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Predictors of Opioid and Alcohol Pharmacotherapy Initiation at Hospital Discharge Among Patients Seen by an Inpatient Addiction Consult Service

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1 **Title:** **Predictors of opioid and alcohol pharmacotherapy initiation at hospital discharge**
2 **among patients seen by an inpatient addiction consult service**

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39
40

41 **Abstract**

42 **Background:** Medications for opioid use disorder (MOUD) and alcohol use disorder (MAUD) are effective
43 and under-prescribed. Hospital-based addiction consult services can engage out-of-treatment adults in
44 addictions care. Understanding which patients are most likely to initiate MOUD and MAUD can inform
45 interventions and deepen understanding of hospitals' role addressing substance use disorders (SUD).

46
47 **Objective:** Determine patient- and consult-service level characteristics associated with MOUD/MAUD
48 initiation during hospitalization

49
50 **Methods:** We analyzed data from a study of the Improving Addiction Care Team (IMPACT), an
51 interprofessional hospital-based addiction consult service at an academic medical center. Researchers
52 collected patient surveys and clinical data from September 2015 to May 2018. We used logistic
53 regression to identify characteristics associated with medication initiation among participants with OUD,
54 AUD, or both. Candidate variables included patient demographics, social determinants, and treatment-
55 related factors.

56
57 **Results:** 339 participants had moderate to severe OUD, AUD, or both and were not engaged in
58 MOUD/MAUD care at admission. Past methadone maintenance treatment (aOR 2.07, 95%CI (1.17,
59 3.66)), homelessness (aOR 2.63, 95%CI (1.52, 4.53)), and partner substance use (aOR 2.05, 95%CI (1.12,
60 3.76) were associated with MOUD/MAUD initiation. Concurrent methamphetamine use disorder (aOR
61 0.32, 95%CI (0.18, 0.56)) was negatively associated with MOUD/MAUD initiation.

62 **Conclusions:** The association of MOUD/MAUD initiation with homelessness and partner substance use
63 suggests that hospitalization may be an opportunity to reach highly-vulnerable people, further

64 underscoring the need to provide hospital-based addictions care as a health-system strategy.

65 Methamphetamine's negative association with MOUD/MAUD warrants further study.

66

67

68 **INTRODUCTION**

69 Hospitalization can be a reachable moment to initiate care for people with substance use disorders
70 (SUD) (Englander et al., 2017). Many people with SUD who are admitted to general medical hospitals are
71 not engaged in treatment and they do not come to the hospital seeking addictions care (Englander et al.,
72 2017; Velez et al., 2017). Hospitalization and acute illness can raise patients awareness of mortality and
73 other harmful effects of substance use, and can be a strong motivation to initiate treatment (Velez et al.,
74 2017). Yet, little is known about who might benefit from hospital-based care. Understanding which
75 patients are most likely to initiate MOUD and MAUD can inform interventions and deepen
76 understanding of hospitals' role addressing substance use disorders (SUD).

77

78 Medications for opioid use disorder (MOUD) and alcohol use disorder (MAUD) are effective and under-
79 prescribed. Opioid agonist therapy (OAT) (methadone and buprenorphine) is first-line treatment for
80 moderate to severe opioid use disorder. Decades of evidence show that OAT reduces overdose and all-
81 cause mortality by over half (Sordo et al., 2017), reduces risk of infectious disease transmission (Gowing
82 et al., 2013; Tsui et al., 2014), and reduces criminal behavior associated with substance use (Rastegar et
83 al., 2016). Further, hospitalization is a high-risk touchpoint after which people with opioid use disorder
84 are at increased risk for overdose and death. A recent study in Massachusetts found that hospitalization
85 for injection-related infection was associated with a 54-fold increase in mortality, and that MOUD can
86 mitigate this risk (Laroche et al., 2019). Medication, combined with psychosocial interventions,
87 comprise first line treatment for moderate to severe alcohol use disorder. MAUD is associated with
88 reduced drinking days, reduced alcohol consumption, and increased abstinence from alcohol (Jonas et
89 al., 2014). Despite their effectiveness, less than 10% of people with alcohol use disorder receive MAUD
90 (Substance Abuse and Mental Health Services Administration, 2017) and only 20%–40% of people with
91 OUDs are receiving life-saving medication treatment (Jones et al., 2015).

