity of methadone take-home doses for patients on methadone maintenance treatment (MMT) to maximize their adherence to government-imposed lockdown restrictions and social distancing measures designed to curtail the spread of SARS-CoV-2. We evaluate the impact of COVID-19 on take-home medication (number of days provided) in a methadone clinic in Barcelona (Catalonia, Spain). This work conveys that we should consider maintaining the take-home practices that we adopted in response to the pandemic, even after the pandemic has abated.

Methadone maintenance treatment (MMT) is a widely used, evidence-based, first-line treatment for opioid use disorder. However, MMT practices and policies vary considerably within and across countries (Jin et al., 2020). At the methadone treatment clinic in our hospital (Santa Creu i Sant Pau Hospital) and in other methadone treatment centers in Barcelona (the major city in Catalonia, an autonomous region located in the northeast part of Spain), the main aim of MMT is harm reduction (Parés-Badell et al., 2020; Torrens et al., 2013). We do not place any limitations on treatment duration or dose levels, and the take-home doses of methadone (i.e., doses for unsupervised use on days between clinic visits) are provided on a case-by-case basis according to a pre-established clinical protocol after carefully weighing the risks and benefits for both the patient and the community.

Health policy planners and clinical administrators frequently overlook the needs of MMT patients, particularly during “big events” such as economic crises, natural disasters, and disease outbreaks. For example, a study that Pouget et al. (2015) carried out to explore the impact of hurricane Sandy on injection drug users in New York City found that practitioners gave only 30.1% of those in opioid maintenance programs sufficient take-home doses to avoid withdrawal. In the context of the COVID-19 pandemic and the state of emergency that the government in Spain declared, the findings that Pouget and colleagues described underscore the importance of ensuring the

availability and accessibility of MMT, including a sufficient quantity of take-home doses, to maximize the likelihood that patients on MMT will adhere to government-imposed lockdown restrictions and social distancing measures designed to curtail the spread of SARS-CoV-2. Accordingly, in regions where MMT is available, governmental and scientific organizations have recommended that methadone clinics switch as many patients as possible from supervised methadone administration to take-home self-administration, and that they temporarily increase the number of take-home doses for patients already in this treatment regimen (e.g., Marsden et al., 2020; Vecchio et al., 2020; Volkow, 2020).

Even though methadone take-home policies are both a matter of considerable debate and a complex area that defies a “one size fits all” approach (Berends et al., 2015), the most restrictive take-home policies are a key barrier to treatment access (Deering et al., 2011; Kourounis et al., 2016) and retention (Pani et al., 1996; Rhoades et al., 1998). It is unsurprising, therefore, that MMT patients highly value take-home doses (Fraser, 2006). Even otherwise satisfied MMT patients have concerns about or are dissatisfied with the lack or the small number of methadone take-home doses (Ezard et al., 1999; Madden et al., 2008).

On March 12, 2020, the Catalan Ministry of Health (Departament de Salut, 2020) issued a series of recommendations to drug dependence treatment centers explicitly supporting the aforementioned measures

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Take-home schedule	Pre-COVID-19	COVID-19
Less than one week	1.0	0
One week	22.5	1.0
Two weeks	24.5	19.6
Three weeks	16.7	31.4
Four weeks	35.3	48.0

Fig. 1. Percentage of methadone-maintained patients according to their take-home schedule before and during the COVID-19 pandemic ($n = 102$).

regarding methadone take-home doses to ensure uninterrupted access to the medication while minimizing the risks of COVID-19; those recommendations included, when appropriate, the provision of naloxone kits for overdose reversal. Consequently, as of March 13, 2020, our methadone clinic increased the number of take-home doses per patient on a case-by-case basis after a thorough risk/benefit assessment. During the COVID-19 outbreak, we incorporated and emphasized new factors in such risk/benefit analysis: i) the increased syndemic vulnerability to SARS-CoV-2 transmission among people who inject drugs (Vasyleva et al., 2020); ii) the potentially worsened outcomes in patients with opioid use disorder who contract COVID-19 (Schimmel & Manini, 2020); and iii) the facilitation of MMT patients' adherence to lockdown restrictions and social distancing measures.

In this context, we sought to evaluate the impact of COVID-19 on MMT service delivery. To do so, we examined changes in the take-home medication (number of days provided). We compared two time periods, "pre-COVID-19" (March 6–12) and "COVID-19" (March 13–May 12). Fig. 1 displays the percentages for each take-home schedule in the two time periods. It is noteworthy that even the number of MMT patients in the 4-week take-home schedule (i.e., the maximum number of take-home doses allowed) increased significantly during the COVID-19 outbreak (McNemar's $\chi^2(1) = 11.077$; $p < 0.001$). In the whole sample of MMT patients, a paired-sample t -test demonstrated a statistically significant increase in take-home days from the pre-COVID-19 period ($t(101) = -7.759$, $p < 0.001$, $d = 0.768$). This increase, however, did not lead to any detectable increase in signs that patients might be misusing or diverting their medication (i.e., early returns for additional doses).

