

Understanding the impact of co-occurring substance use disorders on receipt of medications for  
opioid use disorder in the Veterans Health Administration to inform care improvement

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**Abstract**

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**Background:** A growing majority of people with opioid use disorder (OUD) have co-occurring substance use and/or substance use disorders (SUDs), which are associated with reduced likelihood of receiving life-saving OUD treatment medications (MOUD). Efforts to increase and improve MOUD care should explicitly address the role of co-occurring substance use/SUDs. This work is particularly important in the context of the Veterans Health Administration (VA) healthcare system – the VA is the nation’s largest OUD treatment provider, expanding MOUD access is an important VA priority, and over half of VA patients with OUD have co-occurring SUDs. However, more information is needed to effectively address this issue.

**Objectives:** This dissertation involved three aims which sought to: 1) examine associations between distinct types of co-occurring SUDs and either initiation or continuation of MOUD among outpatients with OUD in the national VA healthcare system; 2) assess whether the VA

Stepped Care for Opioid Use Disorder Train the Trainer (SCOUTT) initiative's effectiveness in increasing MOUD receipt was modified by the presence of co-occurring SUDs; and 3) qualitatively assess the perspectives of VA clinicians providing buprenorphine care in primary care, mental health, and pain settings to understand their approach to addressing OUD in patients with co-occurring substance use/SUDs, barriers and facilitators to MOUD receipt for this patient population, and support needed to increase MOUD receipt in this patient population.

**Methods:** In Aim 1, among national VA outpatients with OUD who received care 8/1/2016-7/31/2017, we used adjusted regression models to estimate the likelihood of following-year MOUD initiation (among patients without prior-year MOUD receipt) and continuation (among patients with prior-year MOUD receipt) for patients with each co-occurring SUD relative to those without. In Aim 2, we used a controlled interrupted time series design to examine the monthly proportion of patients who received MOUD in SCOUTT and/or SUD specialty clinics during pre- and post-implementation years (9/1/2017-8/31/2018 and 9/1/2018-8/31/2019, respectively) among patients with OUD who received care in SCOUTT intervention or comparison clinics. We fit segmented logistic regression models to examine pre-post changes in outcomes (immediate level change, change in trend/slope) in intervention vs. comparison clinics, adjusting for patient characteristics and pre-implementation trends, with interaction terms to assess effect modification by the presence of co-occurring SUDs. In Aim 3, we interviewed 27 clinicians in the VA northwest regional network. Interviews were transcribed and qualitatively analyzed using inductive content analysis.

**Results:** In Aim 1, we found that among 23,990 patients without prior-year MOUD receipt, 12% initiated MOUD in the following year. Alcohol use disorder (adjusted incidence rate ratio [aIRR] 0.80, 95% confidence interval [CI] 0.72-0.90) and cannabis use disorder (aIRR 0.78, 95% CI

0.70-0.87) were negatively associated with initiation. Among 11,854 patients with prior-year MOUD receipt, 83% continued MOUD in the following year. Alcohol use disorder (aIRR 0.94, 95% CI 0.91-0.97), amphetamine/other stimulant use disorder (aIRR 0.94, 95% CI 0.90-0.99), and cannabis use disorder (aIRR 0.95, 95% CI 0.93-0.98) were negatively associated with continuation. In Aim 2, we found that the impact of the SCOUTT initiative on MOUD receipt was not significantly modified by the presence of co-occurring SUDs. However, among patients without co-occurring SUDs, the trend change in MOUD receipt in SCOUTT clinics was greater in intervention vs. comparison clinics (adjusted odds ratio [aOR]: 1.06, 95% confidence interval [CI]: 1.02-1.10), and the immediate level change in MOUD receipt in SUD clinics was greater in intervention vs. comparison clinics (aOR: 1.12, 95% CI: 1.02-1.22), while these changes were not significantly greater in intervention vs. comparison clinics among patients with co-occurring SUDs. In Aim 3, we found that participants reported varied approaches to identifying co-occurring substance use/SUDs and to treating OUD in this patient population. Although they reported that this topic was not clearly addressed in clinical guidelines or training, participants generally felt that patients with co-occurring substance use should receive MOUD. Some viewed their primary role as providing this care, others as facilitating linkage to OUD care in SUD specialty settings. Participants reported multiple barriers and facilitators to providing buprenorphine care to patients with co-occurring substance use/SUDs and linking them to SUD specialty care. They discussed their perceptions of how provider factors, patient factors, organizational factors, and external factors impact MOUD receipt for this population.

**Conclusions:** Current VA efforts to implement MOUD outside of SUD specialty settings may be primarily increasing MOUD receipt for patients without co-occurring SUDs. Providers in these settings report multiple barriers to as well as facilitators of providing MOUD to patients with co-

occurring substance use/SUDs and linking them to SUD specialty care. Ongoing and future MOUD implementation efforts can work to address these barriers and leverage these facilitators to improve MOUD care for patients with co-occurring substance use/SUDs, keeping in mind that barriers specifically related to co-occurring alcohol, cannabis and amphetamine use disorders may need particular focus.

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## Chapter 1: Introduction

An estimated 2.7 million people in the United States have opioid use disorder (OUD),<sup>1</sup> and overdose deaths are at a record high and continue to climb.<sup>2,3</sup> There are three approved medications for opioid use disorder (MOUD), which include buprenorphine, methadone and naltrexone.<sup>4</sup> Buprenorphine and methadone are considered first-line treatment and substantially reduce overdose risk.<sup>5-9</sup> Unfortunately, most people with OUD do not receive these potentially life-saving medications.<sup>1</sup> Increasing MOUD initiation and retention is therefore an important strategy to combat the overdose crisis.

A growing majority of people with OUD use alcohol or other non-opioid drugs and/or have one or more co-occurring non-opioid substance use disorders (SUDs).<sup>10-13</sup> For example, a survey of people entering treatment for OUD across the country found that over 50% reported past-month use of non-opioid substances other than tobacco in 2018,<sup>10</sup> and diagnostic records suggest that the majority of Veterans Health Affairs (VA) patients with OUD have at least one other non-tobacco SUD, with estimates ranging from 59-64%.<sup>13,14</sup> Several studies have found that patients with co-occurring SUDs are less likely to receive MOUD than those with only OUD.<sup>12,15-17</sup> Clinical guidelines state that use of other substances should not prevent MOUD provision,<sup>18</sup> therefore lower receipt of MOUD among patients with co-occurring SUDs is a problem that needs to be addressed. Though polysubstance use and co-occurring SUDs are “the norm rather than the exception” among people with OUD and appear to hinder MOUD receipt, efforts to expand MOUD have tended to overlook this issue.<sup>10,19</sup>

It is unclear what factors drive lower MOUD receipt among patients with co-occurring substance use/SUDs, though factors at multiple levels (including provider, patient, and the healthcare system) likely contribute at multiple points in the care continuum. For example,

providers may be less likely to offer MOUD to patients using other substances,<sup>20,21</sup> patients with co-occurring substance use/SUDs may be more likely to experience problems that increase life instability (e.g., housing instability, legal system involvement) that may make it difficult to engage in MOUD care,<sup>13</sup> and clinic policies requiring abstinence from other substances may hinder MOUD initiation and retention for this patient population.<sup>22</sup> Moving forward, efforts to increase and improve MOUD care should more explicitly address the role of co-occurring substance use/SUDs. However, more information is needed to effectively address this issue.

Better understanding of how specific co-occurring SUDs are associated with MOUD receipt is needed, as this information may inform targeted efforts to improve care. These associations likely vary across different clinical settings and patient populations. In the VA, a few studies have examined associations between individual co-occurring SUDs and MOUD receipt, finding mixed results.<sup>23-25</sup> However, these studies have been limited to specific patient populations (e.g., those with post-traumatic stress disorder) and/or used data from 2012 or prior. Further, they have used methodological approaches that are limited for examining these associations (e.g., stepwise regression and/or models without *a priori* selected covariates, which may not adequately address confounding). It is therefore currently unclear how distinct types of co-occurring SUDs are associated with receipt of MOUD in the national VA, and a study using an analytic approach designed to answer this specific question is needed.

Research addressing the role of co-occurring substance use/SUDs in efforts to expand MOUD provision into new clinical settings is also needed. As patients may face multiple barriers to accessing care in SUD specialty settings,<sup>26</sup> expanding MOUD provision in other clinical settings is a key strategy to increase access.<sup>27,28</sup> It is important to understand whether and how new MOUD care models being implemented outside of SUD specialty settings impact MOUD

access for patients with co-occurring substance use/SUDs, however few studies examining these care models have focused on whether they are effective for this population, and, similar to MOUD efficacy trials,<sup>29</sup> many have excluded patients with co-occurring SUDs from their study sample.<sup>30</sup> These care models may improve access for patients with co-occurring substance use/SUDs through direct MOUD provision and/or improved linkage to SUD specialty settings. However, if they do not, then modified or additional efforts may be needed to improve care for this population.

Additionally, better understanding of how MOUD providers outside of SUD care settings view and address co-occurring substance use/SUDs is needed. Though providers outside of SUD specialty care play a key role in the expansion of MOUD treatment, and research has assessed their perspectives on providing this treatment,<sup>31</sup> little is known about their practices and perspectives regarding providing MOUD to patients with co-occurring substance use/SUDs. Existing research suggests that co-occurring substance use plays a role in MOUD providers' decision-making,<sup>20,21,32-34</sup> but more in-depth, qualitative information from clinicians providing MOUD outside of SUD specialty settings is needed to understand how their experiences and perceptions may drive clinical practices, as well as barriers and facilitators to MOUD for this patient population.

The VA is an important setting in which to address these research gaps for multiple reasons. It is the nation's largest integrated healthcare system and largest OUD treatment provider,<sup>35</sup> and expanding access to MOUD is an important VA priority.<sup>36</sup> Over half of patients with OUD in the national VA have co-occurring SUDs, and those with at least one co-occurring SUD are less likely than those with OUD alone to receive both buprenorphine and methadone.<sup>12</sup> The VA recently implemented the Stepped Care for Opioid Use Disorder Train the Trainer

(SCOUTT) initiative—the system’s largest effort to implement MOUD outside of SUD specialty settings, including primary care, mental health, and pain clinics.<sup>27</sup> Finally, leaders have called for research that leverages the VA’s status as a learning health system (i.e., an integrated system that can broadly implement and test new interventions and care models) to improve care for patients with OUD and polysubstance use.<sup>37</sup>

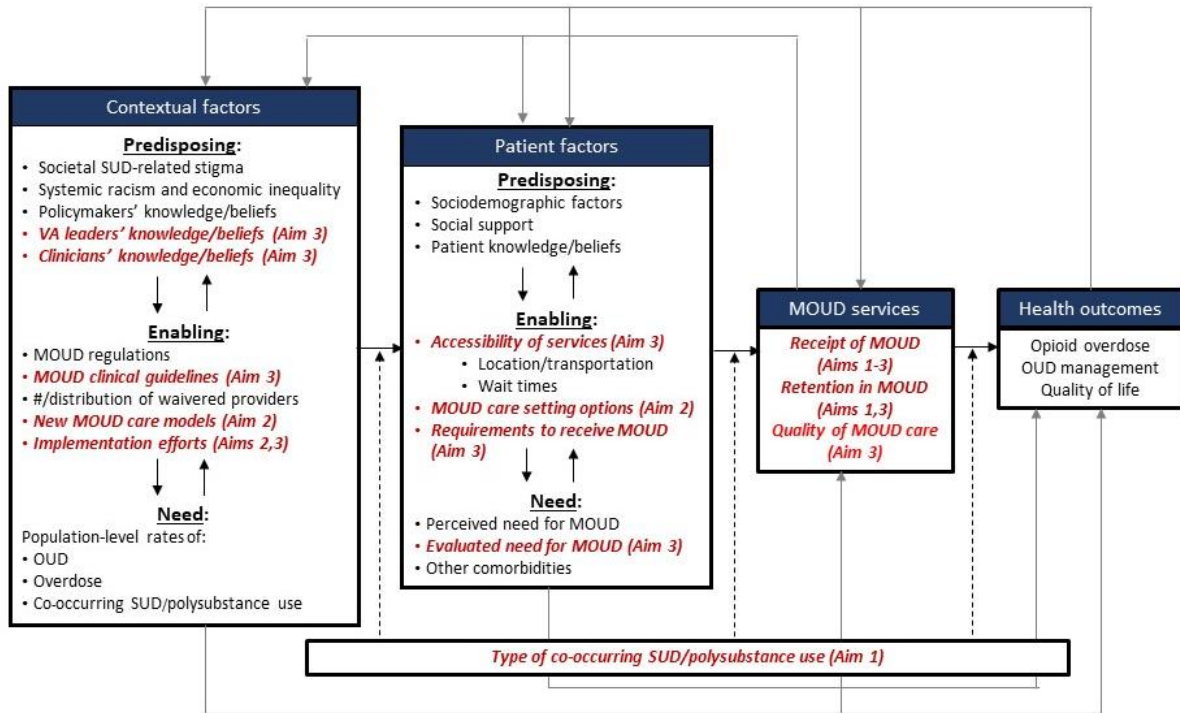
This dissertation addresses the research gaps described above through three research aims conducted in the VA healthcare system. First, using national patient-level electronic health record (EHR) data, we examined associations between distinct types of co-occurring SUDs and either initiation or continuation of MOUD among outpatients with OUD in the national VA healthcare system (Aim 1). Second, using patient-level EHR data from 35 intervention and 35 matched comparison VA clinics, we assessed whether the VA SCOUTT initiative’s effectiveness in increasing MOUD receipt was modified by the presence of co-occurring SUDs (Aim 2). Third, we conducted qualitative interviews with VA clinicians providing buprenorphine care in primary care, mental health, and pain settings to understand 1) their approach to addressing OUD in patients with co-occurring substance use/SUDs, 2) their perspectives on barriers and facilitators to MOUD receipt for this patient population, and 3) support needed to increase MOUD receipt in this patient population (Aim 3). Findings from these aims can inform future efforts to improve MOUD care for patients with co-occurring substance use/SUDs in the VA and other settings.

The conceptual model framing this dissertation was adapted from the Behavioral Model of Health Services Use.<sup>38</sup> Figure 1.1 shows hypothesized contextual and patient-level factors influencing MOUD access for VA patients with OUD with co-occurring substance use/SUDs. Multiple contextual factors at the societal, organizational, and provider levels likely shape receipt

and quality of MOUD services for VA patients with OUD and co-occurring SUDs. These include predisposing factors (e.g., prevailing knowledge/beliefs around SUD treatment among policymakers, VA leadership, and VA clinicians), enabling factors (e.g., MOUD regulations and clinical guidelines, availability of buprenorphine prescribers, new models of MOUD care, implementation efforts), and need factors (e.g., population-level rates of OUD, overdose and co-occurring substance use/SUDs among VA patients with OUD). Contextual factors may impact MOUD access directly or through patient-level factors. Patient-level factors also include predisposing factors (e.g., sociodemographic characteristics, social support, patients' knowledge/beliefs about MOUD), enabling factors (accessibility of VA services, availability of MOUD across different types of care settings, requirements patients must meet to receive MOUD), and need factors (e.g., patients' perceived need for MOUD, clinically evaluated need for MOUD, other non-SUD mental and physical comorbidities).

Factors in the conceptual model that were most directly addressed by our three research aims are indicated in red. Aim 1 assessed whether specific types of co-occurring SUDs are differentially associated with initiation and continuation of MOUD among VA patients with OUD. Aim 2 assessed the impact of co-occurring SUDs on MOUD receipt within the context of a new model of MOUD care being implemented through a train-the-trainer intervention in the VA (SCOUTT), which directly impacts the range of care settings in which MOUD is offered to patients. SCOUTT implementation may also have impacted providers' knowledge and beliefs about MOUD. Aim 3 most directly assessed how providers' perceptions of clinical guidelines and knowledge and beliefs around providing MOUD for patients with co-occurring substance use SUDs impacts their practice, but these interviews also addressed providers' perceptions of other contextual and patient-level factors.

Figure 1.1. Model of MOUD access for VA patients with OUD and co-occurring substance use/SUDs



## **Chapter 2: Associations between distinct co-occurring substance use disorders and receipt of medications for opioid use disorder in the Veterans Health Administration**

### **ABSTRACT**

**Objectives:** Among people with opioid use disorder (OUD), having a co-occurring substance use disorder (SUD) is associated with lower likelihood of receiving OUD treatment medications (MOUD). However, it is unclear how different co-occurring SUDs are associated with MOUD receipt. This study examined associations of distinct co-occurring SUDs with initiation and continuation of MOUD among patients with OUD in the national Veterans Health Administration (VA).

**Methods:** Electronic health record data were extracted for outpatients with OUD who received care 8/1/2016-7/31/2017. Analyses were conducted separately among patients without and with prior-year MOUD receipt to examine initiation and continuation, respectively. SUDs were measured using diagnostic codes; MOUD receipt was measured using prescription fills/clinic visits. Adjusted regression models estimated likelihood of following-year MOUD receipt for patients with each co-occurring SUD relative to those without.

**Results:** Among 23,990 patients without prior-year MOUD, 12% initiated in the following year. Alcohol use disorder (adjusted incidence rate ratio [aIRR] 0.80, 95% confidence interval [CI] 0.72-0.90) and cannabis use disorder (aIRR 0.78, 95% CI 0.70-0.87) were negatively associated with initiation. Among 11,854 patients with prior-year MOUD receipt, 83% continued in the following year. Alcohol use disorder (aIRR 0.94, 95% CI 0.91-0.97), amphetamine/other stimulant use disorder (aIRR 0.94, 95% CI 0.90-0.99), and cannabis use disorder (aIRR 0.95, 95% CI 0.93-0.98) were negatively associated with continuation.

**Conclusions:** In this study of national VA outpatients with OUD, those with certain co-occurring SUDs were less likely to initiate or continue MOUD. Further research is needed to identify barriers related to specific co-occurring SUDs.

## **INTRODUCTION**

An estimated 2.7 million people in the United States have opioid use disorder (OUD).<sup>1</sup> Opioid overdose is a severe public health crisis with overdose deaths at an all-time high.<sup>3</sup> There are three medications approved to treat OUD (MOUD)—buprenorphine, methadone, and naltrexone.<sup>4</sup> Opioid agonist medications (buprenorphine and methadone) reduce overdose risk,<sup>7</sup> and are considered first-line treatment for OUD.<sup>5,6</sup> Despite the effectiveness of these potentially life-saving medications, most people with OUD do not receive them.<sup>1</sup> Increasing MOUD initiation and retention is therefore an important strategy to combat the overdose crisis.

