Take-Home Medication Research Summary

Purpose of this document

The purpose of this document is to provide a general overview of, and set of references, for the evidence-base for the benefits and safety considerations for the release of methadone from opioid treatment programs for at-home dosing. The science presented reflect findings reflect policy changes made during the COVID-19 public health emergency, when the Substance Abuse and Mental Health Services Administration (SAMSHA) revised the methadone take-home dose policy permitting a greater number of patients to take more daily doses at home. This policy shift is referred to as "increased take-home flexibility" in this document.

This pragmatic shift by SAMSHA reflected the acute need for changes in methadone treatment in the context of the public health emergency. The shift also drew from a long history of patient and provider positive experiences with take-home dosing, including improved retention, social, and health outcomes for people in treatment. Shortly following the announcement by SAMSHA, the New York State (NYS) Office of Addiction Services and Supports (OASAS) adopted the new take-home dosing guidelines. Together, SAMSHA and OASAS support increased take-home flexibility as a new best practice. Strategies for advancing its wider implementation necessitate emphasizing the evidence base informing the guideline shift as well as addressing potential provider concerns about patients receiving take-home doses.

Evidence for the Benefits of Take-Home Dosing: Data preceding the COVID-19 pandemic

Important data demonstrating the safety and efficacy of take-home methadone doses up to 30 days at a time comes from experience with seven *Medical Maintenance* programs, authorized under exemptions from federal methadone regulations, which were conducted in six states (two such programs were in New York State).[1-5] These programs achieved very high, long term retention rates with very low rates of substance use. Further, diversion rates in these programs have been low.

The demonstrated benefits of methadone provision with a less restrictive and less punitive approach include improved medical provider-patient trust, reduced patient travel time, and expanded time for employment activities.[4] Increased take-home flexibility makes methadone treatment more attractive to patients and may improve treatment retention.[2,3]

Patient and provider experience of change in take-home dosing policy

Multiple studies demonstrate that increased take-home flexibility during the COVID-19 pandemic has had numerous benefits for patients.[6] Patients had initial questions and some reported initial challenges in adapting to the transition to greater flexibility[7-9], yet patients reported that increased opportunity for take-home doses had the following benefits:

- Promoting increased self-esteem and autonomy and thereby increasing the likelihood of treatment engagement and sustainment in care.[6,8,10,11]

- Allowing more time and resources to pursue employment and/or work, spend time with family, and reducing the time and financial burden of commuting to and attending clinic.[6,10,12-15]
- Staying engaged in methadone treatment.[16]
- Limiting time spent around others who use substances and facilitating the avoidance of triggers.[6,10,14]
- Supporting people to carry out CDC recommendations to prevent COVID-19 infection (especially important given the higher risk for COVID-19-related morbidity and mortality for this population).[17-19]

The research on patient experience is similar to studies of providers' experience of changes to increased take-home flexibility during the COVID-19 pandemic. Providers have expressed modifications to take-home schedules being positively received, reducing the burden of care on patients and reinforcing a sense of autonomy and supporting person-centered care.[20,21]

A recent review of the research on provider experience found that initial hesitation in modifications waned and providers were supportive of increased flexibility once feared negative consequences failed to materialize, new strategies to balance risks were developed and implemented, and betterprovider-patient relationships and general facilitation of person-centered care.[22] Providers' experience of improved provider-patient relationships[11,23-26] following increased flexibility conforms to patients' reports of take-home dose restrictions being a central reason for frustration and anger directed towards treatment and a primary reason for discontinuation of care. [27]

Treatment retention and change in take-home policy

Four studies to date have assessed how change in take-home dosing policy during the COVID-19 pandemic influenced treatment retention. One study observed that patients enrolled in an OTP for greater than 90 days received a statistically significant increase in take-home doses, which was associated with a slightly decreased likelihood of treatment discontinuation associated .[10] One study of individuals dispensed daily methadone found that initiation of take-home doses was associated with a reduced likelihood of treatment discontinuation and prolonged gaps in care compared to those with no change in take-home doses.[28] Another study of nine OTPs compared 6-month retention rates among a group of patients entering care after the change in take-home dosing policy and a control group from the year before. The study observed identical rates of 6-month retention across the two groups (60% vs. 60%).[29] A study of people who inject drugs in New York City found that utilization of syringe services programs declined between the pre-COVID-19 and COVID-19 periods, while OTP utilization was unchanged, suggesting that increased take-home flexibility facilitated maintained access to methadone.[16]