92

93 Nationally, hospital-based addiction medicine consult services are emerging as a way to engage out-of-
94 treatment adults in addictions care (Priest and McCarty, 2019). A study at a Boston academic medical
95 center found that 30% of patients with high risk alcohol and drug use were engaged in treatment prior
96 to admission, and that hospital addiction consultation was associated with increased treatment
97 engagement after discharge (Wakeman et al., 2017). In a study of Oregon Medicaid recipients
98 comparing adults seen by our addiction consult service to matched controls, we found that 17% of
99 patients were engaged in treatment prior to hospitalization. Treatment engagement increased to 39% in
100 the 34 days after discharge among patients seen by our addiction consult service, compared to 23%
101 among matched-controls (Englander et al., 2019a). Healthcare Effectiveness Data and Information Set
102 (HEDIS) identifies SUD treatment initiation and engagement as a national quality measure (National
103 Committee for Quality Assurance, 2017), and hospitalization is an important part of the SUD care
104 continuum.

105

106 Little is known about which hospitalized patients are most likely to initiate MOUD and MAUD, and what
107 consult service factors are associated with medication initiation. The goal of this study was to determine
108 patient- and consult-service level characteristics associated with MOUD and MAUD initiation during
109 hospitalization.

110

111 **METHODS**

112 **Setting and study design:**

113 We analyzed survey data collected as part of a study of the Improving Addiction Care Team (IMPACT) at
114 an urban, academic medical center in Portland, Oregon. IMPACT is a hospital-based addiction consult

115 service that includes care from addiction medicine providers (physicians or advance-practice providers
116 (APPs)), social workers, and peers with lived experience in recovery (Englander et al., 2017; Englander et
117 al., 2019c). Inpatient medical and surgical providers, and hospital social workers refer patients with
118 known or suspected SUD (excluding people with tobacco use disorders alone) to IMPACT, regardless of
119 an individual's readiness to change or interest in SUD treatment. In general, at least one member of
120 IMPACT (MD/APP, SW, peer) visits patients daily during hospitalization, and peers often continue peer
121 support 30-90 days after hospital discharge. Peers are often the first-line for patients who express low
122 interest in treatment or working with IMPACT (Collins et al., 2019; Englander et al., 2019b). IMPACT
123 performs an initial comprehensive assessment; elicits patient-centered goals; initiates SUD treatment,
124 including pharmacotherapy and behavioral treatments; and offers harm reduction services. IMPACT can
125 help manage acute pain and perioperative care, including MOUD/MAUD initiation in this population.
126 IMPACT also includes robust referral pathways to post-hospital SUD care. IMPACT offers MOUD and
127 MAUD to all patients with moderate-to-severe opioid and/or alcohol use disorder, and tailors
128 medication decisions based on patient preferences, acute medical conditions, and post-hospital
129 community treatment resources. For some patients, this includes coordinating treatment plans with
130 skilled nursing facilities (e.g. coordinating take-out dosing from an opioid treatment program (OTP) or
131 daily transportation to support patients to get methadone from an OTP while at SNF). The Oregon
132 Health & Science University Institutional Review Board approved this study.

133

134 **Participants:**

135 Participants included patients seen by IMPACT and enrolled in the IMPACT evaluation between
136 September 2015 and August 2018. Patients were eligible for this analysis if they 1) had moderate to
137 severe opioid use disorder, alcohol use disorder, or both, and 2) were not already receiving MOUD or

138 MAUD upon hospital admission. We operationalized the definition of current use of MOUD or MAUD by
139 baseline questionnaire responses, which asked participants if they were currently receiving medication
140 for opioid use disorder (e.g. methadone, buprenorphine, naltrexone), or medication for alcohol use
141 disorder (e.g. acamprosate).