It is common for people with OUD to use other non-opioid substances and to have other co-occurring substance use disorders (SUDs).<sup>10,11,39</sup> In the Veterans Health Administration (VA) over half of patients with OUD have at least one other SUD,<sup>12</sup> which may negatively impact receipt of and retention in OUD care. A national VA study found that compared to patients who had OUD alone, those with one or more non-opioid SUDs had lower odds of receiving both methadone and buprenorphine.<sup>12</sup> Clinical guidelines state that use of other substances should not prevent MOUD provision,<sup>18</sup> therefore lower receipt of MOUD among patients with co-occurring SUDs is a problem that needs to be addressed.

It is important to understand relationships between distinct types of co-occurring SUDs and MOUD receipt, as this information can inform more targeted efforts to increase MOUD receipt among people with co-occurring SUDs (e.g., provider training/education, addressing

patient barriers related to specific types of co-occurring SUDs). Associations between distinct co-occurring SUDs and MOUD receipt likely vary across different clinical settings, depending on the patient population, provider practices, and available resources. This question is particularly important to understand in the context of the VA healthcare system, as it is the nation's largest OUD treatment provider,<sup>35</sup> most VA patients with OUD have co-occurring SUDs,<sup>12,13</sup> and expanding access to MOUD is a major VA priority.<sup>36</sup> Prior studies reporting associations between distinct co-occurring SUDs and receipt of or retention in MOUD treatment among VA patients have reported inconsistent findings; these studies have either been conducted among restricted groups of patients (e.g., those with certain medical conditions) or lacked adjustment for factors hypothesized to confound these associations.<sup>23-25,40-44</sup> Therefore, we examined associations between distinct types of co-occurring SUDs and either initiation or continuation of MOUD among outpatients with OUD in the national VA healthcare system.

## **METHODS**

### **Data source and study sample**

This study is a secondary analysis of electronic health record (EHR) data extracted for a prior study focused on alcohol use.<sup>45</sup> Data were extracted from the Corporate Data Warehouse (CDW), a repository of national VA EHR data, for outpatients with a documented alcohol screen (administered annually to >90% of outpatients in the VA).<sup>46</sup> Alcohol screens are administered at routine healthcare visits, and the visit date was considered the index date for defining study measures. The sample for this study included all outpatients within each VA facility with a screen between 8/1/2016-7/31/2017 who had an OUD diagnosis documented in the prior year (International Classification of Diseases, 10<sup>th</sup> Revision, Clinical Modification and International

Classification of Diseases, 10<sup>th</sup> Revision, Clinical Modification [ICD] codes for opioid “abuse” or “dependence,” excluding in remission). This study was approved by institutional review boards at the University of Washington and VA Puget Sound; approval included waivers of Health Insurance Portability and Accountability Act (HIPAA) authorization and consent.

## **Measures**

### ***Independent variables of interest***

Co-occurring SUDs were measured as the presence of  $\geq 1$  ICD code for “abuse” or “dependence” (excluding in remission) documented in the year prior to the index date; these included *alcohol use disorder*, *cocaine use disorder*, *amphetamine/other stimulant use disorder*, *cannabis use disorder*, *sedative use disorder*, and *hallucinogen use disorder*. Measure definitions that include diagnostic codes or clinic visit codes are included in Appendix 2A. We secondarily examined *past-year heavy alcohol use* (defined as a score of  $\geq 8$  on the Alcohol Use Disorders Identification Test Consumption screen (AUDIT-C), based on VA clinical guidelines<sup>5</sup>) as the independent variable of interest; other drug use is not systematically screened for in the VA and therefore cannot be obtained from CDW.

### ***Outcome variables***

The primary outcome of interest was *receipt of any MOUD* in the year following the index date, defined as having filled  $\geq 1$  prescription for oral (sublingual/buccal) formulations of buprenorphine,  $\geq 1$  visit to a VA Opioid Treatment Program (OTP) which indicates receipt of methadone, and/or  $\geq 1$  administration of injectable naltrexone with an OUD diagnosis in the year prior to administration.<sup>12,47</sup> While methadone is always administered in an OTP, buprenorphine and injectable naltrexone could have been prescribed across multiple settings (e.g., SUD specialty care, primary care). We did not include the oral formulation of naltrexone as it is not

recommended for OUD in clinical guidelines.<sup>5</sup> We secondarily examined receipt of *buprenorphine*, *methadone* and *injectable naltrexone* separately in the year following the index date to determine whether associations varied across different types of medication.

### ***Covariates***

Covariates included patient characteristics that were considered potential confounders based on previously documented associations with both SUDs and MOUD receipt.<sup>23-25,40-44,47,48</sup> *Age*, *sex*, *race*, *ethnicity*, *marital status*, *VA eligibility status*, *rurality* of patient residence (based on definitions used by the VA's Office of Rural Health<sup>49</sup>), and *U.S. Census region* of VA facility were measured based on documentation in the EHR at the time of the index date. VA eligibility status was considered a proxy for socioeconomic status,<sup>50</sup> and race and ethnicity were considered proxies for exposure to racism. *Homelessness/housing instability* was defined as having  $\geq 1$  clinic visit code, ICD code, or screening documentation from an electronic clinical reminder indicating homelessness or other housing instability in the two years prior to the index date.<sup>51</sup> *Any mental health condition* (depression, post-traumatic stress disorder, anxiety, other mood disorders, bipolar disorder, psychoses, and/or schizophrenia) and *diagnoses included in the Charlson comorbidity index* (adjusted for separately as binary variables rather than a continuous weighted score<sup>52</sup>) were defined as having  $\geq 1$  relevant ICD code in the year prior to the index date. *Hepatitis C* was defined as having  $\geq 1$  ICD code in the two years prior to the index date, and *HIV* was defined as having  $\geq 1$  inpatient or  $\geq 2$  outpatient ICD codes in the two years prior to the index date.<sup>53</sup>

### ***Analyses***

All analyses were conducted in two mutually exclusive subsamples: 1) those with no MOUD receipt in the year prior to the index date to assess MOUD initiation (“initiation

subsample”); and 2) those with MOUD receipt in the year prior to the index date to assess MOUD continuation (“continuation subsample”). When examining continuation of secondary outcomes, the subsample was defined based on the specific medication being examined (i.e., received buprenorphine in the year prior to the index date, received methadone in the year prior to the index date, or received injectable naltrexone in the year prior to the index date).

Sociodemographic and clinical characteristics, co-occurring SUDs, and MOUD outcomes were described within each subsample. Poisson regression models were fit to estimate the incidence rate ratio (relative rate) of outcomes among patients with each distinct co-occurring SUD relative to those without. As outcomes were not expected to be rare and therefore odds ratios not likely to accurately reflect relative risk, Poisson regression was used rather than logistic regression to estimate relative risk.<sup>54</sup> Standard errors accounted for clustering of patients within facilities and were calculated using the robust sandwich estimator to correct for misspecification of the Poisson model variance structure.<sup>54</sup> To examine the magnitude of differences, we calculated the marginal predicted prevalence of outcomes among patients with and without each co-occurring SUD.

Models were unadjusted, then adjusted for demographic characteristics (age, sex, race, ethnicity, marital status, rurality, region), then additionally adjusted for socioeconomic factors and clinical conditions (VA eligibility status, homelessness/housing instability, mental health condition, physical comorbidities); the final adjusted model was considered the primary model. Because socioeconomic factors and clinical conditions might impact risk of SUDs and/or be impacted by SUDs, we wanted to observe whether and how associations changed when adding these covariates. Hallucinogen use disorder was not examined as a predictor of interest in regression models due to small cell counts resulting in unstable coefficient estimates but was

included as a covariate in adjusted models. To account for multiple comparisons, the Holm-Bonferroni sequential correction was applied to statistical tests of primary models, separately for each outcome within each of the two subsamples.<sup>55</sup> Secondary analyses examined associations between past-year heavy alcohol use and initiation and continuation of any MOUD in primary models (adjusted for all covariates), stratified by alcohol use disorder to examine whether these associations differed among patients with and without diagnosed alcohol use disorder. Analyses were conducted in Stata version 17 software.<sup>56</sup>

## **RESULTS**

### **Sample descriptions**

During 8/1/2016-7/31/2017, 35,844 outpatients had a documented OUD diagnosis in the year prior to their index visit; 23,990 had no MOUD in the prior year (initiation subsample) and 11,854 had any MOUD receipt in the prior year (continuation subsample). Patient characteristics in the initiation and continuation subsamples are described in Table 2.1. In both subsamples, mean age was about 50 years, and most patients were male, White, non-Hispanic, and not married. Compared to the initiation subsample, the continuation subsample had a higher proportion of patients in the Northeast and a lower proportion of patients in the South. The continuation subsample also had higher proportions of patients who were living in urban areas, were non-service connected, and who had homelessness/housing instability, a mental health condition, and hepatitis C. HIV and other physical comorbidities were similar across the two subsamples.

In both the initiation and continuation subsamples, just under half of patients (about 47%) had at least one co-occurring SUD (somewhat lower than prior reported prevalence,<sup>12</sup>

likely because our definition excluded codes for in remission and unspecified use; Table 2.1). The most prevalent co-occurring SUD was alcohol use disorder (32% and 29% in initiation and continuation subsamples, respectively), followed by cocaine use disorder (18% and 19%), cannabis use disorder (17% and 16%), amphetamine/other stimulant use disorder (9% and 8%), sedative use disorder (8% and 9%), and hallucinogen use disorder (0.5% and 0.3%).

### **Associations between co-occurring SUDs and initiation of MOUD**

Among the 23,990 patients in the initiation subsample, 12% received any MOUD in the following year (9% received buprenorphine, 4% received methadone, and 1% received injectable naltrexone; Table 2.2).

Associations between co-occurring SUDs and initiation of any MOUD in the following year are presented in Table 2.3. Only alcohol use disorder (adjusted incidence rate ratio [aIRR] 0.80, 95% confidence interval [CI] 0.72-0.90) and cannabis use disorder (aIRR 0.78, 95% CI 0.70-0.87) were significantly negatively associated with initiation of any MOUD after applying the Holm-Bonferroni sequential correction to statistical tests of primary models. Estimates from models that adjusted only for demographic characteristics (Adjusted Model 1) were very similar to those from fully adjusted models (Adjusted Model 2; primary model).

In secondary analyses examining initiation of specific types of MOUD (Appendix 2B, Table 2B.1), alcohol use disorder and cannabis use disorder were significantly negatively associated with initiation of buprenorphine. There were no significant associations for methadone or injectable naltrexone initiation after applying the Holm-Bonferroni sequential correction to primary model statistical tests for each outcome.

In secondary analyses examining heavy alcohol use (Appendix 2B, Table 2B.3), heavy alcohol use was positively associated with initiation of any MOUD among patients with

diagnosed alcohol use disorder (aIRR 1.25, 95% CI 1.07-1.46) and without diagnosed alcohol use disorder (aIRR 1.48, 95% CI 1.21-1.82). The association between heavy alcohol use and MOUD initiation was not modified by diagnosed alcohol use disorder ( $p=0.207$  for interaction term).

### **Associations between co-occurring SUDs and continuation of MOUD**

Among the 11,854 patients in the continuation sample, 83% received any MOUD in the following year (Table 2.2). Among 7,756 who received buprenorphine in the prior year, 83% received buprenorphine in the following year. Among 6,050 who received methadone in the prior year, 75% received methadone in the following year. Among 368 who received injectable naltrexone in the prior year, 41% received injectable naltrexone in the following year.

Associations between co-occurring SUDs and continuation of any MOUD in the following year are presented in Table 2.4. After applying the Holm-Bonferroni sequential correction to statistical tests of primary models, having  $\geq 1$  co-occurring SUD (aIRR 0.92, 95% CI 0.89-0.95), alcohol use disorder (aIRR 0.94, 95% CI 0.91-0.97), amphetamine/other stimulant use disorder (aIRR 0.94, 95% CI 0.90-0.99), and cannabis use disorder (aIRR 0.95, 95% CI 0.93-0.98) were significantly negatively associated with continuation of any MOUD. Estimates from models that adjusted only for demographic characteristics (Adjusted Model 1) were very similar to those from fully adjusted models (Adjusted Model 2; primary model).

In secondary analyses examining continuation of specific types of MOUD (Appendix 2B, Table 2B.2), after applying the Holm-Bonferroni sequential correction to primary model statistical tests for each outcome, having  $\geq 1$  co-occurring SUD, amphetamine/other stimulant use disorder and sedative use disorder were significantly negatively associated with continuing buprenorphine, while having  $\geq 1$  co-occurring SUD and alcohol use disorder were significantly

negatively associated with continuing methadone and there were no significant associations for continuing injectable naltrexone.

In secondary analyses examining heavy alcohol use (Appendix 2B, Table 2B.3), heavy alcohol use was negatively associated with continuation of any MOUD among patients with diagnosed alcohol use disorder (aIRR 0.88, 95% CI 0.81-0.94) and without diagnosed alcohol use disorder (aIRR 0.79, 95% CI 0.65-0.95). The association between heavy alcohol use and MOUD continuation was not modified by diagnosed alcohol use disorder ( $p=0.294$  for interaction term).

## **DISCUSSION**

In this national study of VA outpatients with OUD, certain co-occurring SUDs were negatively associated with initiation and/or continuation of MOUD. Alcohol use disorder and cannabis use disorder were negatively associated with initiating any MOUD, and specifically with initiating buprenorphine in secondary analyses examining separate types of MOUD. Among those with prior year MOUD receipt, alcohol use disorder, amphetamine/other stimulant use disorder, and cannabis use disorder were negatively associated with continuing any MOUD. In secondary analyses amphetamine/other stimulant use disorder and sedative use disorder were negatively associated with buprenorphine continuation, while alcohol use disorder was negatively associated with methadone continuation. These findings can inform future research to better understand barriers to MOUD among patients with co-occurring SUDs, as well as efforts to increase receipt of MOUD among these patients.

Mechanisms driving negative associations between specific co-occurring SUDs and MOUD initiation or continuation in the VA are unclear, and there are likely numerous

contributing factors operating across multiple levels (e.g., clinic, provider, and patient). It is possible that some providers are hesitant to initiate or continue opioid agonist medication for patients using alcohol or sedatives as these may increase risk of respiratory depression.<sup>18</sup> For example, results from a survey of U.S. buprenorphine providers found that they were less likely to prescribe for patients with alcohol or sedative use disorders.<sup>20</sup> Clinical guidelines have been updated to explicitly recommend against withholding or suspending opioid agonist treatment for these patients, however guidelines still highlight potential risks and suggest they may need more frequent monitoring or a higher level of care (e.g., an OTP vs. primary care).<sup>6,18</sup> While these measures could increase safety, they may also increase barriers to initiating or continuing MOUD. VA OTPs are situated within SUD specialty clinics, and VA providers have described barriers to accessing these care settings faced by patients including distance to treatment, long wait times, strict eligibility rules, and addiction-related stigma.<sup>26</sup> Some providers described “inflexibility” in addiction treatment program policies at their facility,<sup>26</sup> and some clinics may require or strongly promote abstinence from other substances to receive MOUD which some patients may be unable or unwilling to do. For example, VA patients who are using cannabis to self-manage symptoms of other conditions such as chronic pain or PTSD may be less willing to stop cannabis use.<sup>57</sup>

It is likely that patients’ experiences outside of the healthcare system also impact associations between co-occurring SUDs and MOUD initiation and continuation. Patients with multiple SUDs may have higher severity SUD, and are more likely to experience problems that may increase life instability (e.g., housing instability, unemployment, legal system involvement, physical and mental health conditions).<sup>13</sup> This may make it difficult for them to engage in MOUD care and may compound other barriers, such as being required to receive MOUD in an

OTP or to engage in more frequent monitoring. Methamphetamine use in particular may be linked to serious health and social problems for some patients.<sup>58</sup> Additionally, people who use methamphetamine and opioids have reported experiencing a balancing effect that helps them function more effectively,<sup>39</sup> and a desire for this effect might contribute to buprenorphine discontinuation and a return to full agonist opioid use for some patients who use amphetamines. Further research incorporating the perspectives of VA providers and VA patients is needed to understand barriers to MOUD for patients with co-occurring SUDs, particularly alcohol, cannabis, amphetamine, and/or sedative use disorder.

It was surprising that, in secondary analyses, past-year heavy drinking documented in an AUDIT-C screen was positively associated with initiating any MOUD but negatively associated with continuation, while diagnosed alcohol use disorder was negatively associated with both initiation and continuation. It is possible that a high alcohol screening score could prompt increased linkage to SUD care settings, though research conducted in the VA suggests that brief intervention connected to positive screening for unhealthy alcohol use does not increase linkage to SUD specialty treatment for alcohol use disorder.<sup>59</sup> It is also possible that patients with OUD who are drinking heavily may be experiencing more severe impacts of OUD, such as more frequent overdose events.<sup>60</sup> This might make them more interested in initiating OUD treatment, though continued heavy drinking may negatively impact treatment retention. More research is needed to understand potential mechanisms underlying these associations.

Efforts are needed to improve MOUD initiation and continuation for VA patients with co-occurring SUDs, particularly alcohol, cannabis, amphetamine/other stimulant, and sedative use disorders. These efforts should be informed by further research with providers and patients aiming to better understand specific barriers. MOUD providers, especially those providing

buprenorphine outside of specialty SUD settings, may need additional clinical guidance and resources related to caring for patients with OUD who use other substances. These resources could more specifically address situations in which patients are unable or unwilling to receive MOUD in a higher-level care setting—for example, strategies to increase the safety of providing buprenorphine to patients using central nervous system depressants and to address other non-opioid substance use in a primary care setting. Efforts could also aim to lower barriers to accessing specialty SUD clinic services, such as improved linkage from other clinical settings and possibly revising clinic policies related to MOUD provision for patients with other substance use. Future research should examine whether associations between specific co-occurring SUDs and MOUD receipt vary across different VA facilities, which may have different clinic policies and provider practices, as well as different clinic settings (e.g., SUD clinics vs. general healthcare settings). Additionally, targeted engagement efforts or additional services (e.g., housing, employment) for patients with OUD and co-occurring SUDs may help address other barriers related to life instability that may be more common among these patients.

This study has limitations. Co-occurring SUDs may not be diagnosed or documented in the EHR, and thus may be undermeasured by ICD codes. These data do not capture MOUD that may have been received outside of the VA. Additionally, these data do not allow examination of the impact of co-occurring SUDs on precise length in MOUD treatment—future studies examining MOUD retention in the VA using time-to-discontinuation data should examine the impact of distinct co-occurring SUDs with appropriate adjustment for confounders. Further, we defined continuation as any MOUD among people who had prior-year MOUD receipt; for some patients this could reflect a distinct MOUD treatment episode rather than continuation of prior treatment. We may have had limited statistical power to detect associations for SUDs that are

less prevalent (particularly hallucinogen use disorder). Although over 90% of VA outpatients receive annual screening for alcohol use,<sup>46</sup> it is possible that patients who did not receive screening and thus are not present in this sample differed from those who did receive screening. These findings may have limited generalizability outside of the VA system, which serves a unique patient population and may differ from other healthcare settings due to its integrated structure and efforts targeting increased provision of MOUD.