Even in a methadone clinic with an already relatively liberal take-home policy, we observed a medium-to-large effect size increase in the number of take-home doses. Although the current evidence base is insufficient to clearly inform clinical decision-making about the provision of take-home doses (e.g., Larance et al., 2014), and there is a lack of robust research comparing the effectiveness of supervised versus unsupervised dosing (Saulle et al., 2017), we may consider maintaining current take-home practices, even after the current pandemic has abated.

That said, larger controlled studies should rigorously evaluate the results of these more liberal take-home practices before incorporating them into routine clinical care. When planning this type of evaluation, future studies must focus not only on the traditional outcomes that clinicians, decision-makers, and community members prioritize (Cotton et al., 2017; Marcus, 2011; Varenbut et al., 2007), but also on the patient-defined ones (Byrne & Wykes, 2020; Harris & Rhodes, 2013; Marchand & Oviedo-Joekes, 2017).

CRedit authorship contribution statement

Joan Trujols: Conceptualization, Methodology, Formal analysis, Writing – original draft, Writing – review & editing, Project administration. **Antonio Larrabeiti:** Investigation, Data curation, Writing – review & editing. **Oriol Sánchez:** Investigation, Data curation, Writing – review & editing. **Maite Madrid:** Investigation, Writing – review & editing. **Sandra De Andrés:** Investigation, Writing – review & editing. **Santiago Duran-Sindreu:** Writing – original draft, Writing – review & editing, Project administration.

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Declaration of competing interest

The authors declare no financial interests or potential conflicts of interest related directly or indirectly to this research note.

References

- Berends, L., Chalmers, J., & Lancaster, K. (2015). Trust, agency and control: Perspectives on methadone takeaway dosing in the context of the Victorian policy review. *Drug and Alcohol Review*, 34(5), 483–486. <https://doi.org/10.1111/dar.12287>.
- Byrne, L., & Wykes, T. (2020). A role for lived experience mental health leadership in the age of Covid-19. *Journal of Mental Health*, 29(3), 243–246. <https://doi.org/10.1080/09638237.2020.1766002>.
- Cotton, A. J., Shipley, L. J., Glynn, L. H., Tracy, J., & Saxon, A. J. (2017). Methadone "callbacks" within a veterans affairs opioid treatment program: Detecting methadone misuse. *American Journal on Addictions*, 26(1), 50–52. <https://doi.org/10.1111/ajad.12479>.
- Deering, D. E. A., Sheridan, J., Sellman, J. D., Adamson, S. J., Pooley, S., Robertson, R., & Henderson, C. (2011). Consumer and treatment provider perspectives on reducing barriers to opioid substitution treatment and improving treatment attractiveness. *Addictive Behaviors*, 36(6), 636–642. <https://doi.org/10.1016/j.addbeh.2011.01.004>.
- Departament de Salut (2020, March 12). *Coronavirus SARS-CoV-2: recomanacions per reduir el risc de contagi de la COVID-19 per a centres d'atenció i seguiment de les drogodependències (CAS)*. Barcelona: Departament de Salut. Retrieved from <https://scientiasalut.gencat.cat/handle/11351/4799> (Accessed on 25 May 2020).
- Ezard, N., Lintzeris, N., Odgers, P., Koutroulis, G., Muhleisen, P., Stowe, A., & Lanagan, A. (1999). An evaluation of community methadone services in Victoria, Australia: Results of a client survey. *Drug and Alcohol Review*, 18(4), 417–423. <https://doi.org/10.1080/09595239996284>.
- Fraser, S. (2006). The chronotope of the queue: Methadone maintenance treatment and the production of time, space and subjects. *International Journal of Drug Policy*, 17(3), 192–202. <https://doi.org/10.1016/j.drugpo.2006.02.010>.
- Harris, M., & Rhodes, T. (2013). Methadone diversion as a protective strategy: The harm reduction potential of "generous constraints". *International Journal of Drug Policy*, 24(6), e43–e50. <https://doi.org/10.1016/j.drugpo.2012.10.003>.
- Jin, H., Marshall, B. D. L., Degenhardt, L., Strang, J., Hickman, M., Fiellin, D. A., ... Larney, S. (2020). Global opioid agonist treatment: A review of clinical practices by country. *Addiction*. <https://doi.org/10.1111/add.15087>.
- Kourounis, G., Richards, B. D. W., Kyprianou, E., Symeonidou, E., Malliori, M. M., & Samartzis, L. (2016). Opioid substitution therapy: Lowering the treatment thresholds. *Drug and Alcohol Dependence*, 161, 1–8. <https://doi.org/10.1016/j.drugalcdep.2015.12.021>.
- Larance, B., Carragher, N., Mattick, R. P., Lintzeris, N., Ali, R., & Degenhardt, L. (2014). A latent class analysis of self-reported clinical indicators of psychosocial stability and adherence among opioid substitution therapy patients: Do stable patients receive more unsupervised doses? *Drug and Alcohol Dependence*, 142, 46–55. <https://doi.org/10.1016/j.drugalcdep.2014.05.018>.
- Madden, A., Lea, T., Bath, N., & Winstock, A. R. (2008). Satisfaction guaranteed? What clients on methadone and buprenorphine think about their treatment. *Drug and Alcohol Review*, 27(6), 671–678. <https://doi.org/10.1080/09595230801935706>.
- Marchand, K., & Oviedo-Joekes, E. (2017). Prioritizing the patient in patient-centered addictions treatment. *Addiction*, 112(3), 466–467. <https://doi.org/10.1111/add.13680>.
- Marcus, S. M. (2011). Accidental death from take home methadone maintenance doses: A report of a case and suggestions for prevention. *Child Abuse & Neglect*, 35(1), 1–2. <https://doi.org/10.1016/j.chiabu.2010.08.003>.
- Marsden, J., Darke, S., Hall, W., Hickman, M., Holmes, J., Humphreys, K., ... West, R. (2020). Mitigating and learning from the impact of COVID-19 infection on addictive disorders. *Addiction*, 115(6), 1007–1010. <https://doi.org/10.1111/add.15080>.
- Pani, P. P., Pirastu, R., Ricci, A., & Gessa, G. L. (1996). Prohibition of take-home dosages: Negative consequences on methadone maintenance treatment. *Drug and Alcohol Dependence*, 41(1), 81–84. [https://doi.org/10.1016/0376-8716\(96\)01240-9](https://doi.org/10.1016/0376-8716(96)01240-9).
- Parés-Badell, O., Barbaglia, G., Robinowitz, N., Majó, X., Torrens, M., Espelt, A., ... Brugal, M. T. (2020). Integration of harm reduction and treatment into care centres for substance use: The Barcelona model. *International Journal of Drug Policy*, 76, 102614. <https://doi.org/10.1016/j.drugpo.2019.102614>.
- Pouget, E. R., Sandoval, M., Nikolopoulos, G. K., & Friedman, S. R. (2015). Immediate