Methadone-related deaths and hospitalizations related to changes in take-home policy

Overall, recent evidence suggests that increased take-home flexibility did not result in increased rates of overdose or hospitalization.[6] Table 1 presents an overview of the nine studies that explored this question. Seven studies[29-35] indicate that increasing flexibility in take-home doses of methadone did not significantly increase the risk of fatal and non-fatal overdoses or adverse events. One article examined

how race, sex, and ethnicity influenced the relationship between change in take-home policy and methadone-involved deaths. This study found that following SAMHSA's take-home guidance in March, 2020, the numbers of methadone-involved deaths decreased for Black and Hispanic males and yet remained unchanged for White men and women, Hispanic women, and Black women.[36] Only one study observed small increases in methadone-related deaths following increased take-home flexibility.[37] In this study, it is unclear whether methadone-involved deaths were attributable to methadone as prescribed for opioid use disorder or for pain. Thus, the preponderance of evidence to date demonstrates that increased take-home flexibility has not led to increased opioid overdose and may have resulted in decreased methadone-related overdose deaths among Black and Hispanic men.

Summary

The scientific research to date demonstrates that increased take-home flexibility for medication provides patients with greater autonomy in pursuing meaningful changes in their treatment, greater retention in treatment over time, and improved outcomes in other areas of their lives. Data also demonstrate that initial concerns expressed by providers regarding take-home flexibility have decreased over time suggesting that the benefits of take-home doses have supplanted many anticipated concerns. Moreover, concerns regarding overdose risks are not substantiated by the data. Overall, the scientific literature underscores the positive impact of SAMSHA's revised take-home dose policies, supporting their wider implementation for enhanced patient care and outcomes.

Recommended articles for further information:

Krawczyk N, Rivera BD, Levin E, Dooling BCE. Synthesizing evidence of the effects of COVID-19 regulatory changes on methadone treatment for opioid use disorder: implications for policy. Lancet Public Health. Mar 2023;8(3):e238-e246. doi:10.1016/S2468-2667(23)00023-3
https://www.ncbi.nlm.nih.gov/pubmed/36841564

Adams A, Blawatt S, MacDonald S, et al. Provider experiences with relaxing restrictions on take-home medications for opioid use disorder during the COVID-19 pandemic: A qualitative systematic review. Int J Drug Policy. Jul 2023;117:104058. doi:10.1016/j.drugpo.2023.104058
https://pubmed.ncbi.nlm.nih.gov/37182352/

Review of the literature on the association of the implementation of SAMHSA's take-home dosing (THD) exemption during COVID-19 Pandemic and overdose

Authors & link	Goal of study	How study was done	Results of study	Main point
Amram et al., 2021[30] https://pubmed.ncbi.nlm.nih.gov/34670453/	Evaluate effects of SAMHSA take-home dosing exemption on OUD-related outcomes	Sample: 183 patients from an OTP in Washington State. Methadone being the primary treatment in the clinic. *Analysis*: Emergency department (ED), Overdose (OD)-related ED visits compared pre- (270 days before exemption) and post- (270 days after exemption) relaxation of take-home dosing (THD) guidelines	The average number of take-home doses increased nearly 200% from an average of 11.4 take-home doses per 30 days before exemption to 22.3 after exemption. Number of ED visits dropped from pre- (40% of patients) to post- (31 of patients) exemption ($p < 0.001$). Number of OD-related ED visits dropped from pre- (9% of patients) to post- (8%) THD exemption.	Although THD in this clinic doubled from pre- and post- in this clinic, ED visits for this population significantly dropped and OD-related ED visits remained unchanged. Overall, this study provides evidence that the SAMHSA take-home dosing flexibility can have positive effects on reducing ED visits and supports the potential benefits of increased flexibility in take-home doses for patients with OUD.
Brothers et al., 2021[31] https://pubmed.ncbi.nlm.nih.gov/34098303/	Evaluate the association of SAMHSA take-home exemption during pandemic with methadone-involved overdose rates in Connecticut.	*Sample*: Study used state-level data on autopsies conducted on confirmed accidental opioid-involved deaths and toxicology reports involved in these fatal events, which were provided by Connecticut state agencies. *Analysis:* Statistical tests compared opioid-involved overdose deaths and methadone-involved overdose deaths during the 5-month period after lockdown (April – August 2020) to the same five-month period during previous five years (2015 – 2019)	Take-home dosing increased significantly among OTPs in CT during COVID-19. The percent of patients receiving 28-day take-home does increased from 0.1% to 17% from pre- to post-COVID-19. The percentage patients receiving 14-day doses increased from 14% to 27% pre- to post-COVID-19. There were 539 opioid-involved fatalities in April-August 2020 and 1,972 in all April-August periods in 2015 – 2019, combined. In 2020, 4% (22/539) and 11 % (59/53) were methadone-only and methadone-involved, respectively. From 2015 – 2019, 4% (74/1972)	The study concluded that the increase in THD flexibility in Connecticut OTPs during the COVID-19 pandemic was not associated with a higher proportion of opioid deaths attributed to methadone. This suggests that the expanded take-home dosing was not a contributing factor to opioid deaths in the state.