## **CONCLUSIONS**

In this study of national VA outpatients with OUD, those with certain co-occurring SUDs were less likely to initiate or continue MOUD in the following year. Specifically, alcohol use disorder and cannabis use disorder were negatively associated with initiation of any MOUD, while alcohol use disorder, amphetamine/other stimulant use disorder, and cannabis use disorder were negatively associated with continuation of any MOUD. Further research with providers and patients is needed to identify barriers to MOUD initiation and continuation related to specific co-occurring SUDs. This information can help inform the development of effective policies and interventions to increase receipt of potentially life-saving treatment among patients with co-occurring SUDs, who make up a large proportion of patients with OUD.

**Table 2.1. Sociodemographic and clinical characteristics among national Veterans Health Administration outpatients with OUD 8/1/16-7/31/17, with and without any MOUD receipt in the past year**

	No MOUD receipt in past year		Any MOUD receipt in past year	
	(Initiation subsample)		(Continuation subsample)	
	(N=23,990)		(N=11,854)	
	N	(%)	N	(%)
Age (mean, SD)	52.7	(14.4)	50.0	(14.1)
Female	1,801	(7.5)	800	(6.8)
Race				
American Indian/Alaska Native	226	(0.9)	88	(0.7)
Asian/Pacific Islander	247	(1.0)	88	(0.7)
Black/African American	4,386	(18.3)	2,353	(19.9)
White	17,987	(75.0)	8,822	(74.4)
Multiple races	243	(1.0)	96	(0.8)
Unknown	901	(3.8)	407	(3.4)
Hispanic/Latino	1,218	(5.1)	740	(6.2)
Marital status				
Divorced/separated	9,942	(41.4)	4,987	(42.1)
Married	7,852	(32.7)	3,298	(27.8)
Never married/single	5,290	(22.1)	3,174	(26.8)
Widowed	835	(3.5)	362	(3.1)
Unknown	71	(0.3)	33	(0.3)
Rurality				
Rural	7,119	(29.7)	2,499	(21.1)
Urban	16,788	(70.0)	9,336	(78.8)
Unknown	83	(0.4)	19	(0.2)
U.S. Census region				
Midwest	4,959	(20.7)	2,386	(20.1)
Northeast	4,615	(19.2)	3,335	(28.1)
South	9,325	(38.9)	3,680	(31.0)
West	4,993	(20.8)	2,415	(20.4)
Other	98	(0.4)	38	(0.3)
VA eligibility status <sup>b</sup>				
Full VA coverage	10,472	(43.7)	4,771	(40.3)
Service connection <50%	4,417	(18.4)	2,294	(19.4)
Non-service connected	9,078	(37.8)	4,777	(40.3)
Other/unknown	23	(0.1)	12	(0.1)
Homelessness/housing instability	8,044	(33.5)	4,619	(39.0)
Mental health condition <sup>a</sup>	17,175	(71.6)	8,965	(75.6)
Charlson score <sup>b</sup> (mean, SD)	1.0	(1.7)	0.8	(1.4)
HIV	304	(1.3)	170	(1.4)
Hepatitis C	4,868	(20.3)	3,711	(31.3)
≥1 non-opioid SUD	11,264	(47.0)	5,650	(47.7)
Alcohol use disorder	7,680	(32.0)	3,475	(29.3)

Cocaine use disorder	4,195	(17.5)	2,220	(18.7)
Amphetamine/other stimulant use disorder	2,128	(8.9)	936	(7.9)
Cannabis use disorder	4,135	(17.2)	1,943	(16.4)
Sedative use disorder	1,908	(8.0)	1,075	(9.1)
Hallucinogen use disorder	108	(0.5)	34	(0.3)

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MOUD = medications for opioid use disorder; OUD = opioid use disorder; SD = standard deviation; SUD = substance use disorder; VA = Veterans Health Administration

<sup>a</sup>Includes depression, post-traumatic stress disorder, anxiety, other mood disorders, bipolar disorder, psychoses, and/or schizophrenia

<sup>b</sup>Not including HIV

**Table 2.2. Receipt of MOUD in the following year among national Veterans Health Administration outpatients with OUD 8/1/16-7/31/17, with and without any MOUD receipt in the past year**

Outcome (in the following year)	No MOUD receipt in past year		MOUD receipt in past year	
	(Initiation subsample)		(Continuation subsample)	
	(N=23,990)		(N=11,854 for any MOUD)	
	N	(%)	N	(%)
Any MOUD	2,871	(12.0)	9,860	(83.2)
Buprenorphine	2,088	(8.7)	6,401	(82.5) <sup>a</sup>
Methadone	1,001	(4.2)	4,555	(75.3) <sup>a</sup>
Injectable naltrexone	318	(1.3)	149	(40.5) <sup>a</sup>

MOUD = medications for opioid use disorder; OUD = opioid use disorder

<sup>a</sup>Percentage out of N who received specific type of MOUD in the past year (N=7,756 for buprenorphine; N=6,050 for methadone; N=368 for injectable naltrexone)

**Table 2.3. Initiation of any MOUD in the following year for patients with past-year co-occurring SUDs compared to those without among national Veterans Health Administration outpatients with OUD and no MOUD receipt in the past year 8/1/16-7/31/17 (N=23,990)**

Predictor of interest	Among those without predictor of interest		Among those with predictor of interest		IRR for those with predictor of interest relative to those without		
	%	(95% CI)	%	(95% CI)	IRR	(95% CI)	p-value
<b>≥1 non-opioid SUD</b>							
Unadjusted Model	10.8	(9.4-12.1)	13.3	(11.9-14.8)	1.24	(1.11-1.39)	<0.001
Adjusted Model 1 <sup>a</sup>	12.4	(11.0-13.7)	11.6	(10.4-12.9)	0.94	(0.85-1.04)	0.239
Adjusted Model 2 <sup>b</sup> (primary)	12.4	(11.1-13.6)	11.6	(10.4-12.8)	0.94	(0.86-1.02)	0.155
<b>Alcohol use disorder</b>							
Unadjusted Model	12.1	(10.7-13.6)	11.6	(10.2-13.0)	0.95	(0.85-1.07)	0.426
Adjusted Model 1 <sup>c</sup>	12.8	(11.6-14.1)	10.4	(9.1-11.7)	0.81	(0.73-0.90)	<0.001
Adjusted Model 2 <sup>b</sup> (primary)	12.9	(11.7-14.1)	10.3	(9.1-11.6)	<b>0.80</b>	<b>(0.72-0.90)</b>	<b>&lt;0.001*</b>
<b>Cocaine use disorder</b>							
Unadjusted Model	11.5	(10.3-12.7)	14.1	(11.9-16.4)	1.23	(1.06-1.43)	0.008
Adjusted Model 1 <sup>c</sup>	11.7	(10.5-12.8)	13.3	(11.4-15.1)	1.14	(1.00-1.29)	0.053
Adjusted Model 2 <sup>b</sup> (primary)	11.7	(10.6-12.8)	13.0	(11.2-14.7)	1.11	(0.98-1.26)	0.119
<b>Amphetamine/other stimulant use disorder</b>							
Unadjusted Model	11.6	(10.4-12.9)	15.5	(13.2-17.8)	1.33	(1.16-1.54)	<0.001
Adjusted Model 1 <sup>c</sup>	11.8	(10.7-12.9)	13.3	(11.4-15.2)	1.12	(1.00-1.26)	0.054
Adjusted Model 2 <sup>b</sup> (primary)	11.9	(10.8-13.0)	12.8	(11.0-14.6)	1.08	(0.96-1.21)	0.210
<b>Cannabis use disorder</b>							
Unadjusted Model	12.0	(10.7-13.3)	11.9	(10.4-13.3)	0.99	(0.88-1.11)	0.845
Adjusted Model 1 <sup>c</sup>	12.6	(11.3-13.9)	9.6	(8.6-10.7)	0.77	(0.69-0.86)	<0.001
Adjusted Model 2 <sup>b</sup> (primary)	12.5	(11.3-13.8)	9.8	(8.7-10.9)	<b>0.78</b>	<b>(0.70-0.87)</b>	<b>&lt;0.001*</b>
<b>Sedative use disorder</b>							
Unadjusted Model	11.8	(10.6-13.0)	14.2	(11.6-16.7)	1.20	(1.04-1.39)	0.013
Adjusted Model 1 <sup>c</sup>	11.9	(10.8-13.0)	12.9	(10.8-15.1)	1.09	(0.96-1.23)	0.182
Adjusted Model 2 <sup>b</sup> (primary)	11.9	(10.8-12.9)	13.2	(11.0-15.4)	1.11	(0.98-1.26)	0.093

IRR = incidence rate ratio; MOUD = medications for opioid use disorder; OUD = opioid use disorder

<sup>a</sup>Adjusted for age, sex, race, ethnicity, marital status, rurality, U.S. Census region

<sup>b</sup>Adjusted for all covariates in Model 1, plus VA eligibility status, homelessness/housing instability, mental health condition, cancer, cerebrovascular disease, chronic obstructive pulmonary disease, congestive heart failure, dementia, diabetes, diabetes with complications, metastatic solid tumor, mild liver disease, moderate/severe liver disease, myocardial infarction, paralysis, peptic ulcer, peripheral vascular disease, renal disease, rheumatic disease, HIV, hepatitis C

<sup>c</sup>Adjusted for other co-occurring substance use disorders (including hallucinogen use disorder), age, sex, race, ethnicity, marital status, rurality, U.S. Census region

\*significant after Holm-Bonferroni sequential correction applied to all primary model statistical tests in the table

**Table 2.4. Continuation of any MOUD in the following year for patients with past-year co-occurring SUDs compared to those without among national Veterans Health Administration outpatients with OUD and any MOUD receipt in the past year 8/1/16-7/31/17 (N=11,854)**

Predictor of interest	Among those without predictor of interest		Among those with predictor of interest		IRR for those with predictor of interest relative to those without		
	%	(95% CI)	%	(95% CI)	IRR	(95% CI)	p-value
<b>≥1 non-opioid SUD</b>							
Unadjusted Model	86.9	(83.1-90.6)	79.1	(77.0-81.2)	0.91	(0.87-0.95)	<0.001
Adjusted Model 1 <sup>a</sup>	87.0	(84.0-90.0)	79.0	(76.8-81.2)	0.91	(0.88-0.94)	<0.001
Adjusted Model 2 <sup>b</sup> (primary)	86.5	(83.7-89.2)	79.5	(77.4-81.6)	<b>0.92</b>	<b>(0.89-0.95)</b>	<b>&lt;0.001*</b>
<b>Alcohol use disorder</b>							
Unadjusted Model	85.4	(82.5-88.4)	77.7	(75.5-79.9)	0.91	(0.88-0.95)	<0.001
Adjusted Model 1 <sup>c</sup>	84.8	(82.2-87.4)	79.1	(76.8-81.4)	0.93	(0.90-0.96)	<0.001
Adjusted Model 2 <sup>b</sup> (primary)	84.6	(82.2-87.1)	79.5	(77.3-81.8)	<b>0.94</b>	<b>(0.91-0.97)</b>	<b>&lt;0.001*</b>
<b>Cocaine use disorder</b>							
Unadjusted Model	84.3	(81.6-86.9)	78.4	(75.3-81.5)	0.93	(0.89-0.97)	0.001
Adjusted Model 1 <sup>c</sup>	83.8	(81.6-85.9)	80.5	(77.2-83.7)	0.96	(0.93-0.99)	0.010
Adjusted Model 2 <sup>b</sup> (primary)	83.7	(81.6-85.7)	80.9	(77.7-84.2)	0.97	(0.94-1.00)	0.034
<b>Amphetamine/other stimulant use disorder</b>							
Unadjusted Model	84.0	(81.6-86.4)	73.9	(70.4-77.5)	0.88	(0.84-0.92)	<0.001
Adjusted Model 1 <sup>c</sup>	83.6	(81.3-85.9)	78.2	(74.7-81.7)	0.94	(0.89-0.98)	0.005
Adjusted Model 2 <sup>b</sup> (primary)	83.5	(81.3-85.7)	78.7	(75.3-82.2)	<b>0.94</b>	<b>(0.90-0.99)</b>	<b>0.010*</b>
<b>Cannabis use disorder</b>							
Unadjusted Model	84.4	(81.8-87.0)	77.0	(74.6-79.5)	0.91	(0.88-0.95)	<0.001
Adjusted Model 1 <sup>c</sup>	83.8	(81.6-86.1)	79.7	(77.0-82.3)	0.95	(0.92-0.98)	<0.001
Adjusted Model 2 <sup>b</sup> (primary)	83.8	(81.6-86.0)	79.8	(77.2-82.4)	<b>0.95</b>	<b>(0.93-0.98)</b>	<b>0.001*</b>
<b>Sedative use disorder</b>							
Unadjusted Model	83.7	(81.3-86.1)	78.2	(74.1-82.4)	0.93	(0.89-0.98)	0.011
Adjusted Model 1 <sup>c</sup>	83.4	(81.2-85.6)	80.9	(76.6-85.1)	0.97	(0.93-1.01)	0.177
Adjusted Model 2 <sup>b</sup> (primary)	83.3	(81.3-85.4)	81.4	(77.2-85.6)	0.98	(0.93-1.02)	0.302

IRR = incidence rate ratio; MOUD = medications for opioid use disorder; OUD = opioid use disorder

<sup>a</sup>Adjusted for age, sex, race, ethnicity, marital status, rurality, U.S. Census region

<sup>b</sup>Adjusted for all covariates in Model 1, plus VA eligibility status, homelessness/housing instability, mental health condition, cancer, cerebrovascular disease, chronic obstructive pulmonary disease, congestive heart failure, dementia, diabetes, diabetes with complications, metastatic solid tumor, mild liver disease, moderate/severe liver disease, myocardial infarction, paralysis, peptic ulcer, peripheral vascular disease, renal disease, rheumatic disease, HIV, hepatitis C

<sup>c</sup>Adjusted for other co-occurring substance use disorders (including hallucinogen use disorder), age, sex, race, ethnicity, marital status, rurality, U.S. Census region

\*significant after Holm-Bonferroni sequential correction applied to all primary model statistical tests in the table

## Appendix 2A. Measure definitions

**Table 2A.1. Definitions for measures using diagnostic codes and/or clinic visit codes**

Measure	Definition
Opioid use disorder	<p><u>ICD-9-CM codes:</u> 304.00-304.02, 304.70-304.72, 305.50-305.52</p> <p><u>ICD-10-CM codes:</u> F11.1* excluding F11.11 F11.2* excluding F11.21</p>
Receipt of methadone	VHA stop code 523 (VA opioid agonist treatment clinic)
Homelessness/housing instability	<p><u>ICD-9-CM codes:</u> V60.0; V60.1</p> <p><u>ICD-10-CM codes:</u> Z59.0, Z59.1, Z59.3, Z59.8, Z59.9</p> <p><u>VHA stop codes:</u> 504, 507, 508, 511, 522, 528, 529, 530, 555, 556, 590</p> <p><u>Inpatient treatment specialty codes:</u> 28, 37</p> <p><u>Health factors data (text notes generated by provider documentation):</u> “Housing, level 3 (major concerns)”, “Housing, level 4 (crisis)”, “Lives in shelter”, “Presenting issue – housing”</p>
Mental health condition	<p><u>ICD-9-CM codes:</u> 296.2-296.3*, 296.82, 311, 309.81, 300.0, 300.01, 300.02, 300.09, 300.20, 300.21, 300.23, 300.29, 300.3, 293.83, 296.9*, 300.4, 301.12, 309.0, 309.1, 296.0-296.1*, 296.4-296.8*, 297-298*, 295.0-295.4*, 295.6-295.9*</p> <p><u>ICD-10-CM codes:</u> F32.0-F32.5, F32.9, F33.0-F33.4*, F33.9, F06.31-F06.32, F32.8*, F33.8, F43.1*, F06.4, F40*, F41.0-F41.9, F42*, F45.20-F45.21, F45.29, F93.0, F06.30, F39, F34.1, F34.8*, F43.21, F30*, F31*, F34.0, F06.0, F06.2, F22-F24, F28-F29, F20*, F21, F25*</p>
Alcohol use disorder	<p><u>ICD-9-CM codes:</u> 303.90-303.92, 305.00-305.02</p> <p><u>ICD-10-CM codes:</u> F10.1* excluding F10.11 F10.2* excluding F10.21</p>
Cocaine use disorder	<p><u>ICD-9-CM codes:</u> 304.20-304.22, 305.60-305.62</p> <p><u>ICD-10-CM codes:</u> F14.1* excluding F14.11 F14.2* excluding F14.21</p>
Amphetamine/other stimulant use disorder	<p><u>ICD-9-CM codes:</u> 304.40-304.42, 305.70-305.72</p> <p><u>ICD-10-CM codes:</u> F15.1* excluding F15.11 F15.2* excluding F15.21</p>
Cannabis use disorder	<p><u>ICD-9-CM codes:</u> 304.30-304.32, 305.20-305.22</p> <p><u>ICD-10-CM codes:</u> F12.1* excluding F12.11 F12.2* excluding F12.21</p>
Sedative use disorder	<p><u>ICD-9-CM codes:</u> 304.10-304.12, 305.40-304.42</p> <p><u>ICD-10-CM codes:</u> F13.1* excluding F13.11 F13.2* excluding F13.21</p>
Hallucinogen use disorder	<u>ICD-9-CM codes:</u>