142 **Study procedures and data sources:**

143 Early in hospitalization, a trained research assistant who was not part of the clinical team administered
144 an in-person survey. Surveys focused on demographics, substance use, and patient experience, and took
145 approximately 15-20 minutes to complete. The research assistant collected patient surveys and directly
146 entered responses into an online survey and database management system, REDCap, reviewing surveys
147 afterwards for accuracy. At discharge, IMPACT clinical team members completed a case closure form
148 during the daily team huddle. Case closure forms included information about a patient's diagnoses,
149 hospital course, and treatment plan. Trained research assistants validated information from case closure
150 forms by chart review in the electronic health record, and then entered this information into REDCap.
151 Finally, research team members abstracted data from electronic medical records.

152 **Measures:**

153 We selected potential covariates based on *a priori* hypotheses and face validity.
154 Covariates from the patient survey included gender (male/female), race (American Indian/Alaska Native,
155 Asian, African American/Black, Native Hawaiian/other Pacific Islander, white, more than one race,
156 refused), income in the previous year (\$10,000 increments, \$0 to >\$50,000), housing status
157 (housed/unhoused), partner with substance use (yes/no), rural home zip code (yes/no), history of past
158 but not current methadone maintenance engagement (yes/no) and access to a usual primary care clinic
159 (yes/no). We identified rural zip codes using the Federal Office of Rural Health Policy designated rural zip
160 codes (Health Resources & Services Administration, 2018). We determined past but not current

161 methadone maintenance therapy using the Addiction Severity Index Lite (ASI-lite) measurement tool;
162 and considered patients who identified past methadone maintenance therapy without use in the last 30
163 days (Cacciola et al., 2007). Covariates from the case closure form included opioid use disorder (yes/no),
164 alcohol use disorder (yes/no), methamphetamine use disorder (yes/no), peer support delivered in
165 hospital (yes/no). Discussion with members of the clinical and research team suggested that cocaine and
166 benzodiazepine use would be very low in our population; hence, we did not consider these covariates in
167 our research. Covariates from chart review included patient age (years), insurance status (any Oregon
168 Medicaid, Medicare, other), and number of IMPACT clinician and social worker visits per day
169 (continuous).

170 Our outcome measure was in-hospital initiation of MOUD, MAUD, or both, and was determined from
171 case closure forms and validated via chart review. MOUD included the three FDA-approved medications
172 for opioid use disorder: methadone, buprenorphine (including buprenorphine-naloxone), and
173 naltrexone. MAUD included naltrexone, acamprosate, disulfiram, and gabapentin. We included
174 gabapentin only if it was prescribed for treatment of alcohol use disorder. We elected to include
175 gabapentin even though it is a not FDA approved for treatment of AUD because in hospitalized adults
176 with AUD and acute pain on opioids who are reluctant to take multiple three-time daily medication, it
177 can be the best alternative for MAUD. We felt including it was better reflective of MAUD initiation than
178 excluding it. We excluded all medications if there was no plan to continue after hospital discharge; for
179 example, methadone for withdrawal only with no plan for methadone maintenance post-discharge.

180 **Covariate manipulation**

181 We reclassified race as Caucasian/non-Caucasian because of sample size among non-Caucasian patients;
182 we included patients who did not know their race, were missing race information or refused to answer

183 as Caucasian. One participant was transgender; we reclassified this person the gender they identify with.
184 If participants were unsure if they had any income in the previous year, we classified them as no income.
185 Finally, we created a “dose indicator” for IMPACT delivery, defined as the total number of documented
186 IMPACT provider or social worker encounters during hospitalization, divided by the total number of
187 hospital days. We dichotomized this as a binary covariate (at least 1 visit per day/less than 1 visit per
188 day). We report this variable in our table but did not consider this for inclusion in our analyses, as it may
189 be challenging to interpret without a measure of patient motivation for treatment and could represent
190 confounding by indication.