			and 9% (181/1972) were methadone-only and methadone-involved, respectively. These differences were not statistically significant.	
Welsh et al., 2022[32] https://pubmed.ncbi.nlm.nih.gov/35085855/	Evaluation of changes in exposures involving methadone reported to poison control centers across the U.S. before and after loosening of THD regulations.	*Sample*: Intentional methadone exposures among US adults reported to the National Poison Control Data System from March, 19 2019 to March 15, 2021 (2 years) *Analysis*: Statistical tests assessed changes in intentional methadone exposures, and outcomes of exposures, one-year before loosening of THD regulations and one year after.	The number of intentional exposures increased by 5.3% $p <$ .0.05) from pre- to post-change in THD regulations. There was no statistically significant difference in the overall distribution outcomes pre- and post- regulation change, including being treated and released from the emergency department, admission to non-critical care, admission to critical care, admission to in-patient psychiatry, or death.	In summary, the loosening of THD regulations was associated with a modest increase in intentional methadone exposures. However, this increase did not result in significant changes in adverse outcomes such as hospitalization or death. The authors noted that other factors in addition to the regulatory change may have contributed to the observed increase in intentional methadone exposures.
Joseph et al., 2021[33] https://pubmed.ncbi.nlm.nih.gov/33353790/	Report on the experience of a large OTP system in Bronx, NY with their adaptation to the change in THD dosing regulations during the early phase of COVID-19 pandemic.	*Sample*: Events reported to OTP medical staff during hospital verification of MOUD doses, inpatient admission notes, discharge summaries, family reports, and counselor notes from March 16, 2020 to May 31, 2020 *Analysis*: Compare the counts of overdoses during March 16, 2020, to May 31, 2020, compared to January 1, 2020 to March 15, 2020.	Prior, to the change in THD regulation (1/1/2015 – 3/15/2020), there were two nonfatal and one fatal overdose. From 3/16/2020 – 5/31/2020, there were six non-fatal overdoses and no fatal overdoses. During this time, THD had increased significantly.	The findings indicated that there was little change in the numbers of overdoses, including fatal overdoses, before and after the change in THD regulations. However, it is important to note that this report did not employ statistical tests, and further research is needed to fully assess the impact of THD regulation changes on overdose outcomes.
Ezie et al., 2022[34] https://pubmed.ncbi.nlm.nih.gov/35480781/	Report on comparison of clinical outcomes at a Veterans Health Administration pre- and	*Sample*: Patients enrolled in an OTP during period 1 (3/16/2020 – 3/15/2020) and period 2 (3/16/2020 – 6/15/2020). Data derived from patient medical records.	There were 3 overdoses during period 1 (2% of sample) compared to 1 overdose in period 2 (0.7% of sample).	The findings indicated that there was no significant difference in the number of overdoses between the two periods. However, it is