	304.50-304.52 305.30-305.32 <u>ICD-10-CM codes:</u> F16.1* excluding F16.11 F16.2* excluding F16.21
Coronary Heart Disease/Heart Failure	<u>ICD-9-CM codes:</u> 428* <u>ICD-10-CM codes:</u> I50.1-I50.4*, I50.9
Chronic Pulmonary Disease	<u>ICD-9-CM codes:</u> 490-496*, 500-505*, 506.4 <u>ICD-10-CM codes:</u> J40-J47*, J60-J67*, J68.4
Cerebrovascular Disease	<u>ICD-9-CM codes:</u> 430-438* <u>ICD-10-CM codes:</u> G45-G46*, I60-I66*, I67.0-I67.848*, I67.89-I67.9, I68* I69*
Dementia	<u>ICD-9-CM codes:</u> 290* <u>ICD-10-CM codes:</u> F01-F03*, F05
Diabetes	<u>ICD-9-CM codes:</u> 250.0-250.3*, 250.7* <u>ICD-10-CM codes:</u> E10.1*, E10.5*, E10.641, E10.65, E10.69, E10.9, E11.0* E11.5*, E11.641, E11.65, E11.69, E11.9, E13.0-E13.1* E13.5*, E13.641, E13.9
Diabetic Complications	<u>ICD-9-CM codes:</u> 250.4-250.6* <u>ICD-10-CM codes:</u> E10.2-E10.4*, E10.61*, E11.2-E11.4*, E11.61*, E13.2-E13.4*, E13.61*
Cancer	<u>ICD-9-CM codes:</u> 140-172*, 174-195*, 200-207*, 208.00-208.91 <u>ICD-10-CM codes:</u> C00-C43*, C4A*, C45.0-C45.7, C46-C75*, C76*, C81-C96*, D03*, D45
Myocardial infarction	<u>ICD-9-CM codes:</u> 410*, 412 <u>ICD-10-CM codes:</u> I21.0-I21.4*, I22*, I25.2
Mild Liver Disease	<u>ICD-9-CM codes:</u> 571.2, 571.4-571.6* <u>ICD-10-CM codes:</u> K70.0-K70.3*, K73-K74*, K75.4
Severe Liver Disease	<u>ICD-9-CM codes:</u> 456.0-456.2*, 572.2-572.8* <u>ICD-10-CM codes:</u> I85*, K70.41, K71.11, K71.2-K71.9*, K72*, K76.6-K76.7
Metastatic Solid Tumor	<u>ICD-9-CM codes:</u> 196-198*, 199.0-199.1 <u>ICD-10-CM codes:</u> C45.9, C7A-C7B*, C77-C80*
Paralysis	<u>ICD-9-CM codes:</u> 342*, 344.1 <u>ICD-10-CM codes:</u> G04.1, G81-G82*
Peptic Ulcer Disease	<u>ICD-9-CM codes:</u> 531-534* <u>ICD-10-CM codes:</u>

	K25-K28*, K56.60*
Peripheral Vascular Disease	<u>ICD-9-CM codes:</u> 440.20-440.24, 440.31-440.32, 440.8-440.9 441*, 443.9, 785.4, V43.4 <u>ICD-10-CM codes:</u> I70-I71*, I73.01-I73.1, I73.9, I79.0, I96, Z95.8-Z95.9*
Renal Disease	<u>ICD-9-CM codes:</u> 582*, 583.0-583.7, 585*, 586, 588* <u>ICD-10-CM codes:</u> N03*, N05.2-N05.5*, N05.9, N06.2-N06.5, N07.2-N07.5, N08, N17.1-N17.2, N18*, N19, N25*
Rheumatic Disease	<u>ICD-9-CM codes:</u> 710.0-710.1, 710.4, 714.0-714.2, 714.81 725 <u>ICD-10-CM codes:</u> M05-M06*, M32, M33.00-M33.02, M33.09, M33.10-M33.12, M33.19, M33.2*, M33.90-M33.92, M33.99 M34*, M35.3
HIV	<u>ICD-9-CM codes:</u> 042, V08 (≥2 outpatient codes or ≥1 inpatient code) <u>ICD-10-CM codes:</u> B20, Z21 (≥2 outpatient codes or ≥1 inpatient code)
Hepatitis C	<u>ICD-9-CM codes:</u> 070.41, 070.44, 070.51, 070.54, 070.70 070.71, V02.62 <u>ICD-10-CM codes:</u> B17.1*, B18.2, B19.2*, Z22.52

ICD-9-CM = International Classification of Diseases, 9th Revision, Clinical Modification; ICD-10-CM = International Classification of Diseases, 10th Revision, Clinical Modification

\*Indicates inclusion of all sub-codes under parent code

Appendix 2B. Results from secondary analyses

Table 2B.1. Initiation of specific types of MOUD in the following year for patients with past-year co-occurring SUDs compared to those without among national Veterans Health Administration outpatients with OUD and no MOUD receipt in the past year 8/1/16-7/31/17 (N=23,990)

Predictor of interest	Among those without predictor of interest		Among those with predictor of interest		IRR for those with predictor of interest relative to those without		
	%	(95% CI)	%	(95% CI)	IRR	(95% CI)	p-value
<b>Outcome: Buprenorphine receipt in the following year</b>							
<b>≥1 non-opioid SUD</b>							
Unadjusted Model	8.1	(7.1-9.2)	9.4	(8.2-10.5)	1.15	(1.02-1.31)	0.024
Adjusted Model 1 <sup>a</sup>	9.2	(8.2-10.2)	8.2	(7.2-9.2)	0.89	(0.80-1.00)	0.048
Adjusted Model 2 <sup>b</sup> (primary)	9.2	(8.2-10.2)	8.2	(7.3-9.2)	0.89	(0.80-0.99)	0.035
<b>Alcohol use disorder</b>							
Unadjusted Model	9.1	(8.0-10.3)	7.8	(6.7-8.9)	0.85	(0.75-0.96)	0.011
Adjusted Model 1 <sup>c</sup>	9.5	(8.5-10.5)	7.2	(6.1-8.2)	0.76	(0.67-0.86)	<0.001
Adjusted Model 2 <sup>b</sup> (primary)	9.5	(8.6-10.5)	7.2	(6.1-8.2)	<b>0.75</b>	<b>(0.66-0.85)</b>	<b>&lt;0.001*</b>
<b>Cocaine use disorder</b>							
Unadjusted Model	8.6	(7.6-9.5)	9.3	(7.5-11.2)	1.09	(0.91-1.30)	0.362
Adjusted Model 1 <sup>c</sup>	8.5	(7.6-9.4)	9.6	(8.1-11.1)	1.13	(0.97-1.31)	0.114
Adjusted Model 2 <sup>b</sup> (primary)	8.5	(7.7-9.4)	9.5	(8.0-10.9)	1.11	(0.95-1.28)	0.181
<b>Amphetamine/other stimulant use disorder</b>							
Unadjusted Model	8.4	(7.4-9.4)	11.5	(9.4-13.5)	1.36	(1.14-1.62)	0.001
Adjusted Model 1 <sup>c</sup>	8.6	(7.8-9.5)	9.5	(7.8-11.1)	1.10	(0.95-1.28)	0.209
Adjusted Model 2 <sup>b</sup> (primary)	8.6	(7.8-9.5)	9.2	(7.6-10.8)	1.07	(0.92-1.23)	0.392
<b>Cannabis use disorder</b>							
Unadjusted Model	8.8	(7.7-9.8)	8.3	(7.2-9.4)	0.94	(0.83-1.07)	0.338
Adjusted Model 1 <sup>c</sup>	9.2	(8.2-10.2)	6.9	(6.1-7.7)	0.75	(0.67-0.85)	<0.001
Adjusted Model 2 <sup>b</sup> (primary)	9.2	(8.2-10.1)	7.0	(6.1-7.8)	<b>0.76</b>	<b>(0.68-0.86)</b>	<b>&lt;0.001*</b>
<b>Sedative use disorder</b>							
Unadjusted Model	8.6	(7.6-9.5)	10.4	(8.4-12.5)	1.22	(1.03-1.44)	0.019
Adjusted Model 1 <sup>c</sup>	8.6	(7.8-9.5)	9.4	(7.8-11.0)	1.08	(0.95-1.24)	0.250
Adjusted Model 2 <sup>b</sup> (primary)	8.6	(7.8-9.5)	9.5	(7.9-11.1)	1.10	(0.96-1.26)	0.158
<b>Outcome: Methadone receipt in the following year</b>							
<b>≥1 non-opioid SUD</b>							
Unadjusted Model	3.7	(2.6-4.9)	4.7	(3.3-6.0)	1.24	(1.04-1.48)	0.015
Adjusted Model 1 <sup>a</sup>	4.3	(3.1-5.6)	4.0	(2.9-5.2)	0.93	(0.78-1.11)	0.426
Adjusted Model 2 <sup>b</sup> (primary)	4.4	(3.1-5.6)	4.0	(2.9-5.1)	0.92	(0.78-1.08)	0.294
<b>Alcohol use disorder</b>							
Unadjusted Model	4.1	(2.9-5.3)	4.3	(3.0-5.6)	1.05	(0.87-1.27)	0.618
Adjusted Model 1 <sup>c</sup>	4.4	(3.2-5.6)	3.7	(2.6-4.9)	0.85	(0.70-1.02)	0.080
Adjusted Model 2 <sup>b</sup> (primary)	4.4	(3.3-5.6)	3.7	(2.6-4.8)	0.84	(0.70-1.00)	0.055
<b>Cocaine use disorder</b>							
Unadjusted Model	3.9	(2.7-5.0)	5.6	(3.8-7.4)	1.45	(1.16-1.81)	0.001
Adjusted Model 1 <sup>c</sup>	4.1	(2.9-5.2)	4.6	(3.2-6.0)	1.14	(0.93-1.40)	0.213

Adjusted Model2 <sup>b</sup> (primary)	4.1	(3.0-5.2)	4.5	(3.1-5.8)	1.10	(0.90-1.34)	0.342
<b>Amphetamine/other stimulant use disorder</b>							
Unadjusted Model	4.1	(2.9-5.3)	4.9	(3.0-6.8)	1.19	(0.84-1.68)	0.320
Adjusted Model1 <sup>c</sup>	4.1	(3.0-5.2)	4.8	(3.1-6.4)	1.15	(0.88-1.52)	0.302
Adjusted Model2 <sup>b</sup> (primary)	4.1	(3.0-5.3)	4.5	(3.0-6.0)	1.09	(0.84-1.42)	0.527
<b>Cannabis use disorder</b>							
Unadjusted Model	4.2	(3.0-5.4)	4.0	(2.7-5.3)	0.95	(0.74-1.23)	0.717
Adjusted Model1 <sup>c</sup>	4.4	(3.2-5.7)	3.3	(2.3-4.2)	0.74	(0.59-0.94)	0.012
Adjusted Model2 <sup>b</sup> (primary)	4.4	(3.2-5.6)	3.4	(2.4-4.3)	0.77	(0.61-0.96)	0.020
<b>Sedative use disorder</b>							
Unadjusted Model	4.1	(3.0-5.3)	4.7	(3.0-6.4)	1.13	(0.89-1.44)	0.322
Adjusted Model1 <sup>c</sup>	4.1	(3.0-5.2)	4.7	(2.9-6.4)	1.13	(0.88-1.43)	0.337
Adjusted Model2 <sup>b</sup> (primary)	4.1	(3.0-5.2)	4.8	(3.0-6.6)	1.17	(0.91-1.51)	0.226
<b>Outcome: Injectable naltrexone receipt in the following year</b>							
<b>≥1 non-opioid SUD</b>							
Unadjusted Model	0.8	(0.5-1.2)	1.9	(1.4-2.4)	2.23	(1.48-3.36)	<0.001
Adjusted Model1 <sup>a</sup>	1.0	(0.6-1.4)	1.6	(1.1-2.0)	1.57	(1.05-2.35)	0.029
Adjusted Model2 <sup>b</sup> (primary)	1.0	(0.6-1.5)	1.5	(1.1-2.0)	1.50	(0.98-2.29)	0.062
<b>Alcohol use disorder</b>							
Unadjusted Model	1.1	(0.7-1.5)	1.8	(1.3-2.2)	1.57	(1.13-2.17)	0.007
Adjusted Model1 <sup>c</sup>	1.3	(0.9-1.7)	1.4	(1.0-1.8)	1.12	(0.82-1.52)	0.482
Adjusted Model2 <sup>b</sup> (primary)	1.3	(0.9-1.7)	1.4	(1.0-1.8)	1.08	(0.80-1.46)	0.603
<b>Cocaine use disorder</b>							
Unadjusted Model	1.1	(0.8-1.5)	2.3	(1.5-3.1)	2.01	(1.35-2.99)	0.001
Adjusted Model1 <sup>c</sup>	1.2	(0.8-1.6)	1.8	(1.3-2.4)	1.56	(1.09-2.22)	0.014
Adjusted Model2 <sup>b</sup> (primary)	1.2	(0.8-1.6)	1.8	(1.2-2.4)	1.49	(1.03-2.15)	0.034
<b>Amphetamine/other stimulant use disorder</b>							
Unadjusted Model	1.3	(0.9-1.6)	2.0	(1.2-2.8)	1.56	(1.02-2.39)	0.039
Adjusted Model1 <sup>c</sup>	1.3	(0.9-1.7)	1.4	(0.8-2.0)	1.06	(0.70-1.60)	0.786
Adjusted Model2 <sup>b</sup> (primary)	1.3	(0.9-1.7)	1.3	(0.7-1.9)	0.99	(0.65-1.52)	0.971
<b>Cannabis use disorder</b>							
Unadjusted Model	1.2	(0.8-1.5)	2.0	(1.3-2.6)	1.67	(1.28-2.17)	<0.001
Adjusted Model1 <sup>c</sup>	1.3	(1.0-1.7)	1.3	(0.8-1.8)	0.99	(0.78-1.26)	0.935
Adjusted Model2 <sup>b</sup> (primary)	1.3	(1.0-1.7)	1.3	(0.9-1.8)	1.00	(0.79-1.27)	0.977
<b>Sedative use disorder</b>							
Unadjusted Model	1.3	(0.9-1.6)	2.0	(1.1-2.9)	1.57	(1.06-2.33)	0.025
Adjusted Model1 <sup>c</sup>	1.3	(0.9-1.7)	1.5	(0.8-2.1)	1.11	(0.75-1.65)	0.605
Adjusted Model2 <sup>b</sup> (primary)	1.3	(1.0-1.7)	1.5	(0.8-2.2)	1.14	(0.77-1.68)	0.513

IRR = incidence rate ratio; MOUD = medications for opioid use disorder; OUD = opioid use disorder

<sup>a</sup>Adjusted for age, sex, race, ethnicity, marital status, urbanicity/rurality, U.S. Census region

<sup>b</sup>Adjusted for all covariates in Model 1, plus VA eligibility status, homelessness/housing instability, mental health condition, cancer, cerebrovascular disease, chronic obstructive pulmonary disease, congestive heart failure, dementia, diabetes, diabetes with complications, metastatic solid tumor, mild liver disease, moderate/severe liver disease, myocardial infarction, paralysis, peptic ulcer, peripheral vascular disease, renal disease, rheumatic disease, HIV, hepatitis C

<sup>c</sup>Adjusted for other co-occurring substance use disorders (including hallucinogen use disorder), age, sex, race, ethnicity, marital status, urbanicity/rurality, U.S. Census region

\*significant after Holm-Bonferroni sequential correction applied to all primary model statistical tests for each outcome

**Table 2B.2. Continuation of specific types of MOUD in the following year for patients with past-year co-occurring SUDs compared to those without among national Veterans Health Administration outpatients with OUD and MOUD receipt in the past year 8/1/16-7/31/17**

Predictor of interest	Among those without predictor of interest		Among those with predictor of interest		IRR for those with predictor of interest relative to those without		
	%	(95% CI)	%	(95% CI)	IRR	(95% CI)	p-value
<b>Outcome: Buprenorphine receipt in the following year (N=7,756)</b>							
<b>≥1 non-opioid SUD</b>							
Unadjusted Model	87.2	(85.6-88.8)	77.2	(75.3-79.2)	0.89	(0.86-0.91)	<0.001
Adjusted Model 1 <sup>a</sup>	87.0	(85.4-88.6)	77.4	(75.6-79.3)	0.89	(0.87-0.91)	<0.001
Adjusted Model 2 <sup>b</sup> (primary)	86.0	(84.3-87.6)	78.5	(76.7-80.3)	<b>0.91</b>	<b>(0.89-0.94)</b>	<b>&lt;0.001*</b>
<b>Alcohol use disorder</b>							
Unadjusted Model	84.7	(83.1-86.3)	77.1	(74.9-79.3)	0.91	(0.88-0.94)	<0.001
Adjusted Model 1 <sup>c</sup>	83.7	(82.0-85.3)	79.6	(77.4-81.8)	0.95	(0.92-0.98)	0.001
Adjusted Model 2 <sup>b</sup> (primary)	83.3	(81.7-85.0)	80.5	(78.4-82.6)	0.97	(0.94-1.00)	0.027
<b>Cocaine use disorder</b>							
Unadjusted Model	83.9	(82.4-85.4)	75.6	(72.2-79.0)	0.90	(0.86-0.94)	<0.001
Adjusted Model 1 <sup>c</sup>	83.1	(81.7-84.6)	79.3	(75.9-82.7)	0.95	(0.91-1.00)	0.030
Adjusted Model 2 <sup>b</sup> (primary)	82.9	(81.5-84.4)	80.4	(77.0-83.7)	0.97	(0.93-1.01)	0.136
<b>Amphetamine/other stimulant use disorder</b>							
Unadjusted Model	83.7	(82.3-85.2)	69.7	(66.1-73.3)	0.83	(0.79-0.88)	<0.001
Adjusted Model 1 <sup>c</sup>	83.3	(81.8-84.8)	73.6	(69.8-77.4)	0.88	(0.84-0.93)	<0.001
Adjusted Model 2 <sup>b</sup> (primary)	83.2	(81.7-84.7)	74.7	(70.9-78.5)	<b>0.90</b>	<b>(0.85-0.95)</b>	<b>&lt;0.001*</b>
<b>Cannabis use disorder</b>							
Unadjusted Model	83.9	(82.4-85.3)	76.1	(73.3-78.9)	0.91	(0.88-0.94)	<0.001
Adjusted Model 1 <sup>c</sup>	83.1	(81.6-84.5)	79.7	(77.0-82.5)	0.96	(0.93-0.99)	0.011
Adjusted Model 2 <sup>b</sup> (primary)	83.0	(81.6-84.4)	80.0	(77.3-82.7)	0.96	(0.93-0.99)	0.020
<b>Sedative use disorder</b>							
Unadjusted Model	83.5	(82.1-85.0)	72.5	(69.0-75.9)	0.87	(0.83-0.91)	<0.001
Adjusted Model 1 <sup>c</sup>	83.2	(81.8-84.6)	75.7	(72.2-79.2)	0.91	(0.87-0.95)	<0.001
Adjusted Model 2 <sup>b</sup> (primary)	83.1	(81.7-84.5)	76.6	(73.1-80.1)	<b>0.92</b>	<b>(0.88-0.96)</b>	<b>&lt;0.001*</b>
<b>Outcome: Methadone receipt in the following year (N=6,050)</b>							
<b>≥1 non-opioid SUD</b>							
Unadjusted Model	78.3	(71.7-84.9)	72.1	(67.1-77.1)	0.92	(0.85-0.99)	0.030
Adjusted Model 1 <sup>a</sup>	78.6	(73.3-84.0)	71.8	(66.9-76.7)	0.91	(0.86-0.97)	0.005
Adjusted Model 2 <sup>b</sup> (primary)	78.5	(73.5-83.5)	71.9	(66.9-76.8)	<b>0.92</b>	<b>(0.86-0.97)</b>	<b>0.003*</b>
<b>Alcohol use disorder</b>							
Unadjusted Model	77.8	(72.1-83.5)	69.1	(63.7-74.5)	0.89	(0.83-0.95)	0.001
Adjusted Model 1 <sup>c</sup>	77.5	(72.7-82.2)	69.9	(64.8-74.9)	0.90	(0.85-0.95)	<0.001
Adjusted Model 2 <sup>b</sup> (primary)	77.4	(72.8-82.0)	70.0	(64.9-75.0)	<b>0.90</b>	<b>(0.86-0.95)</b>	<b>&lt;0.001*</b>
<b>Cocaine use disorder</b>							
Unadjusted Model	76.4	(71.1-81.7)	71.3	(65.2-77.4)	0.93	(0.87-1.00)	0.067
Adjusted Model 1 <sup>c</sup>	76.1	(71.6-80.6)	72.3	(66.6-78.0)	0.95	(0.90-1.00)	0.048
Adjusted Model 2 <sup>b</sup> (primary)	76.1	(71.8-80.4)	72.2	(66.3-78.0)	0.95	(0.90-1.00)	0.046