191 We were concerned that medication initiation would differ significantly by diagnosis (AUD, OUD or
192 both). We chose to include an interaction term to determine if IMPACT delivery differed by diagnosis; if
193 the interaction term was significant, we planned to present the terms separately in the paper.

194

195 **Data analysis**

196 *Primary analysis and fit*

197 We built a logistic regression model to estimate the relationship of baseline participant characteristics
198 with the binary outcome variable MOUD and/or MAUD initiation. We fit our logistic regression model
199 using a conservative estimated covariate ratio of 10 events per degree of freedom (Cacciola et al., 2007).
200 We used backwards stepwise elimination with a relaxed p-value of 0.20 to finalize our model and did not
201 force any covariates into our model. We evaluated our continuous covariates for linearity in the log-
202 odds using Lowess scatter plot (comparing medication intention and continuous covariates individually
203 and evaluated all covariates for collinearity using a correlation matrix). Finally, we used a Hosmer-
204 Lemeshow test to evaluate model goodness-of-fit (Hosmer and Lemeshow, 2000).

205 For patients who were admitted more than once, we used only the first encounter to both comply with
206 the assumption of independence in logistic regression testing and because we were primarily interested
207 in associations with MOUD/MAUD initiation following a first encounter with IMPACT. We did not adjust
208 for multiple comparisons in this exploratory study.

209 *Missing Data*

210 We anticipated minimal missingness in surveys conducted in the hospital, and so only included patients
211 with complete covariate data, other than as listed in data manipulations above (Figure).

212 *Sensitivity analysis*

213 We conducted two sensitivity analyses. First, we identified influential observations using Pregibon's
214 Delta-Beta statistic. Observations with a Delta-Beta statistic greater than 0.20 were removed. Second,
215 we re-ran our analyses without imputing Caucasian when race was missing. We planned to report
216 results alongside the primary analysis if directionality or significance of any covariate changed.

217 **RESULTS**

218 During the study period, 760 patients were referred to IMPACT. Researchers approached 689 patients,
219 and 486 consented to participate in surveying. Of those, 401 had moderate to severe OUD and/or AUD
220 and 349 had no pharmacotherapy for OUD/AUD before admission (Figure). Two patients were identified
221 as in "sustained remission" from both alcohol and opioid use and were excluded. One patient died in the
222 hospital. 346 participants were eligible for inclusion in the model. Of those, 248 (71.7%) initiated
223 MOUD/MAUD during hospitalization. Study participants were predominantly Caucasian (80.9%), had
224 opioid use disorder without alcohol use disorder (52.0%), were experiencing homelessness (55.0%), had
225 Medicaid insurance (76.3%), and had an established primary care clinic (61.3%). 30.0% of participants
226 had a co-occurring moderate or severe methamphetamine use disorder (Table 1).

227 In our analysis, past methadone maintenance treatment initiation (aOR 2.24, 95%CI (1.28, 3.94)),
228 homelessness (aOR 2.52, 95%CI (1.47, 4.30)), and having a partner with substance use (aOR 2.06, 95%CI
229 (1.13, 3.74) were associated with MOUD/ MAUD initiation. Concurrent methamphetamine use disorder
230 (aOR 0.32, 95%CI (0.18, 0.56)) was negatively associated with MOUD/MAUD initiation (Table 2). In
231 addition to these covariates, backwards selection also included age and gender in our final model,
232 though they are not statistically significant. Neither sensitivity analysis changed the direction or
233 significance of results. The interaction term evaluating if the IMPACT dose indicator varied by diagnosis
234 (AUD only vs any OUD) was not significant, and was not included in the final model ($p=0.97$).

235 Among participants with any OUD ($n=219$), methadone was the most common MOUD ($n=80$; 36.5%),
236 followed by buprenorphine ($n=62$, 28.3%). Eight participants with OUD (3.7%) received intramuscular
237 naltrexone. Among participants with any AUD ($n=166$), 41 (24.7%) received any naltrexone (oral or
238 intramuscular), and 39 (23.5%) received acamprosate (Table 3).

