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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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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

INTRODUCTION

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

Medications for opioid use disorder (MOUD) and alcohol use disorder (MAUD) are effective and under-prescribed. Opioid agonist therapy (OAT) (methadone and buprenorphine) is first-line treatment for moderate to severe opioid use disorder. Decades of evidence show that OAT reduces overdose and all-cause mortality by over half (Sordo et al., 2017), reduces risk of infectious disease transmission (Gowing et al., 2013; Tsui et al., 2014), and reduces criminal behavior associated with substance use (Rastegar et al., 2016). Further, hospitalization is a high-risk touchpoint after which people with opioid use disorder are at increased risk for overdose and death. A recent study in Massachusetts found that hospitalization for injection-related infection was associated with a 54-fold increase in mortality, and that MOUD can mitigate this risk (Larochelle et al., 2019). Medication, combined with psychosocial interventions, comprise first line treatment for moderate to severe alcohol use disorder. MAUD is associated with reduced drinking days, reduced alcohol consumption, and increased abstinence from alcohol (Jonas et al., 2014). Despite their effectiveness, less than 10% of people with alcohol use disorder receive MAUD (Substance Abuse and Mental Health Services Administration, 2017) and only 20%–40% of people with 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, 3.74were 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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