**Amphetamine/other stimulant use disorder**

Unadjusted Model	75.8	(70.5-81.0)	68.8	(61.2-76.3)	0.91	(0.81-1.01)	0.087
Adjusted Model 1 <sup>c</sup>	75.3	(70.7-80.0)	74.8	(67.9-81.7)	0.99	(0.91-1.09)	0.880
Adjusted Model 2 <sup>b</sup> (primary)	75.3	(70.8-79.8)	74.9	(68.0-81.7)	0.99	(0.91-1.08)	0.898

**Cannabis use disorder**

Unadjusted Model	76.5	(71.2-81.9)	68.6	(63.1-74.1)	0.90	(0.83-0.97)	0.005
Adjusted Model 1 <sup>c</sup>	76.0	(71.3-80.6)	71.5	(66.5-76.6)	0.94	(0.89-1.00)	0.033
Adjusted Model 2 <sup>b</sup> (primary)	76.0	(71.5-80.6)	71.3	(66.1-76.4)	0.94	(0.89-0.99)	0.020

**Sedative use disorder**

Unadjusted Model	75.7	(70.5-80.8)	71.7	(64.5-79.0)	0.95	(0.87-1.04)	0.252
Adjusted Model 1 <sup>c</sup>	75.3	(70.7-79.8)	75.7	(69.0-82.4)	1.01	(0.93-1.09)	0.882
Adjusted Model 2 <sup>b</sup> (primary)	75.2	(70.8-79.7)	75.9	(69.4-82.4)	1.01	(0.94-1.09)	0.811

**Outcome: Injectable naltrexone receipt in the following year (N=368)**

**≥1 non-opioid SUD**

Unadjusted Model	43.1	(27.3-59.0)	40.1	(35.4-44.7)	0.93	(0.63-1.37)	0.709
Adjusted Model 1 <sup>a</sup>	41.6	(25.5-57.8)	40.3	(35.5-45.1)	0.97	(0.64-1.47)	0.877
Adjusted Model 2 <sup>b</sup> (primary)	40.4	(22.8-58.1)	40.5	(35.8-45.2)	1.00	(0.63-1.61)	0.994

**Alcohol use disorder**

Unadjusted Model	37.5	(28.0-47.0)	41.7	(36.5-46.8)	1.11	(0.84-1.47)	0.462
Adjusted Model 1 <sup>c</sup>	36.5	(27.1-45.9)	42.1	(36.7-47.5)	1.15	(0.86-1.55)	0.340
Adjusted Model 2 <sup>b</sup> (primary)	35.8	(26.1-45.5)	42.5	(37.1-47.8)	1.19	(0.87-1.62)	0.284

**Cocaine use disorder**

Unadjusted Model	41.4	(34.3-48.6)	39.0	(32.6-45.5)	0.94	(0.73-1.22)	0.655
Adjusted Model 1 <sup>c</sup>	40.3	(33.5-47.0)	40.8	(32.8-48.8)	1.01	(0.76-1.35)	0.928
Adjusted Model 2 <sup>b</sup> (primary)	39.8	(33.0-46.6)	41.6	(32.8-50.4)	1.05	(0.77-1.43)	0.778

**Amphetamine/other stimulant use disorder**

Unadjusted Model	40.5	(35.6-45.4)	40.3	(27.8-52.9)	1.00	(0.71-1.39)	0.977
Adjusted Model 1 <sup>c</sup>	40.4	(35.6-45.2)	41.0	(28.8-53.2)	1.02	(0.74-1.39)	0.924
Adjusted Model 2 <sup>b</sup> (primary)	40.0	(35.2-44.9)	42.9	(30.6-55.3)	1.07	(0.78-1.47)	0.663

**Cannabis use disorder**

Unadjusted Model	45.2	(39.6-50.7)	30.8	(23.7-37.9)	0.68	(0.53-0.88)	0.004
Adjusted Model 1 <sup>c</sup>	44.8	(38.8-50.8)	31.3	(23.3-39.3)	0.70	(0.52-0.95)	0.020
Adjusted Model 2 <sup>b</sup> (primary)	44.6	(38.6-50.5)	31.7	(23.2-40.2)	0.71	(0.52-0.98)	0.037

**Sedative use disorder**

Unadjusted Model	40.8	(35.7-46.0)	38.7	(27.0-50.4)	0.95	(0.67-1.33)	0.757
Adjusted Model 1 <sup>c</sup>	40.8	(35.6-46.0)	39.1	(27.1-51.1)	0.96	(0.68-1.36)	0.810
Adjusted Model 2 <sup>b</sup> (primary)	41.2	(35.9-46.5)	37.2	(27.0-47.4)	0.90	(0.66-1.24)	0.530

IRR = incidence rate ratio; MOUD = medications for opioid use disorder; OUD = opioid use disorder

<sup>a</sup>Adjusted for age, sex, race, ethnicity, marital status, urbanicity/rurality, U.S. Census region

<sup>b</sup>Adjusted for all covariates in Model 1, plus VA eligibility status, homelessness/housing instability, mental health condition, cancer, cerebrovascular disease, chronic obstructive pulmonary disease, congestive heart failure, dementia, diabetes, diabetes with complications, metastatic solid tumor, mild liver disease, moderate/severe liver disease, myocardial infarction, paralysis, peptic ulcer, peripheral vascular disease, renal disease, rheumatic disease, HIV, hepatitis C

<sup>c</sup>Adjusted for other co-occurring substance use disorders (including hallucinogen use disorder), age, sex, race, ethnicity, marital status, urbanicity/rurality, U.S. Census region

\*significant after Holm-Bonferroni sequential correction applied to all primary model statistical tests for each outcome

**Table 2B.3. Initiation and continuation of any MOUD in the following year for patients with past-year heavy drinking compared to those without among national Veterans Health Administration outpatients with OUD 8/1/16-7/31/17**

	Among those without heavy drinking		Among those with heavy drinking		aIRR for those with heavy drinking relative to those without <sup>a</sup>		
	%	(95% CI)	%	(95% CI)	aIRR	(95% CI)	p-value
<b>Initiation subsample (no MOUD receipt in the past year)</b>							
Patients with AUD (N=7,680)	9.8	(8.6-10.9)	12.2	(9.9-14.5)	1.25	(1.07-1.46)	0.005
Patients without AUD (N=16,310)	12.7	(11.5-13.9)	18.9	(15.0-22.7)	1.48	(1.21-1.82)	<0.001
<b>Continuation subsample (any MOUD receipt in the past year)</b>							
Patients with AUD (N=3,475)	80.5	(78.3-82.8)	70.5	(65.2-75.9)	0.88	(0.81-0.94)	<0.001
Patients without AUD (N=8,379)	84.8	(82.4-87.2)	66.8	(53.6-80.0)	0.79	(0.65-0.95)	0.013

AUD = alcohol use disorder; aIRR = adjusted incidence rate ratio; MOUD = medications for opioid use disorder; OUD = opioid use disorder

<sup>a</sup>Adjusted for cocaine use disorder, amphetamine/other stimulant use disorder, cannabis use disorder, sedative use disorder, hallucinogen use disorder, age, sex, race, ethnicity, marital status, urbanicity/rurality, U.S. Census region, VA eligibility status, homelessness/housing instability, mental health condition, cancer, cerebrovascular disease, chronic obstructive pulmonary disease, congestive heart failure, dementia, diabetes, diabetes with complications, metastatic solid tumor, mild liver disease, moderate/severe liver disease, myocardial infarction, paralysis, peptic ulcer, peripheral vascular disease, renal disease, rheumatic disease, HIV, hepatitis C

### **Chapter 3: Impact of an opioid use disorder treatment implementation intervention among patients with and without co-occurring substance use disorders in the Veterans Health Administration**

#### **ABSTRACT**

**Introduction:** Co-occurring substance use disorders (SUDs) are common among people with opioid use disorder (OUD) and negatively associated with receipt of medications for OUD (MOUD). It is important to understand how MOUD care implemented outside of SUD specialty settings impacts access for patients with co-occurring SUDs. The Veterans Health Administration's (VA) Stepped Care for Opioid Use Disorder Train the Trainer (SCOUTT) initiative increased MOUD receipt in primary care, mental health, and pain clinics. This study assessed whether the SCOUTT initiative's effectiveness was modified by the presence of co-occurring SUDs.

**Methods:** This study used a controlled interrupted time series design. Electronic health record data were extracted for patients with OUD with visits in intervention or comparison clinics (matched based on facility complexity, number of patients with OUD, and pre-implementation trends in MOUD prescribing) during the post-implementation year (9/1/2018-8/31/2019). We examined the monthly proportion of patients who received MOUD in SCOUTT and/or SUD specialty clinics during the pre- and post-implementation years. We fit segmented logistic regression models to examine pre-post changes in outcomes (immediate level change, change in trend/slope) in intervention vs. comparison clinics, adjusting for patient characteristics and pre-

implementation trends. Models included interaction terms to assess effect modification by the presence of co-occurring SUDs and obtain stratified estimates.

**Results:** During the pre-implementation year, patients with  $\geq 1$  co-occurring SUD received MOUD in SCOUTT clinics less frequently than those without co-occurring SUDs, but they received MOUD more frequently overall. The impact of the SCOUTT initiative on MOUD receipt was not significantly modified by the presence of co-occurring SUDs. However, among patients without co-occurring SUDs, the trend change in MOUD receipt in SCOUTT clinics was greater in intervention vs. comparison clinics (adjusted odds ratio [aOR]: 1.06, 95% confidence interval [CI]: 1.02-1.10), and the immediate level change in MOUD receipt in SUD clinics was greater in intervention vs. comparison clinics (aOR: 1.12, 95% CI: 1.02-1.22), while these changes were not significantly greater in intervention vs. comparison clinics among patients with co-occurring SUDs.

**Conclusions:** The SCOUTT initiative may have increased MOUD receipt primarily among patients without co-occurring SUDs. Focusing on increasing MOUD receipt for patients with co-occurring SUDs may improve the overall effectiveness of MOUD implementation efforts. Further research is needed to examine the effectiveness of implementation efforts for patients with co-occurring SUDs in facilities where this patient population has lower overall MOUD receipt.

## INTRODUCTION

The United States is facing an ongoing overdose crisis—overdose deaths are at a record high and continue to climb.<sup>2,3</sup> Effective medications approved to treat opioid use disorder (MOUD) include methadone, buprenorphine and naltrexone;<sup>4</sup> first-line medications (methadone

and buprenorphine)<sup>5,6</sup> substantially reduce risk of opioid-related overdose and mortality.<sup>7-9</sup> Unfortunately, most people with OUD do not receive this potentially life-saving treatment.<sup>1</sup> This treatment gap has resulted in numerous efforts to improve MOUD access.<sup>28,61-63</sup>

Although co-occurring substance use disorders (SUDs) and polysubstance use are common among people with OUD and have been found to be negatively associated with MOUD receipt,<sup>11-13,15,16</sup> efforts to expand MOUD have generally overlooked this issue.<sup>10,19</sup> Because many patients may face barriers to receiving MOUD in SUD specialty settings,<sup>26</sup> one important strategy to increase access is expanding MOUD provision outside of these settings.<sup>4,35,62</sup> It is important to understand whether and how new MOUD care models being implemented outside of SUD specialty settings impact MOUD access for patients with co-occurring SUDs. These care models may improve access for this patient population through direct MOUD provision and/or improved linkage to SUD specialty settings. However, if they do not, then modified or additional efforts may be needed to improve care for this population.

The Veterans Health Administration (VA) is the country's largest OUD treatment provider, and improving MOUD access is an important VA priority.<sup>35,36</sup> Over half of patients with OUD in the national VA have co-occurring SUDs, and those with at least one co-occurring SUD are less likely than those with OUD alone to receive both buprenorphine and methadone.<sup>12</sup> The Stepped Care for Opioid Use Disorder Train the Trainer (SCOUTT) initiative is the VA's largest effort to implement MOUD outside of SUD specialty settings (specifically in primary care, mental health, and pain clinics).<sup>27</sup> The SCOUTT initiative supports a stepped care model, which promotes ongoing OUD care for every patient in a non-SUD setting, with a "step up" to higher intensity care in an SUD specialty setting as needed.<sup>27</sup> The evaluation of the SCOUTT initiative found that it increased MOUD receipt in intervention clinics.<sup>64</sup> However, to our

knowledge, no studies have assessed the effectiveness of a stepped care model of MOUD implemented through a train-the-trainer intervention for patients with co-occurring SUDs compared to those without, and it is unknown whether the SCOUTT initiative differentially impacted patients with co-occurring SUDs compared to those without. This study aimed to assess whether the VA SCOUTT initiative's effectiveness in increasing MOUD receipt was modified by the presence of co-occurring SUDs.

## **METHODS**

### **Setting and study design**

SCOUTT was implemented in 35 primary care, mental health, and pain clinics across 18 facilities (one facility in each VA regional network). Details of the intervention and implementation procedures have been previously described.<sup>27,64</sup> Briefly, the intervention involved training an implementation team from each facility in evidence-based MOUD care models; these teams then worked to implement MOUD in their facility's selected clinics with ongoing external facilitation support.

The SCOUTT evaluation used a controlled interrupted time series design to assess whether implementation impacted the level of and trend in MOUD receipt in intervention clinics relative to comparison clinics. SCOUTT implementation launched 9/1/2018; the pre-implementation period was defined as 9/1/2017-8/31/2018 and the post-implementation period as 9/1/2018-8/31/2019. Thirty-five comparison clinics were selected that were similar to intervention clinics in facility complexity, number of patients with OUD, and pre-implementation trends in MOUD prescribing.<sup>64</sup> A control series was included to account for the

potential influence of external factors, such as a changing societal landscape related to substance use and other national VA initiatives to increase MOUD prescribing.<sup>65</sup>

This secondary analysis of SCOUTT evaluation data also uses a controlled interrupted time series design, with interaction terms to assess whether the impact of the intervention on level of and trend in MOUD receipt in intervention clinics relative to comparison clinics differed among patients with and without co-occurring SUDs. This study was approved by the University of Washington and VA Puget Sound institutional review boards, with waivers of consent and Health Insurance Portability and Accountability Act (HIPAA) authorization.

### **Data source and study sample**

This study is a secondary analysis of electronic health record (EHR) data extracted from the VA Corporate Data Warehouse for the SCOUTT evaluation, in accordance with a Data Use Agreement with the VA Office of Mental Health and Suicide Prevention. The study sample included patients who 1) were  $\geq 18$  years of age, 2) had  $\geq 1$  outpatient visit in a SCOUTT intervention or comparison clinic during the post-implementation period, and 3) had a documented OUD diagnosis during either the pre- or post-implementation periods.

### **Measures**

#### ***Outcomes***

Outcomes were measured as monthly proportions in the 12 months prior to and 12 months following SCOUTT implementation. We examined the proportion of patients who were prescribed MOUD in SCOUTT intervention or comparison clinics (buprenorphine or injectable naltrexone) and/or in VA SUD specialty clinics (methadone, buprenorphine, or injectable naltrexone). This outcome included MOUD in both SCOUTT and SUD specialty settings to account for the possibility that some patients were referred to a setting offering more specialized

care. Clinic codes associated with prescriptions were examined to determine if prescriptions originated in SCOUTT intervention or comparison clinics. As SUD clinic codes were not tied to prescription information in these data, MOUD prescribed in SUD specialty clinics was defined as having either 1) a methadone treatment program order on file or clinic visit code 523 (VA Opioid Treatment Program), and/or 2) an SUD clinic visit code combined with buprenorphine or injectable naltrexone prescribed in a non-SCOUTT VA clinic. We also examined MOUD prescribed in SCOUTT clinics and MOUD prescribed in SUD specialty clinics as separate outcomes.

### ***Effect modifier***

The presence of co-occurring SUDs was considered a potential effect modifier and was defined as having  $\geq 1$  documented diagnosis for alcohol use disorder or any non-opioid drug use disorder during the pre-implementation period.

### ***Covariates***

Sociodemographic and clinical covariates were included based on known associations with SUDs and MOUD receipt.<sup>15,16,23-25,48,66-70</sup> These covariates were measured during the pre-implementation period and included age, sex, race, ethnicity, marital status, VA service-connected disability rating  $\geq 50\%$ , housing instability, depression, anxiety, post-traumatic stress disorder, serious mental illness (including bipolar, psychoses, and schizophrenia disorders), and Charlson Comorbidity Index score.<sup>71</sup> Clinic type (primary care, mental health, pain) was also included as a covariate to account for differences in practice across settings. Three time-varying (monthly) binary variables were additionally included as covariates when examining MOUD receipt in SCOUTT clinics as the outcome to account for whether patients had an opportunity to receive MOUD in that clinic: having  $\geq 1$  visit in the SCOUTT intervention or comparison clinic,

having  $\geq 1$  visit to a VA SUD specialty clinic, and receipt of MOUD outside of the SCOUTT intervention or comparison clinic.

## **Analyses**

We descriptively compared patient characteristics across the presence of co-occurring SUDs in intervention and comparison clinics. We also described the proportion of patients who had each outcome during at least one month during the pre- and post-implementation years across the presence of co-occurring SUDs in intervention and comparison clinics.

Interrupted time series analyses used segmented logistic regression models with interaction terms for intervention vs. comparison to examine pre-post changes in outcomes (including immediate level change and change in trend/slope) in intervention vs. comparison clinics, adjusting for patient characteristics and pre-implementation trends.<sup>65,72</sup> Models also included interaction for co-occurring SUDs to: 1) determine if the impact of the intervention was significantly modified by the presence of co-occurring SUDs, and 2) obtain estimates stratified by the presence of co-occurring SUDs (a detailed explanation of model parameters and estimates is included in Appendix 3A). We also obtained the marginal adjusted prevalence of the outcome stratified across 4 subgroups (patients with co-occurring SUDs in intervention clinics, patients with co-occurring SUDs in comparison clinics, patients without co-occurring SUDs in intervention clinics, patients without co-occurring SUDs in comparison clinics) and graphed these over each month. Models used generalized estimating equations (GEE) with a logit link that accounted for patient-level correlation (each patient had multiple observations corresponding to multiple months in the dataset) and included a fixed effect for implementation facility to account for facility-level correlation. Models were fit with an autoregressive (AR1) correlation structure and robust standard errors, and included the covariates described above. We fit three

models examining each outcome: 1) MOUD prescribed in SCOUTT and/or SUD clinics (primary outcome), 2) MOUD prescribed in SCOUTT clinics, and 3) MOUD prescribed in SUD clinics.