239 **Discussion**

240 Our study identifies predictors of MOUD and/or MAUD initiation among hospitalized adults seen by an
241 addiction consult service. We found that current homelessness or a partner with substance use
242 predicted MOUD/MAUD initiation. Co-occurring methamphetamine use disorder, however, was
243 negatively associated with MOUD/MAUD initiation. Residing in a rural area, having a usual source of
244 primary care, and Medicaid insurance had no association with MOUD/MAUD initiation. To our
245 knowledge, this is the first study describing patterns of MOUD/MAUD initiation among hospitalized
246 adults seen by an addiction consult service. Our findings suggest ways in which hospital-based addiction
247 care may differ from community treatment, and highlight how the reachable moment of hospitalization
248 may differentially effect people with co-occurring methamphetamine use, those experiencing
249 homelessness or those with a partner with substance use.

250 This research builds on existing research in several important ways. The finding that 74% of people with
251 moderate to severe OUD and/or AUD initiated medication supports earlier work showing that
252 hospitalization can be a reachable moment and opportunity engage non-treatment seeking adults by
253 interrupting drug use and serving as a “wakeup call” (Velez et al., 2017). Though this study was not
254 designed to examine post-hospital treatment engagement, our findings are contextualized and
255 promising in light of earlier work showing that hospital-initiated addictions care is associated with
256 increased treatment engagement after discharge (Englander et al., 2019a).

257 This study highlights ways in which hospitalization may present a unique opportunity to initiate care.
258 Notably, most research in community settings suggests that homelessness is associated with lower
259 MOUD/MAUD initiation and engagement (Appel et al., 2004; Prangnell et al., 2016; Damian et al., 2017;
260 Lo et al., 2018; Watkins et al., 2018), and some studies find no association (Simon et al., 2017; Tsui et al.,
261 2018). Previous studies in community settings found that having a partner with substance use is
262 associated with lower readiness to engage in treatment (Riehman et al., 2000). By contrast, our study
263 found increased rates of MOUD/MAUD initiation in this population. Though we do not have data to
264 explain this unexpected finding, we speculate that there may be an important interplay between
265 motivation to initiate treatment and barriers to care. Specifically, patients with fewer barriers who are
266 motivated to initiate treatment may do so prior to hospitalization. Our findings suggest that
267 hospitalization may serve as an opportunity to engage hard-to-reach populations.

268 The finding that co-occurring methamphetamine use disorder is negatively associated with MOUD/
269 MAUD initiation is important. Methamphetamine hospitalizations are surging (Winkelman et al., 2018)
270 and methamphetamine use is an emerging public health issue, with an estimated 250% increase in
271 stimulant-related deaths nationally from January 2015 to October 2018 (Ahmad et al., 2019). In Oregon,
272 rates appear even worse, with a 400% increase in deaths related to methamphetamines between 2010
273 and 2018 (Oregon-Idaho HIDTA Program, 2019).

274 Little is known about the association of methamphetamine use and treatment with medications for
275 opioid and alcohol use in general, and specifically among hospitalized adults. However, our research is
276 consistent with earlier work in community settings. One study of clients with opioid and
277 methamphetamine use who accessed services across 17 Washington State syringe exchanges found that
278 recent methamphetamine use was negatively associated with interest in getting help for OUD
279 (AOR=0.49; 95% CI: 0.26, 0.91) (Frost et al., 2018). Another primary care based study among people
280 with OUD and recent stimulant use found that clinic policies eliminating the requirement for stimulant
281 abstinence were associated with higher rates of buprenorphine initiation, but also with lower
282 buprenorphine treatment retention (Payne et al., 2019).