- impact of Hurricane Sandy on people who inject drugs in New York City. *Substance Use & Misuse*, 50(7), 878–884. <https://doi.org/10.3109/10826084.2015.978675>.
- Rhoades, H. M., Creson, D., Elk, R., Schmitz, J., & Grabowski, J. (1998). Retention, HIV risk, and illicit drug use during treatment: Methadone dose and visit frequency. *American Journal of Public Health*, 88(1), 34–39. <https://doi.org/10.2105/ajph.88.1.34>.
- Saulle, R., Vecchi, S., & Gowing, L. (2017). Supervised dosing with a long-acting opioid medication in the management of opioid dependence. *Cochrane Database of Systematic Reviews*, 4(4), Article CD011983. <https://doi.org/10.1002/14651858.CD011983.pub2>.
- Schimmel, J., & Manini, A. F. (2020). Opioid use disorder and COVID-19: Biological plausibility for worsened outcomes. *Substance Use and Misuse*, 55(11), 1900–1901. <https://doi.org/10.1080/10826084.2020.1791184>.
- Torrens, M., Fonseca, F., Castillo, C., & Domingo-Salvany, A. (2013). Methadone maintenance treatment in Spain: The success of a harm reduction approach. *Bulletin of the World Health Organization*, 91(2), 136–141. <https://doi.org/10.2471/BLT.12.111054>.
- Varenbut, M., Teplin, D., Daiter, J., Raz, B., Worster, A., Emadi-Konjin, P., ... Snider-Adler, M. (2007). Tampering by office-based methadone maintenance patients with methadone take home privileges: A pilot study. *Harm Reduction Journal*, 4, 15. <https://doi.org/10.1186/1477-7517-4-15>.
- Vasylyeva, T. I., Smyrnov, P., Strathdee, S., & Friedman, S. R. (2020). Challenges posed by COVID-19 to people who inject drugs and lessons from other outbreaks. *Journal of the International AIDS Society*, 23(7), Article e25583. <https://doi.org/10.1002/jia2.25583>.
- Vecchio, S., Ramella, R., Drago, A., Carraro, D., Littlewood, R., & Somaini, L. (2020). COVID19 pandemic and people with opioid use disorder: Innovation to reduce risk. *Psychiatry Research*, 289, 113047. <https://doi.org/10.1016/j.psychres.2020.113047>.
- Volkow, N. D. (2020). Collision of the COVID-19 and addiction epidemics. *Annals of Internal Medicine*, 173(1), 61–62. <https://doi.org/10.7326/M20-1212>.