We conducted post-hoc, exploratory analyses to examine whether findings related to MOUD prescribed in SCOUTT clinics differed across clinic type (repeated Model 2 in subgroups limited to primary care clinics, mental health clinics, and pain clinics). Analyses were conducted with Stata version 17 software.<sup>56</sup>

## **RESULTS**

### **Sample characteristics and outcome prevalence**

Sample characteristics across the presence of co-occurring SUDs in intervention and comparison clinics are presented in Table 3.1. In both intervention and comparison clinics, patients with co-occurring SUDs were more likely than those without to be younger, Black, Hispanic, and not married, to have unstable housing and physical and mental health comorbidities, and to be seen in mental health clinics. In intervention clinics patients with co-occurring SUDs were more likely than those without to be male, while in comparison clinics they were more likely to have VA service-connected disability  $\geq 50\%$ .

The annual unadjusted prevalence of outcomes during the pre- and post-implementation years across the presence of co-occurring SUDs in intervention and comparison clinics is presented in Table 3.2. In both intervention and comparison clinics, patients with co-occurring SUDs had significantly higher prevalence of MOUD receipt in SCOUTT and/or SUD clinics and in SUD clinics alone during both the pre- and post-implementation years. In both intervention and comparison clinics, there was no significant difference across the presence of co-occurring

SUDs in MOUD receipt in SCOUTT clinics during the pre-implementation year, and in the post-implementation year prevalence was significantly lower among patients with co-occurring SUDs compared to those without. For all outcomes, the increase in prevalence from pre- to post-implementation was smaller among patients with co-occurring SUDs compared to those without, and these increases were larger in intervention clinics.

### **Interrupted time series results**

#### ***MOUD receipt in SCOUTT and/or SUD clinics***

The difference in the immediate level change in MOUD received in SCOUTT and/or SUD clinics between intervention vs. comparison clinics was not significantly modified by the presence of co-occurring SUDs (p-value for interaction term=0.864). Among patients with co-occurring SUDs, the immediate level change was greater in intervention vs. comparison clinics (aOR: 1.08, 95% CI: 1.00-1.17, p=0.043). Among patients without co-occurring SUDs, the immediate level change was also greater in intervention vs. comparison clinics (aOR: 1.10, 95% CI: 1.00-1.19, p=0.026). The difference in the trend (slope) change between intervention vs. comparison clinics was not significantly modified by the presence of co-occurring SUDs (p-value for interaction term=0.828). Among patients with co-occurring SUDs, the trend change did not significantly differ in intervention vs. comparison clinics (aOR: 1.00, 95% CI: 0.98-1.02, p=0.988). Among patients without co-occurring SUDs, the trend change also did not significantly differ in intervention vs. comparison clinics (aOR: 1.00, 95% CI: 0.99-1.02, p=0.771). Adjusted monthly proportions of patients who received MOUD in SCOUTT and/or SUD clinics across the presence of co-occurring SUDs in intervention and comparison clinics are presented in Figure 3.1. Patients with and without co-occurring SUDs in intervention and comparison clinics had a monthly increase in MOUD receipt in SCOUTT and/or SUD clinics

following implementation; this increase was steepest among patients without co-occurring SUDs in intervention clinics.

### ***MOUD receipt in SCOUTT clinics***

The difference in the immediate level change in MOUD received in SCOUTT clinics between intervention vs. comparison clinics was not significantly modified by the presence of co-occurring SUDs (p-value for interaction term=0.740). Among patients with co-occurring SUDs, the immediate level change did not significantly differ in intervention vs. comparison clinics (aOR: 1.17, 95% CI: 0.89-1.54, p=0.263). Among patients without co-occurring SUDs, the immediate level change also did not significantly differ in intervention vs. comparison clinics (aOR: 1.11, 95% CI: 0.93-1.33, p=0.264). The difference in the trend change between intervention vs. comparison clinics was not significantly modified by the presence of co-occurring SUDs (p-value for interaction term=0.241). However, there did appear to be differences in stratified estimates: Among patients with co-occurring SUDs, the trend change did not significantly differ in intervention vs. comparison clinics (aOR: 1.02, 95% CI: 0.97-1.08, p=0.455); among patients without co-occurring SUDs, the trend change was greater in intervention vs. comparison clinics (aOR: 1.06, 95% CI: 1.02-1.10, p=0.002). Adjusted monthly proportions of patients who received MOUD in SCOUTT clinics across the presence of co-occurring SUDs in intervention and comparison clinics are presented in Figure 3.2. Patients with and without co-occurring SUDs who were seen in intervention clinics had a monthly increase in MOUD receipt in SCOUTT clinics following implementation; this increase was steeper among patients without co-occurring SUDs.

### ***MOUD receipt in SUD clinics***

The difference in immediate level change in MOUD received in SUD clinics between intervention vs. comparison clinics was not significantly modified by the presence of co-occurring SUDs (p-value for interaction term=0.541). However, there did appear to be differences in stratified estimates: Among patients with co-occurring SUDs, the immediate level change did not significantly differ in intervention vs. comparison clinics (aOR: 1.08, 95% CI: 0.99-1.17, p=0.079); among patients without co-occurring SUDs, the immediate level change was greater in intervention vs. comparison clinics (aOR: 1.12, 95% CI: 1.02-1.22, p=0.013). The difference in the trend change between intervention vs. comparison clinics was not significantly modified by the presence of co-occurring SUDs (p-value for interaction term=0.706). Among patients with co-occurring SUDs, the trend change did not significantly differ in intervention vs. comparison clinics (aOR: 0.99, 95% CI: 0.98-1.01, p=0.415). Among patients without co-occurring SUDs, the trend change also did not significantly differ in intervention vs. comparison clinics (aOR: 0.99, 95% CI: 0.97-1.01, p=0.199). Adjusted monthly proportions of patients who received MOUD in SUD clinics across the presence of co-occurring SUDs in intervention and comparison clinics are presented in Figure 3.3. Patients without co-occurring SUDs who were seen in intervention clinics and patients with and without co-occurring SUDs who were seen in comparison clinics had a monthly increase in MOUD receipt in SUD clinics following implementation, while there was not a monthly increase for patients with co-occurring SUDs in intervention clinics following implementation.

Results from post-hoc analyses examining whether trends in MOUD prescribed in SCOUTT clinics differed across clinic type are presented in Appendix 3B. Estimates from these interrupted time series models mirror the main analyses, except that in pain clinics the trend

change was no longer significantly greater in intervention vs. comparison clinics among patients without co-occurring SUDs.

## **DISCUSSION**

In this evaluation of the largest effort to date to implement MOUD outside of SUD specialty settings in the VA, we did not find that the presence of co-occurring SUDs significantly modified the effectiveness of SCOUTT. However, analyses stratified by the presence of co-occurring SUDs suggest that the initiative may have primarily increased MOUD among patients without co-occurring SUDs. Specifically, we observed a steeper increase over time in MOUD receipt in SCOUTT clinics, as well as an immediate increase in MOUD receipt in SUD clinics, among patients without co-occurring SUDs but not in patients with co-occurring SUDs.

Though findings from the main SCOUTT evaluation suggest that it is a promising model for implementing MOUD care outside of SUD specialty settings,<sup>64</sup> the present study suggests that focusing on increasing MOUD receipt among patients with co-occurring SUDs could improve the overall effectiveness of ongoing and future MOUD implementation efforts. This could include improving linkage to SUD specialty care for this patient population. However, as many patients may face barriers to receiving SUD specialty care or prefer to receive MOUD in lower-intensity settings,<sup>26</sup> implementation efforts should also aim to support provision of MOUD to patients with co-occurring SUDs in primary care, mental health, and pain clinics. For example, implementation could include specific training on providing buprenorphine to patients with co-occurring substance use as well as principles of harm reduction and patient-centered care.

Additionally, this study suggests that VA patients with co-occurring SUDs may be more likely to be Black and/or Hispanic, to experience housing instability, and to have physical and

mental health comorbidities. These groups of patients are known to experience disparities in MOUD receipt, particularly of buprenorphine.<sup>12,41,68,70</sup> Addressing barriers to MOUD receipt specifically related to co-occurring SUD may be one means of increasing equity in MOUD receipt, though other efforts addressing contextual factors including systemic racism and economic inequality are also needed.<sup>73</sup>

It is important to consider that facilities included in the SCOUTT initiative may not reflect other VA facilities with respect to existing barriers to MOUD faced by patients with co-occurring SUDs. During the pre-implementation period, these patients received MOUD in SCOUTT clinics less frequently but received MOUD more frequently overall, which differs from prior research in the national VA finding that patients with co-occurring SUDs are less likely to receive MOUD.<sup>12</sup> SCOUTT intervention facilities were selected by leadership from each VA regional network,<sup>27</sup> and it is possible that selected facilities tended to have lower barriers to MOUD (particularly in SUD clinics) for patients with co-occurring SUDs than facilities that were not selected. This may have impacted findings from this analysis – for example, providers in SCOUTT clinics may have been less likely to provide MOUD to patients with co-occurring SUDs if they were already more likely to receive this care in an SUD clinic. However, it is also possible that the positive association between co-occurring SUDs and overall MOUD receipt during the pre-implementation period resulted from patients who received MOUD in SUD clinics being more likely to have other SUDs recognized and subsequently diagnosed. In any case, further research is needed to examine the effectiveness of MOUD implementation efforts for patients with co-occurring SUDs in facilities where this patient population has lower overall MOUD receipt.

This study has limitations. The sample may have provided limited power to detect statistically significant effect modification by the presence of co-occurring SUDs, despite apparent differences in results from stratified analyses. Although we adjusted for patient-level covariates, there may have been unmeasured confounding. Although we adjusted for the pre-implementation outcome trend and included a control series, there may have been residual bias from external factors occurring contemporaneously with the intervention (e.g., a changing societal landscape related to substance use and other VA MOUD initiatives).<sup>65</sup> Co-occurring SUDs may have been underdiagnosed or not documented in the EHR for some patients,<sup>74</sup> and these data did not capture substance use which may impact MOUD receipt differently than SUD. Additionally, our measure of MOUD received in VA SUD clinics may have overestimated this outcome, as some patients theoretically could have received MOUD in a non-SUD, non-SCOUTT clinic while also having an SUD clinic visit within the same month. Finally, these findings may have limited generalizability in other VA facilities and in non-VA clinical settings.

## **CONCLUSIONS**

This study examining the impact of an MOUD implementation initiative among patients with and without co-occurring SUDs did not find statistically significant effect modification by the presence of co-occurring SUDs, however it appears the initiative may have increased MOUD receipt primarily for patients without co-occurring SUDs. Focusing on increasing MOUD receipt among patients with co-occurring SUDs could improve the overall effectiveness of ongoing and future MOUD implementation efforts. Further research is needed to examine the effectiveness of MOUD implementation efforts for patients with co-occurring SUDs in facilities where this patient population has lower overall MOUD receipt.

**Table 3.1. Baseline patient characteristics compared across presence of co-occurring SUD in SCOUTT clinics**

	Intervention Clinics				p-value <sup>b</sup>	Comparison Clinics				p-value <sup>b</sup>
	No co-occurring SUD (N=3,765)		≥1 co-occurring SUD (N=3,723)			No co-occurring SUD (N=3,636)		≥1 co-occurring SUD (N=3,922)		
	N	(%)	N	(%)		N	(%)	N	(%)	
Age (mean, SD, t-test)	55.3	(14.4)	51.4	(13.8)	<0.001	55.0	(14.3)	51.9	(13.6)	<0.001
Sex					0.003					0.090
Female	353	(9.4)	277	(7.4)		316	(8.7)	299	(7.6)	
Male	3,412	(90.6)	3,446	(92.6)		3,320	(91.3)	3,623	(92.4)	
Race and ethnicity					<0.001					<0.001
Black	624	(16.6)	852	(22.9)		562	(15.5)	901	(23.0)	
Hispanic	190	(5.1)	227	(6.1)		173	(4.8)	232	(5.9)	
White	2,711	(72.0)	2,451	(65.8)		2,638	(72.6)	2,558	(65.2)	
Other/Multiple races	124	(3.3)	115	(3.1)		126	(3.5)	118	(3.0)	
Unknown	116	(3.1)	78	(2.1)		137	(3.8)	113	(2.9)	
Marital status					<0.001					<0.001
Married	1,533	(40.7)	899	(24.2)		1,372	(37.7)	910	(23.2)	
Not married <sup>b</sup>	2,217	(58.9)	2,808	(75.4)		2,250	(61.9)	3,006	(76.6)	
Unknown	15	(0.4)	16	(0.4)		14	(0.4)	6	(0.2)	
Service disability ≥50%	2,040	(54.2)	2,063	(55.4)	0.285	1,865	(51.3)	2,111	(53.8)	0.028
Housing instability	342	(9.1)	1,458	(39.2)	<0.001	360	(9.9)	1,683	(42.9)	<0.001
Charlson Comorbidity Index					<0.001					<0.001
0	2,036	(54.1)	1,753	(47.1)		1,885	(51.8)	1,663	(42.4)	
1	676	(18.0)	874	(23.5)		710	(19.5)	1,021	(26.0)	
≥2	1,053	(28.0)	1,096	(29.4)		1,041	(28.6)	1,238	(31.6)	
Depression	1,303	(34.6)	2,051	(55.1)	<0.001	1,251	(34.4)	2,107	(53.7)	<0.001
Anxiety	820	(21.8)	1,606	(43.1)	<0.001	921	(25.3)	1,783	(45.5)	<0.001
Post-traumatic stress disorder	1,200	(31.9)	2,067	(55.5)	<0.001	1,004	(27.6)	1,971	(50.3)	<0.001
Serious mental illness <sup>c</sup>	346	(9.2)	963	(25.9)	<0.001	336	(9.2)	1,089	(27.8)	<0.001
Clinic type					<0.001					<0.001
Primary care	2,032	(54.0)	2,140	(57.5)		1,828	(50.3)	1,785	(45.5)	
Mental health	1,003	(26.6)	1,290	(34.7)		978	(26.9)	1,660	(42.3)	
Pain	730	(19.4)	293	(7.9)		830	(22.8)	477	(12.2)	

SD = standard deviation; SUD = substance use disorder

<sup>a</sup>From chi-square test unless otherwise indicated

<sup>b</sup>Includes never married, divorced, or widowed

<sup>c</sup>Includes bipolar-spectrum disorders and/or schizophrenia-spectrum disorders

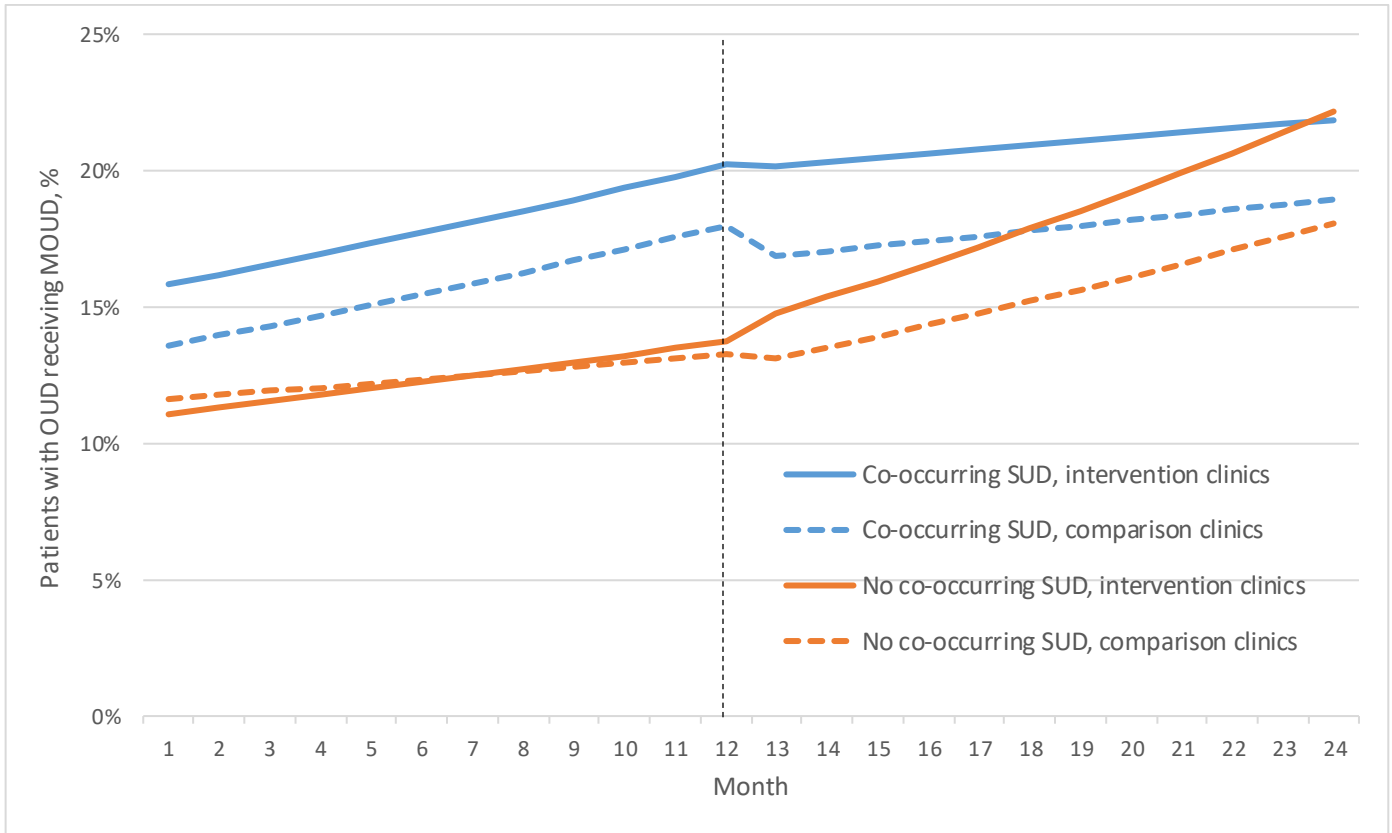
**Table 3.2. MOUD receipt during pre- and post-implementation years compared across presence of co-occurring SUD**