283 The negative association of methamphetamine use with MOUD/MAUD initiation warrants further
284 exploration, and could be due to a variety of system-, provider-, or patient-factors. We speculate that
285 patients with methamphetamine use may perceive their alcohol and/or opioid use as secondary and not
286 needing MOUD/MAUD or that methamphetamine withdrawal, cravings, or psychiatric symptoms may
287 interfere with patients or providers' ability to initiate MOUD/MAUD. It is also possible that community
288 SUD treatment policies influence patients' decisions about MOUD/MAUD, as methadone and
289 buprenorphine treatment programs commonly dismiss patients if their urine drug screens result positive
290 for methamphetamine. Though unknown, it is also possible that methamphetamine use is a marker for
291 social marginalization or other factors that might make people less likely to initiate MOUD/MAUD. Co-
292 use of methamphetamines and opioids is increasingly common due to synergistic euphoric or balancing
293 effects; easier access to methamphetamine; social pressures to co-use; and co-use as a marker for more
294 severe SUD (Ellis et al., 2018). How these factors effect non-treatment seeking, hospitalized adults
295 remains unclear.

296 This study has several limitations. It is a single-site study and all patients received care from an addiction
297 consult service. Findings may not be transferable to settings without a consult service or where the

298 consult service is comprised of different team members or has different activities. Second, not all
299 IMPACT patients agreed to participate in the survey. It is possible that people who participated were
300 more or less likely to initiate MOUD/MAUD. Further, this study took place in Oregon and participants
301 had low racial and ethnic diversity. Additionally, we asked patients about past methadone use because
302 this is included in the ASI-lite, but we did not ask about other past MOUD or MAUD exposure.
303 Associations between all types of past MOUD/MAUD treatment may be important to test in predicting
304 hospital MOUD/MAUD in future studies. Further, our analysis not adjust for multiple comparisons as the
305 nature of this work was exploratory. Additionally, we looked only at the association of MOUD/MAUD
306 initiation following a first encounter with IMPACT. Future research should explore effects of repeated
307 exposure to addiction consult services for individuals who are readmitted to hospitals and have repeat
308 addiction consultation. Future studies should also explore additional patient- and consult-service factors
309 that promote MOUD/MAUD initiation such as patient readiness to change. This analysis included all
310 participants regardless of AMA discharge. Our hypothesis is that AMA discharge would be strongly
311 predictive of not initiating MOUD/MAUD with a plan to continue; future studies could explore this more
312 closely. Finally, while important, medication initiation does not reflect long-term treatment
313 engagement. Future studies of treatment engagement and retention specific to MOUD/MAUD will be
314 important.

315

316 Our study has several important implications for clinical care and research. First, the findings that
317 homelessness and having a partner with substance use was positively associated with MOUD/MAUD
318 initiation suggests that these vulnerable people may not be accessing treatment outside of the hospital.
319 It also supports the potential value of an interprofessional hospital-based addictions team with
320 resources dedicated to addressing social factors that may influence treatment retention after discharge.
321 For IMPACT, this includes social workers and peers who work to connect people with housing, engage

322 partners in addictions care, develop relapse prevention plans, and tailor post hospital treatment plans to
323 support retention in care. Our findings also have implications for community treatment, highlighting the
324 importance of addressing social determinants of health across the continuum of hospital and
325 community SUD to support treatment engagement and retention.

326 The fact that methamphetamine use is associated with lower MOUD/MAUD initiation is important,
327 especially as we consider drivers for the opioid overdose crisis. Most opioid overdose deaths involve
328 multiple substances (Barocas et al., 2019) and initiation of MOUD during acute care encounters is critical
329 to overdose prevention (Larochelle et al., 2018). Our findings suggest the need for further research to
330 explore the association of methamphetamine use and MOUD, MAUD, and hospital-based addiction
331 medicine care. Future studies should also examine effect of MOUD/MAUD initiation during
332 hospitalization on pertinent clinical outcomes including substance use, long-term SUD treatment
333 engagement, healthcare utilization, quality of life, overdose risks, and other health outcomes.

334

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