	post- THD regulation change	*Analysis*: The number of overdoses in period 2 were compared to period 1.		important to note that this report did not employ statistical tests, and further research is needed to fully assess the impact of THD regulation changes on clinical outcomes in this population.
Jones et al., 2022[38] https://pubmed.ncbi.nlm.nih.gov/35830198/	Determine whether methadone involved-overdose deaths in the US increased due to THD regulation change.	*Sample*: Data from US Centers for Disease Control and Prevention National Vital Statistics System, multiple causes of death 2020 and 2021 provisional data. *Analysis*: Examined drug overdose deaths both involving and not involving methadone before (1/2019 – 2/2020) and after the March 2020 changes in THD regulation (4/2020 – 8/2021).	Estimated rates of overdose deaths not involving methadone increased from 78 deaths per month before March 2020, to 1078 in March 2020, and by 69 deaths per month after March 2020. Methadone-involved overdose deaths were stable prior to March, 2020 and increased by 94 deaths per month by March, 2020. Monthly overdose deaths from methadone remained stable after March, 2020.	While there was an increase in methadone-involved overdose deaths in the US in March 2020, this increase can be attributed to the larger surge in national drug overdoses. The rates of methadone overdose deaths have remained stable after the changes in THD regulations in March 2020.
Williams et al., 2023[29] http://dx.doi.org/10.2139/ssrn.4439150	Compare retention in treatment, opioid use, and adverse events among patients newly entering methadone treatment in the post-policy change period in comparison with year-prior, unexposed controls	*Sample:* 9 OTPs, geographically dispersed nationally, in the National Institute of Drug Abuse Clinical Trials Network. Newly enrolled OTP methadone treatment patients for a new care episode between April 15-October 14, 2020 (post-COVID-19, post policy-change period) v. March 15-September 14, 2019 (pre-COVID-19, unexposed controls) were assessed.	Six-month retention rates were equivalent between groups (60·0% vs 60·1%) and hazards of discontinuation (HR=1·02,95%CI=0·81-1·27) and adverse events (including ED visits, hospitalizations, overdose, and death) in the aggregate (X2 (1)=0·55,p=0·46) were non-inferior in the post-COVID-19 period. However, rates of opioid use throughout care were higher among post-COVID-19 intakes compared to pre-COVID-19 controls (64·8% v 51·1%,p<0·001).	Meaningful increases in take-home schedules were not associated with worse retention or adverse events despite slightly elevated rates of measured opioid use. Relaxed guidelines were not associated with increased harms and findings could inform permanent system redesign.
Kleinman et al., 2023[37]	Characterize change in the number of methadone-involved	*Sample*: Data from a US Centers for Disease Control and Prevention data	An increase in methadone-involved overdoses of 105.4 deaths per month (95 % CI: 73.8-	The current study found an increase in methadone-involved overdose deaths.

https://pubmed.ncbi.nlm.nih.gov/36516551/	overdose deaths occurring before take-home dosing policy change (1/2007 – 2/2020) and after 4/2020 – 3/2021.	set, monthly between January 2007 and March 2021 *Analysis*: Examined drug overdose deaths both involving and not involving methadone before (1/2007 – 2/2020) and after the March 2020 changes in THD regulation (4/2020 – 3/2021).	137.0) occurred starting in April 2020 compared with earlier data ($p < 0.001$). Trends in methadone-involved overdose deaths increased starting in April 2020 both with (54.2 deaths per month; 95 % CI: 39.4-68.9) and without (51.7 deaths per month; 95 % CI: 23.4-78.0) synthetic opioid involvement ($p < 0.001$ for both).	While increases occurred during the period coinciding with change in take-home policy, these changes also co-occurred with societal change during the COVID-19 pandemic and are small in comparison with the total number of opioid overdose deaths occurring during the same period.
Harris et al., 2023[36] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10257097/	Assess whether the methadone take-home policy change was associated with drug overdose deaths among different racial, ethnic, and gender groups.	*Sample*: Data from a US Centers for Disease Control and Prevention data set, monthly from 1/2018 – 6/2022 for 6 demographic groups: Hispanic men and women (racial categories Black and White), non-Hispanic Black men and women, and non-Hispanic White men and women. *Analysis*: Compared monthly methadone-involved overdose death trends in the pre- and post-take-home dosing policy change periods by demographic group.	Among Black men, there was a decrease in monthly methadone deaths associated with the March 2020 policy change (change of slope from the preintervention period, −0.55 [95%CI, −0.95 to −0.15]). Hispanic men also experienced a decrease in monthly methadone deaths associated with the policy change (−0.42 [95%CI, −0.68 to −0.17]). No significant changes were observed for the other demographic groups.	For monthly methadone-involved overdose deaths, the take-home policy may have helped reduce deaths for Black and Hispanic men but had no association with deaths of Black or Hispanic women or White men or women.

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