	No co-occurring SUD (N=3,765)		≥1 co-occurring SUD (N=3,723)		p-value <sup>b</sup>	Total (N=7,488)	
	N	(%)	N	(%)		N	(%)
<b>Intervention Clinics</b>							
<b>Buprenorphine/naltrexone in intervention clinic and/or any MOUD in SUD clinic</b>							
Pre-implementation year	726	(19.3)	1,333	(35.8)	<0.001	2,059	(27.5)
Post-implementation year	1,368	(36.3)	1,549	(41.6)	<0.001	2,917	(39.0)
<b>Buprenorphine/naltrexone in intervention clinic</b>							
Pre-implementation year	226	(6.0)	246	(6.6)	0.282	472	(6.3)
Post-implementation year	618	(16.4)	398	(10.7)	<0.001	1,016	(13.6)
<b>Any MOUD in SUD clinic</b>							
Pre-implementation year	574	(15.3)	1,229	(33.0)	<0.001	1,803	(24.1)
Post-implementation year	935	(24.8)	1,369	(36.8)	<0.001	2,304	(30.8)
<b>Comparison Clinics</b>							
<b>Buprenorphine/naltrexone in comparison clinic and/or any MOUD in SUD clinic</b>							
Pre-implementation year	638	(17.6)	1,112	(28.4)	<0.001	1,750	(23.2)
Post-implementation year	993	(27.3)	1,316	(33.6)	<0.001	2,309	(30.6)
<b>Buprenorphine/naltrexone in comparison clinic</b>							
Pre-implementation year	145	(4.0)	173	(4.4)	0.360	318	(4.2)
Post-implementation year	255	(7.0)	206	(5.3)	0.001	461	(6.1)
<b>Any MOUD in SUD clinic</b>							
Pre-implementation year	543	(14.9)	1,069	(27.3)	<0.001	1,612	(21.3)
Post-implementation year	834	(22.9)	1,218	(31.1)	<0.001	2,052	(27.2)

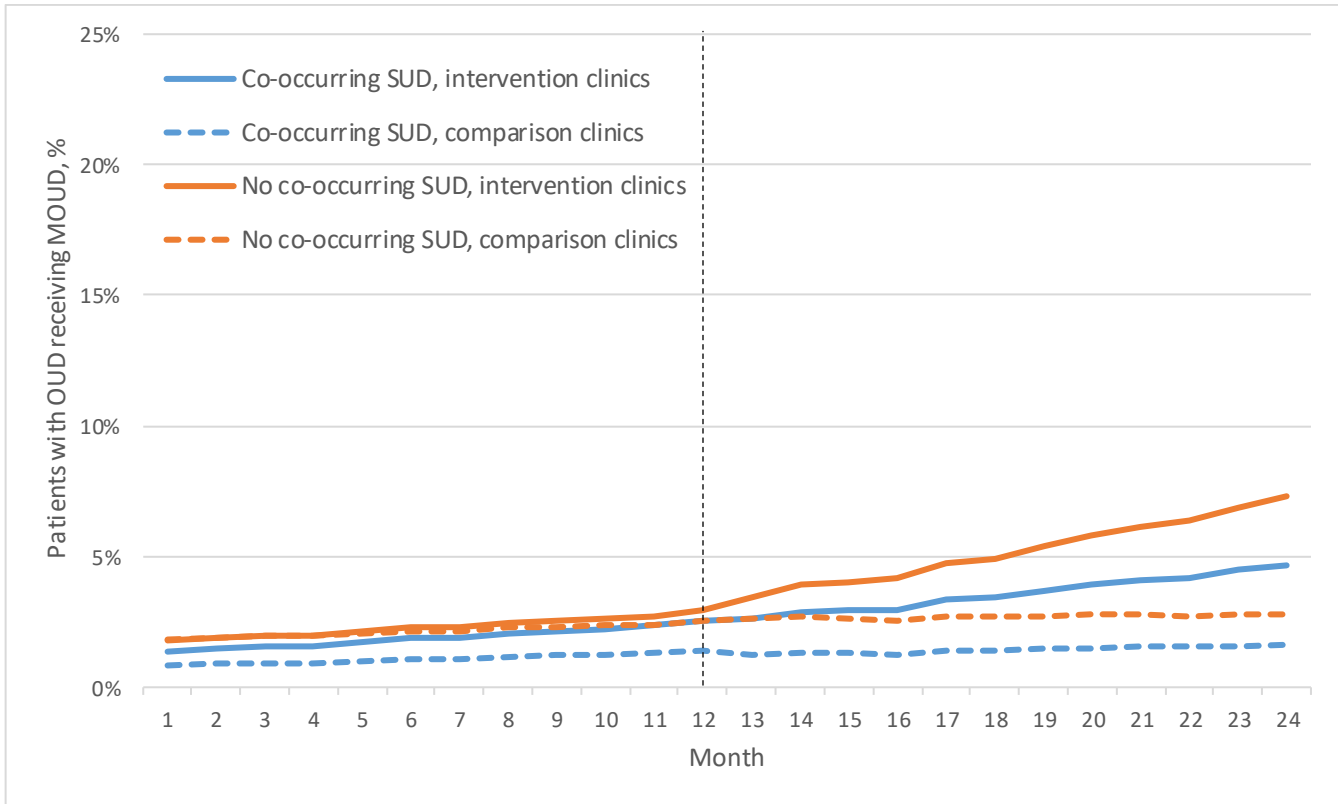
MOUD = medications for opioid use disorder; SUD = substance use disorder

<sup>a</sup>From chi-square test

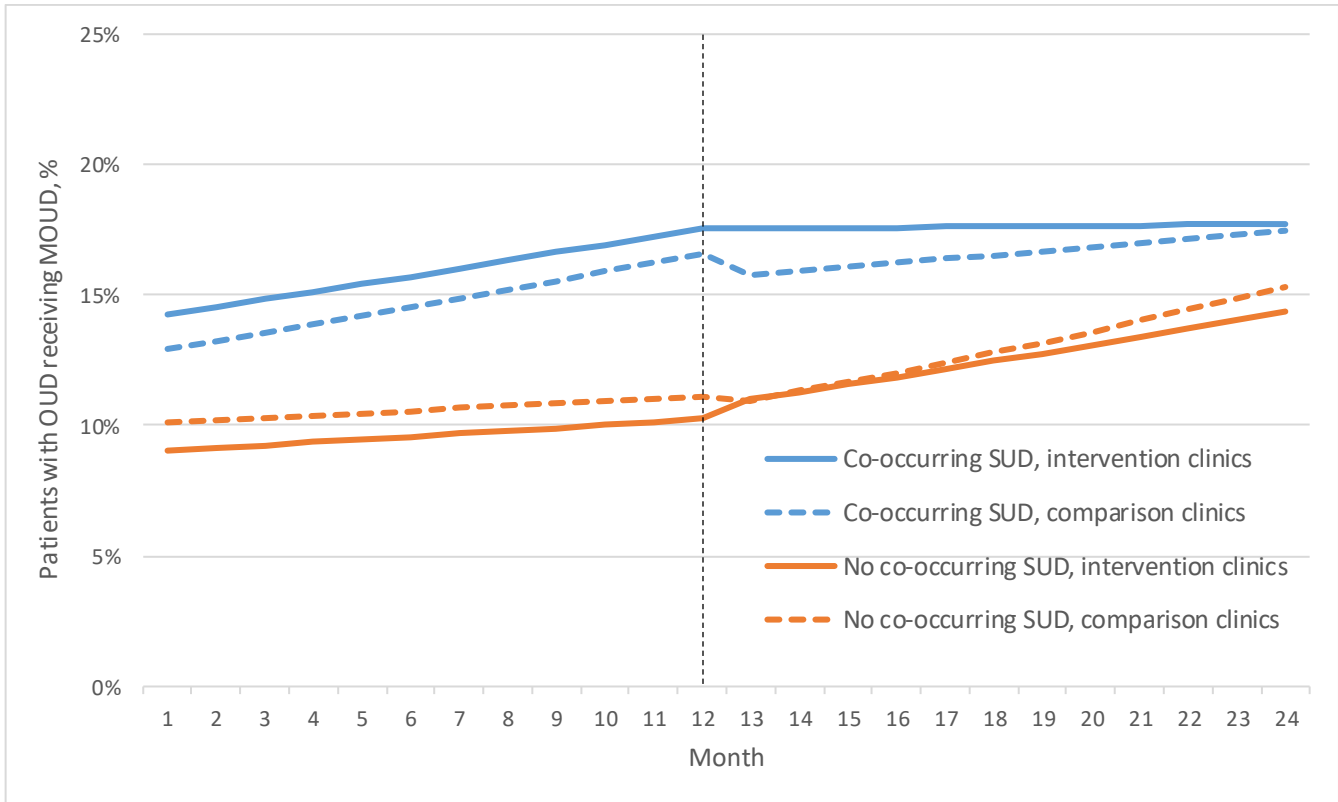
**Figure 3.1. Adjusted Percentage of Patients Receiving Medications for Opioid Use Disorder in SCOUTT and/or SUD clinics**



**Figure 3.2. Adjusted Percentage of Patients Receiving Medications for Opioid Use Disorder in SCOUTT clinics**



**Figure 3.3. Adjusted Percentage of Patients Receiving Medications for Opioid Use Disorder in SUD clinics**



### Appendix 3A. Detailed explanation of interrupted time series models

Models estimated changes in the immediate level and slope of outcomes 12 months prior to and 12 months following implementation, adjusting for the trend in the outcome during the pre-implementation period. Models included 3-way interactions to assess whether the difference in pre/post-implementation changes (immediate level change and change in slope) between intervention and comparison clinics was modified by the presence of co-occurring SUD. The model was specified as:

$$\text{logit}(p)_{jt} = \beta_0 + \beta_1 X_{jt} + \beta_2 \text{TIME}_{jt} + \beta_3 \text{IMP}_{jt} + \beta_4 \text{TIMEAFT}_{jt} + \beta_5 \text{TX}_{jt} + \beta_6 \text{SUD}_{jt} + \beta_7 \text{TX}_{jt} * \text{TIME}_{jt} + \beta_8 \text{SUD}_{jt} * \text{TIME}_{jt} + \beta_9 \text{TX}_{jt} * \text{IMP}_{jt} + \beta_{10} \text{SUD}_{jt} * \text{IMP}_{jt} + \beta_{11} \text{TX}_{jt} * \text{TIMEAFT}_{jt} + \beta_{12} \text{SUD}_{jt} * \text{TIMEAFT}_{jt} + \beta_{13} \text{TX}_{jt} * \text{SUD}_{jt} + \beta_{14} \text{TX}_{jt} * \text{SUD}_{jt} * \text{TIME}_{jt} + \beta_{15} \text{TX}_{jt} * \text{SUD}_{jt} * \text{IMP}_{jt} + \beta_{16} \text{TX}_{jt} * \text{SUD}_{jt} * \text{TIMEAFT}_{jt} + \epsilon$$

For patient  $j$  at time  $t$ ,  $X$ =set of covariates included for confounder adjustment (multiple beta coefficients),  $\text{TIME}$ =time since start of the study;  $\text{IMP}$ =pre- vs. post-implementation (0/1);  $\text{TIMEAFT}$ =time after implementation;  $\text{TX}$ =intervention vs. comparison clinic (0/1); and  $\text{SUD}$ =presence of co-occurring SUD (0/1). We compared two estimates stratified across co-occurring SUD using linear combinations of coefficients: 1) difference between intervention and comparison clinics in the immediate level change in the outcome pre- to post-implementation (SUD=0 group:  $\beta_9$ ; SUD=1 group:  $\beta_9 + \beta_{15}$ ); and 2) difference between intervention and comparison clinics in the change in the slope (trend) of the outcome from pre- to post-implementation (SUD=0 group:  $\beta_{11}$ ; SUD=1 group:  $\beta_{11} + \beta_{16}$ ). We also tested for statistical significance of effect modification by co-occurring SUD by examining the p-values of coefficients  $\beta_{15}$  and  $\beta_{16}$  ( $p < 0.05$ ).

#### Coefficients relevant to assessing immediate level change:

	Difference in level pre/post (intervention clinics)	Difference in level pre/post (comparison clinics)	Difference-in-difference between intervention and comparison clinics
SUD=0	$\beta_0 + \beta_3 + \beta_9$	$\beta_0 + \beta_3$	$\beta_9$
SUD=1	$\beta_0 + \beta_3 + \beta_9 + \beta_{10} + \beta_{15}$	$\beta_0 + \beta_3 + \beta_{10}$	$\beta_9 + \beta_{15}$
			Difference-in-difference-in-difference = $\beta_{15}$

#### Coefficients relevant to assessing slope change:

	Difference in slope pre/post (intervention clinics)	Difference in slope pre/post (comparison clinics)	Difference-in-difference between intervention and comparison clinics
SUD=0	$\beta_4 + \beta_{11}$	$\beta_4$	$\beta_{11}$
SUD=1	$\beta_4 + \beta_{11} + \beta_{12} + \beta_{16}$	$\beta_4 + \beta_{12}$	$\beta_{11} + \beta_{16}$
			Difference-in-difference-in-difference = $\beta_{16}$

**Appendix 3B. Results from post-hoc analyses examining MOUD receipt in SCOUTT clinics stratified by clinic type**

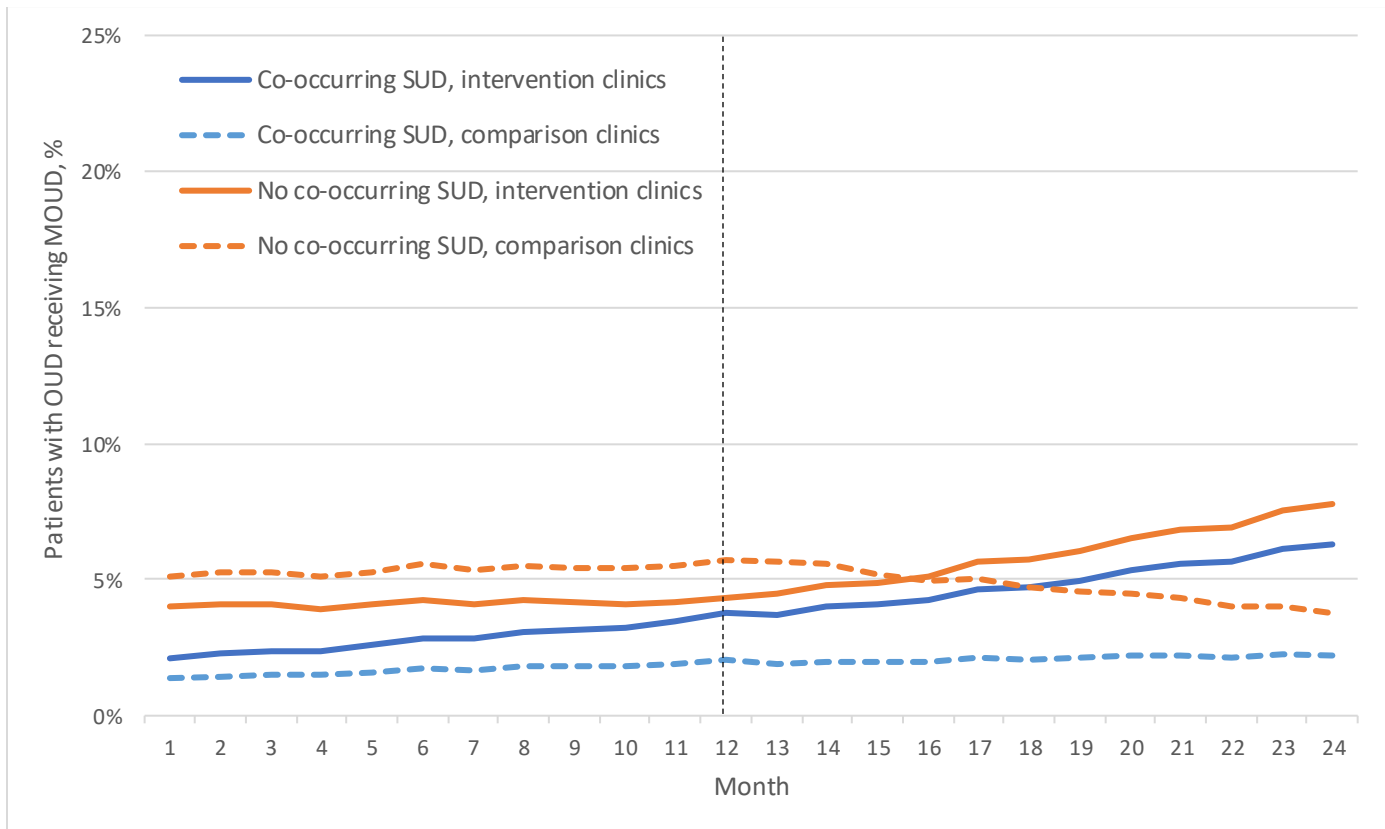
**Figure 3B.1. Adjusted Percentage of Patients Receiving Medications for Opioid Use Disorder in SCOUTT Primary Care Clinics**



When examining MOUD receipt in SCOUTT primary care clinics:

- The difference in the immediate level change between intervention vs. comparison clinics did not significantly differ across co-occurring SUD (p-value for interaction term=0.926).
  - Among patients with co-occurring SUD, the immediate level change did not significantly differ in intervention vs. comparison clinics (aOR: 1.21, 95% CI: 0.77-1.90, p=0.418)
  - Among patients without co-occurring SUD, the immediate level change did not significantly differ in intervention vs. comparison clinics (aOR: 1.17, 95% CI: 0.82-1.68, p=0.383)
- The difference in the slope change between intervention vs. comparison clinics did not significantly differ across co-occurring SUD (p-value for interaction term=0.691).
  - Among patients with co-occurring SUD, the slope change did not significantly differ in intervention vs. comparison clinics (aOR: 1.05, 95% CI: 0.98-1.14, p=0.178)
  - Among patient without co-occurring SUD, the slope change was greater in intervention vs. comparison clinics (aOR: 1.08, 95% CI: 1.01-1.15, p=0.031).

**Figure 3B.2. Adjusted Percentage of Patients Receiving Medications for Opioid Use Disorder in SCOUTT Mental Health Clinics**



When examining MOUD receipt in SCOUTT mental health clinics:

- The difference in the immediate level change between intervention vs. comparison clinics did not significantly differ across co-occurring SUD (p-value for interaction term=0.690).
  - Among patients with co-occurring SUD, the immediate level change did not significantly differ in intervention vs. comparison clinics (aOR: 1.02, 95% CI: 0.72-1.45, p=0.901)
  - Among patients without co-occurring SUD, the immediate level change did not significantly differ in intervention vs. comparison clinics (aOR: 0.94, 95% CI: 0.73-1.20, p=0.610)
- The difference in the slope change between intervention vs. comparison clinics did not significantly differ across co-occurring SUD – but closer to significant than any other interaction term assessing effect modification (p-value for interaction term=0.054).
  - Among patients with co-occurring SUD, the slope change did not significantly differ in intervention vs. comparison clinics (aOR: 1.02, 95% CI: 0.95-1.09, p=0.546)
  - Among patient without co-occurring SUD, the slope change was greater in intervention vs. comparison clinics (aOR: 1.11, 95% CI: 1.06-1.16, p<0.001).

