# A Rapid Methadone Initiation Protocol for Stabilization of **Opioid Withdrawal in the Fentanyl Era**



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### INTRODUCTION

Patients with opioid use disorder (OUD) frequently leave the hospital due to undertreated opioid withdrawal (Simon et al., 2020). Patient-directed discharges contribute to the significant mortality and readmission risk in patients with OUD.

Increased synthetic opioids, including fentanyl, in the opioid drug supply has led to higher opioid tolerances and a need for innovative means to safely and rapidly titrate methadone (Hemmons et al., 2019). Rapid stabilization of opioid withdrawal symptoms is necessary to ensure patients with OUD receive adequate medical care and initiate OUD treatment.

We describe a novel rapid methadone initiation protocol for inpatient stabilization of opioid withdrawal in the fentanyl era.

# General Approach to Rapid Methadone Initiation Protocol Initiation Methadone 20-30 mg PO once a day Day 1 Methadone 10 mg PO g4hour PRN opioid withdrawal Titration Day 2 - 4 Methadone 40-50 mg PO once a day Methadone 10 mg PO g4hour PRN opioid withdrawal Day Consolidate approximate average total methadone dose received per day and administer as once daily dose \*Short-acting opioids PRN for opioid withdrawal provided throughout

## **Table 1: Primary Outcomes**

	Case 1	Case 2	Case 3
Day 1	Methadone 20mg x 1 Methadone 10mg x 3 Hydromorphone 4mg x 1	Methadone 20mg x 1 Methadone 10mg x 2	Methadone 20mg x 1
Day 2	Methadone 40mg x 1 Methadone 10 mg x 4 Hydromorphone 4mg x 1, 5 mg x 1, 10mg x 4	Methadone 40mg x 1 Methadone 10mg x 2	Methadone 20mg x 1 Hydromorphone 15mg x 1
Day 3	Methadone 50mg x 1 Methadone 10mg x 2 Hydromorphone 10mg x 8	Methadone 50mg x 1 Methadone 10mg x 2	Methadone 20mg x 2 Methadone 10mg x 3
Day 4	Methadone 50mg x 1 Methadone 10mg x 2 Hydromorphone 5mg x 1, 10mg x 8, 15mg x 1	Methadone 60mg x 2 Methadone 10mg x 2	Methadone 40mg x 1 Methadone 20mg x 1 Methadone 10 mg x 2
Day 5	Methadone 70mg x 1 Hydromorphone 10mg x 4, 12 mg x 1, 14 mg x 1	Methadone 70mg x 1	Methadone 50mg x 1 Methadone 20mg x 1 Hydromorphone 20mg x 2
Day 6	Note: Methadone reported as PO equivalents; Hydromorphone reported as PO equivalents.		Methadone 80mg x 1 Hydromorphone 25mg x 2
Day 7	Case 3 was not seen by the addi rapid methadone initiation prote Day 3 of admission	ction consult service and	Methadone 80mg x 1 Hydromorphone 15mg x 2

#### **METHODS**

We present a series of three patients with OUD admitted to a tertiary center experiencing opioid withdrawal. A rapid methadone initiation protocol was implemented based on prior published literature (Hemmons et al., 2019). See "General Approach to Rapid Methadone Initiation Protocol." The Clinical Opioid Withdrawal Scale (COWS) was not used to manage opioid withdrawal, Instead, as needed methadone for opioid withdrawal was patient-initiated with hold parameters for sedation or respiratory depression. Equivalent IV methadone doses were used if the patient could not tolerate PO.

Cases were reviewed for primary outcomes of total methadone and short-acting opioids administered per day (Table 1). Secondary outcomes were collected including events of respiratory depression, patient-directed discharges (PDD), and continuation of medication for opioid use disorder on discharge (Table 2).

2. Hemmons P, Bach P, Colizza K, Nolan S. Initiation and Rapid Titration of Methadone in an Acute Care Setting for the Treatment of Opioid Use Disorder: A Case Report. J Addict Med. 2019 Sep/Ox; 13(5):408-411. doi: 10.1097/ADM.000000000000507. PMID: 30741835; PMCID: PMC6682456. 3. The ASAM National Practice Guideline for the Treatment of Opioid Use Disorder: 2020 Focused Update. J Addict Med. 2020 Mar/Jap;14(2) Suppl 1):1-91. doi: 10.1097/ADM.00000000000033. Erratum in: J Addict Med. 2020 May/Jun;14(3):267. PMID: 32511106.

# **Table 2: Secondary Outcomes**

	Case 1	Case 2	Case 3
Age	34	35	40
Admission Dx	Endocarditis	Gastroparesis	Hypoxic Respiratory Failure
Respiratory Depression	No	No	No
Patient-directed Discharge	Yes	No	No
Completion of medical care	No	Yes	Yes
Continuation of MOUD	N/A	Referral	Referral

#### DISCUSSION

Our results suggest that a rapid methadone initiation protocol can be well tolerated and promotes retention in medical care. There were no adverse events secondary to rapid methadone titration. This approach allows for a safe and rapid initiation of methadone to stabilize patients in the acute care setting, which is particularly valuable in the fentanyl era.

Current methadone prescribing quidelines recommend low dose initiation and slow titration to avoid the risks of respiratory depression and overdose (ASAM, 2020). This gradual approach does not account for high opioid tolerances associated with individuals using high potency synthetic opioids and often leads to undertreatment of opioid withdrawal. Challenges associated with implementation is prescriber unfamiliarity with safety and efficacy of protocol as well as possible hospital limitations on maximum daily dose of methadone indicated for OUD.

### CONCLUSIONS

Early evidence suggests that the use of a rapid methadone initiation schedule is well tolerated and safe in patients experiencing opioid withdrawal in medical or surgical units. Appropriate management of opioid withdrawal symptoms can help improve retention and decrease patient directed discharges in patients with OUD admitted for other medical problems.

Simon R. Snow R. Wakeman S. Understanding why natients with substance use disorders leave the hosoital against medical advice: A qualitative study. Subst Abus. 2020;41(4):519-525. doi: 10.1080/08897077.2019.1671942. Epub 2019 Oct 22. PMID: 31638863