**Figure 3B.3. Adjusted Percentage of Patients Receiving Medications for Opioid Use Disorder in SCOUTT Pain Clinics**



When examining MOUD receipt in SCOUTT pain clinics:

- The difference in immediate level change between intervention vs. comparison clinics did not significantly differ across co-occurring SUD (p-value for interaction term=0.689).
  - Among patients with co-occurring SUD, the immediate level change did not significantly differ in intervention vs. comparison clinics (aOR: 1.57, 95% CI: 0.72-3.43, p=0.254)
  - Among patients without co-occurring SUD, the immediate level change did not significantly differ in intervention vs. comparison clinics (aOR: 1.31, 95% CI: 0.88-1.97, p=0.186)
- The difference in the slope change between intervention vs. comparison clinics did not significantly differ across co-occurring SUD (p-value for interaction term=0.580).
  - Among patients with co-occurring SUD, the slope change did not significantly differ in intervention vs. comparison clinics (aOR: 0.96, 95% CI: 0.78-1.17, p=0.685)
  - Among patient without co-occurring SUD, the slope change did not significantly differ in intervention vs. comparison clinics (aOR: 1.02, 95% CI: 0.93-1.12, p=0.653).

## **Chapter 4: Treating opioid use disorder in veterans with co-occurring substance use: A qualitative study with buprenorphine providers in primary care, mental health, and pain settings**

### **ABSTRACT**

**Introduction:** A growing majority of people with opioid use disorder (OUD) have co-occurring substance use and/or substance use disorders (SUDs), which are associated with reduced likelihood of receiving life-saving OUD treatment medications (MOUD). Expanding MOUD provision and care linkage outside of SUD specialty settings is a key strategy to increase access. Therefore, it is important to understand how MOUD providers in these settings approach care for patients with co-occurring substance use/SUDs. This qualitative study of Veterans Health Administration (VA) clinicians providing buprenorphine care in primary care, mental health, and pain clinics aimed to understand 1) their approach to addressing OUD in patients with co-occurring substance use/SUDs, 2) their perspectives on barriers and facilitators to MOUD receipt for this population, and 3) support needed to increase MOUD receipt for this population.

**Methods:** We interviewed 27 clinicians in the VA northwest regional network. Interviews were transcribed and qualitatively analyzed using inductive content analysis.

**Results:** Participants reported varied approaches to identifying co-occurring substance use/SUDs and to treating OUD in this patient population. Although they reported that this topic was not clearly addressed in clinical guidelines or training, participants generally felt that patients with co-occurring substance use should receive MOUD. Some viewed their primary role as providing this care, others as facilitating linkage to OUD care in SUD specialty settings. Participants

reported multiple barriers and facilitators to providing buprenorphine care to patients with co-occurring substance use/SUDs and linking them to SUD specialty care. They discussed their perceptions of how provider factors, patient factors, organizational factors, and external factors impact MOUD receipt for this population.

**Conclusions:** Efforts are needed to support clinicians outside of SUD specialty settings in providing buprenorphine care to patients with co-occurring substance use/SUDs. These could include clearer guidelines and policies, more specific training, and increased care integration or cross-disciplinary collaboration. Simultaneously, efforts are needed to improve linkage to specialty SUD care for patients who would benefit from and are willing to receive this care, which could include increased service availability and improved referral/hand-off processes. These efforts may increase MOUD receipt and improve OUD care quality for patients with co-occurring substance use/SUDs.

## **INTRODUCTION**

Overdose deaths in the United States are at a record high,<sup>2,3</sup> and most people with opioid use disorder (OUD) do not receive recommended treatment.<sup>1</sup> There are three approved medications for opioid use disorder (MOUD): buprenorphine, methadone and naltrexone.<sup>4</sup> Buprenorphine and methadone are considered first-line treatment and substantially reduce overdose risk.<sup>5-9</sup> While methadone for OUD must be administered through a federally regulated treatment center, buprenorphine can be prescribed outside of substance use disorder (SUD) specialty settings.<sup>4</sup>

A growing majority of people with OUD use alcohol or other non-opioid drugs and/or have co-occurring non-opioid SUDs.<sup>10-13</sup> Studies have found that patients with co-occurring

SUDs are less likely to receive MOUD than those with only OUD.<sup>12,15-17</sup> Efforts to increase MOUD access have tended to overlook the role of polysubstance use and co-occurring SUDs, even though these are highly prevalent among people with OUD and appear to hinder MOUD receipt.<sup>10,19</sup> As patients may face multiple barriers to accessing care in SUD specialty settings,<sup>26</sup> expanding MOUD provision in other clinical settings is a key strategy to increase access.<sup>27,28</sup> It is therefore important to understand how clinicians providing buprenorphine care outside of SUD specialty settings approach care for patients with co-occurring substance use/SUDs, who likely make up a large proportion of their patients with OUD.

Existing research examining providers' perspectives on this topic is limited. Surveys of U.S. buprenorphine providers (including providers in SUD and non-SUD settings) suggest they may be less likely to prescribe buprenorphine to patients with alcohol or benzodiazepine use disorders relative to those with OUD alone, or may increase monitoring frequency for patients using benzodiazepines.<sup>20,32</sup> A study reviewing a random sample of patient charts found that clinicians were less likely to recommend MOUD for patients with OUD and co-occurring stimulant use disorder.<sup>33</sup> A qualitative study assessing implementation of buprenorphine provision in primary care settings found that most clinics increased monitoring or required additional psychosocial treatment for patients using other substances, and had varying "thresholds" at which they dismissed patients or referred them to specialty SUD care due to other substance use.<sup>34</sup> However, this study was not specifically focused on co-occurring substance use and did not assess providers' experiences and perceptions that may drive clinical practices. More in-depth qualitative information from clinicians providing buprenorphine care outside of SUD specialty settings is needed to better understand varying approaches to addressing OUD in patients with co-occurring substance use/SUDs, potential barriers and facilitators to treating them

and/or linking them to SUD specialty care, and what support providers need to care for this population.

The Veterans Health Administration (VA) is the largest OUD treatment provider in the country,<sup>35</sup> over half of VA patients with OUD have co-occurring SUDs, and those with co-occurring SUDs have lower MOUD receipt than those without.<sup>12</sup> Increasing MOUD receipt—including increasing buprenorphine provision outside of SUD specialty settings—is a VA priority,<sup>35,36</sup> and leaders have called for research that leverages the VA's status as a learning health system (i.e., an integrated system that can broadly implement and test new interventions and care models) to improve care for patients with OUD and polysubstance use.<sup>37</sup> This qualitative study of VA clinicians providing buprenorphine care in primary care, mental health, and pain settings aimed to understand 1) their approach to addressing OUD in patients with co-occurring SUDs and/or other substance use, 2) their perspectives on barriers and facilitators to MOUD receipt for this patient population, and 3) support needed to increase MOUD receipt in this population.

## **METHODS**

### **Study sample and recruitment**

We interviewed clinicians in the VA northwest regional network (Veterans Integrated Services Network 20) who provide OUD care outside of SUD specialty settings.<sup>75</sup> Clinicians were eligible to participate if 1) they currently provided OUD care outside of an SUD clinic, and 2) they had prescribed buprenorphine for OUD or managed buprenorphine care (e.g., clinical pharmacy specialists who cannot prescribe but sometimes manage this care<sup>76</sup>) for  $\geq 5$  patients. To identify potentially eligible participants, we obtained a list of buprenorphine prescribers in the

network from VA Pharmacy Benefits Management Services. The list included clinicians who 1) had a waiver to provide buprenorphine for OUD<sup>77</sup> and 2) had prescribed buprenorphine to  $\geq 1$  patient within the past 90 days on 2/16/2022. The list excluded one facility that had switched to a new electronic health record system, for which prescribing information was not available. We also employed snowball sampling to expand recruitment beyond this list.<sup>78</sup> Potential participants were sent a recruitment email and up to two follow-up emails. We used purposive sampling to obtain perspectives across training (physician, nurse practitioner/physician assistant, pharmacist), clinical setting (primary care, mental health, pain), VA facility, and clinic rurality. This study was approved by institutional review boards at the University of Washington and VA Puget Sound Healthcare System.

### **Data collection**

Telephone interviews were conducted from 3/8/2022-5/26/2022 by two interviewers with experience in qualitative data collection and researching and/or providing MOUD care (MCF, CEA). The semi-structured interview guide addressed the following topics: clinicians' training and professional experience; their current practices and perspectives related to providing buprenorphine to patients with co-occurring substance use/SUDs; their perception of how training and clinical guidelines address this topic; what factors impact MOUD receipt for VA patients with co-occurring substance use/SUDs; and what support is needed to increase MOUD receipt for this patient population. The interview guide was developed to assess domains in the Tailored Implementation for Chronic Diseases (TICD) Checklist,<sup>79,80</sup> an implementation science tool that organizes factors influencing provision of evidence-based care into categories including individual health professional factors, providers' perceptions of patient factors, professional

interactions, incentives and resources, capacity for organizational change, and social, political and legal factors. All interviews were audio-recorded and transcribed.

## **Analysis**

Participant characteristics were quantitatively summarized. Transcripts were qualitatively analyzed using inductive content analysis,<sup>81</sup> in which codes were derived from the data and added to the codebook as transcripts were analyzed. All transcripts were independently coded by two analysts with experience in qualitative analysis and substance use-related research (MCF, EMS). The analysts met regularly to review each coded transcript, resolve discrepancies, and add to/refine the codebook as needed. Transcripts were coded using Atlas.ti 22 software.<sup>82</sup> Codes and example quotations were iteratively reviewed by the full investigative team to ensure that themes were supported by the data and reach final themes by consensus. Factors impacting MOUD receipt for patients with co-occurring substance use/SUDs organized under TICD checklist domains.<sup>79</sup>

## **RESULTS**

### **Sample description**

Twenty-seven providers participated in interviews, a 30% response rate among 90 providers who were contacted (this rate excludes 9 providers who responded but did not meet eligibility criteria). Participant characteristics are presented in Table 4.1. Just under three-quarters of participants provided buprenorphine care at a VA medical center (larger facilities that provide a wider range of general and specialty services), and just under half provided buprenorphine care at one or more community-based outpatient clinics (smaller facilities that provide primary care and other common outpatient services; types of services provided vary

across clinics).<sup>83</sup> Most provided buprenorphine care in urban locations, and over one-third provided buprenorphine care in rural locations.<sup>84</sup> The most common clinic type was primary care, followed by mental health, and pain (clinical pharmacy specialists managed care across different clinic types). The most common clinical training was physician, followed by nurse practitioner/physician assistant and pharmacist. Most participants had completed buprenorphine waiver training outside of the VA, and most had received some other type of MOUD education (e.g., in residency, VA meetings or trainings). Participants had been in their current position for an average of 3.5 years and had worked at the VA for an average of 6.9 years. They had provided buprenorphine care for an average of 4.9 years (ranging from 8 months to 16 years) and were currently providing buprenorphine care for an average of 20.4 patients (ranging from zero to 80).

### **Approaches to addressing OUD in patients with co-occurring substance use/SUDs**

#### ***Perceptions of co-occurring substance use/SUDs among patients with OUD***

Most participants reported that co-occurring substance use/SUDs were common among their patients with OUD. Alcohol and cannabis were frequently described as the most common substances, and some participants reported that methamphetamine use was also common or increasing. Benzodiazepines, cocaine, and other drugs were less frequently mentioned. Some participants contrasted patients who use illicit opioids to those who use prescription opioids, perceiving that the former were more likely to use other illicit substances.

#### ***Assessment for co-occurring substance use/SUDs among patients with OUD***

Participants typically assessed other substance use through unstructured questions and/or biological tests (e.g., urine drug screens, blood tests). Less common approaches included administering structured assessments or reviewing health record information (e.g., chart notes,

SUD diagnoses, prescribed medications). Participants expressed mixed opinions on the value of biological tests—some felt they were useful for obtaining more objective information and discouraging other substance use, while others felt repeated testing could be detrimental to their relationship with the patient.

*“I think urine drug screens are a deterrent for them to go out and seek other drugs.” [P2, pain]*

*“I think building rapport with the patient in serial interviews about their relationship with other substances, I find that to be more effective. Particularly because for some individuals, providing urine samples was associated with a punitive system, and it can be detrimental to serially test someone, detrimental to your therapeutic alliance.” [P1, primary care]*

### ***Providing OUD treatment to patients with other substance use/SUDs***

Many participants reported that they prescribed buprenorphine or managed buprenorphine care for patients with co-occurring substance use/SUDs. Most recommended additional services to address other substance use (e.g., treatment for other SUDs, support groups). Some also provided medications for co-occurring alcohol use disorder; these participants noted that buprenorphine and naltrexone cannot be used at the same time, and some reported that they typically prioritized buprenorphine and prescribed alcohol use disorder medications other than naltrexone. Others provided injectable naltrexone instead of buprenorphine to simultaneously treat co-occurring OUD and alcohol use disorder, though some felt naltrexone was a less effective OUD treatment and required high patient motivation.

*“If somebody is really motivated to treat both alcohol and opioid use disorder, [injectable] naltrexone is a great option.” [P8, mental health]*

Some participants described additional measures they took when providing buprenorphine to patients with other substance use, including educating patients about potential risks, motivational interviewing to encourage reduction or cessation, and increasing monitoring through increased frequency of visits, shorter refill periods, and/or increased screening for substance use. Some reported that they sometimes prescribed a lower dose of buprenorphine to patients with co-occurring substance use due to concern about respiratory depression.

*“...we might...lower the [buprenorphine] dose if they’re on max dose and we’re worried about respiratory depression.” [P12, pharmacy]*

Another participant said they increased the dose for patients using methamphetamine due to concerns about fentanyl contamination.

*“With my patients that are actively using meth, given the amount of fentanyl that is in meth, [I] do try to have them on higher doses. I think there is some data that there is a decrease in meth use at higher doses of buprenorphine.” [P23, primary care]*

Although many participants in this study provided buprenorphine to patients with other substance use, several perceived that most VA buprenorphine providers outside of SUD specialty settings do not:

*“Most providers that I work with outside of [SUD] specialty care do not touch patients that use other substances. And they do not start buprenorphine in those patients.” [P13, pharmacy]*

### ***Referring to SUD specialty care for OUD treatment***

Several participants reported referring patients with other substance use to specialty SUD settings for OUD treatment, either for any level of use or more severe

use. Some were willing to provide a short-term prescription until the patient was able to start SUD specialty care or would consider providing buprenorphine if the patient was unwilling to go to the SUD clinic, but others indicated they would not initiate or continue prescribing buprenorphine for these patients.

*“If it’s someone who is not going to abstain from alcohol use, or not wanting treatment for that and is heavily using, that’s someone we would not consider starting in the primary care setting, that’s someone who needs to be seen in the [SUD specialty clinic].” [P15, primary care]*

### **Factors impacting MOUD receipt for patients with co-occurring substance use/SUDs**

Factors impacting MOUD receipt are organized under the TICD Checklist domains and summarized in Table 4.2.

#### ***Providers’ awareness of recommendations***

In general, participants reported that there are not clear recommendations around buprenorphine care for patients with co-occurring substance use/SUDs in guidelines or training. About half of the participants were not familiar with formal clinical guidelines related to this issue, and some noted that providers outside of SUD specialty settings may be less likely to be aware of these guidelines compared to SUD specialists.

*“I should know...if there is [a guideline] I would imagine it’s provided to the [SUD specialty clinic] staff, but not necessarily to primary care providers.” [P15, primary care]*

Similarly, most participants said this topic was not addressed in training they had received on buprenorphine care, or that they did not recall if it was addressed.

*“I went back and looked at the buprenorphine waiver training...no detailed information that I could really easily come up with for clarification or guidance on what’s the best way to manage patients who are not interested in giving up methamphetamines.” [P17, mental health]*

Those who did recall specific recommendations from guidelines or training described varied content, including assessing for other substance use, providing buprenorphine regardless of other substance use, being aware of potential risks and using caution when prescribing, increasing monitoring, and referring patients with other substance use to SUD specialty care rather than prescribing.

*“They say...you give the buprenorphine if [patients] need the buprenorphine, even if they are using other substances. I think I’m pretty much in line with what they’ve been telling me on the teleconferences and the courses I’ve been taking.”*  
[P7, pain]

*“...there wasn’t a lot of discussion [in trainings] about concomitant treatment of opioid dependence and alcohol use disorder. I think the recommendation was to move them onto a more specialized care setting.”* [P4, primary care]

Despite reporting low familiarity with formal guidelines and inconsistent training, participants generally felt that patients should receive MOUD in the presence of other substance use/SUDs. Some viewed their primary role as providing this care, while others viewed their primary role as facilitating linkage to OUD care in SUD specialty settings. Participants described other sources of information that shaped their understanding of OUD care for patients with co-occurring substance use SUDs, including modeling their practice after other providers in their facility, consulting with colleagues (including SUD specialists), and doing their own research.

*“I think most of my practice is more informed by just discussion with colleagues who are specialty trained about how they handle situations.”* [P20, primary care]

### ***Other individual health professional factors***

Participants also described a range of perceptions and attitudes (both their own and their perceptions of other providers) that may influence approaches to addressing OUD in patients with co-occurring substance use/SUDs. Many participants had safety concerns about combining buprenorphine with other substances, which sometimes led to extra precautions (e.g., increased monitoring) or referral to an SUD specialty setting for OUD care. Most were specifically concerned about alcohol and benzodiazepines because they may increase risk of respiratory depression.

*“The biggest concern is if they’re using something else that increases risk of respiratory depression...like benzodiazepines or alcohol, I’d be much more concerned than with cannabis use.”* [P10, mental health]

However, some providers expressed more concern about “illicit” substances.

*“If a veteran ever popped for cocaine, amphetamines, things like this, then that would be immediately a [SUD specialty clinic] situation...Because...they’re illicit substances. There’s already a component of, I’m doing something illegal, unsafe.”*  
[P16, pain]

Participants also described other concerns, including other substance use interfering with adherence to buprenorphine and diversion of buprenorphine to obtain other substances.

*“...there might be some concern for diversion for patients who are using other substances...like diverting half of it in order to obtain money for whatever their other substance of choice is.”* [P12, pharmacy]

Many participants endorsed a “harm reduction” philosophy of buprenorphine provision emphasizing that it is more dangerous to let OUD go untreated than to prescribe buprenorphine to patients with co-occurring substance use. This belief was usually tied to a willingness to prescribe to these patients outside of SUD specialty settings.

*“I think from a harm reduction standpoint, regardless of other substance use, patients should be offered treatment to lower the risk of adverse outcomes from opioid use, including overdose. Because we know that buprenorphine reduces that risk.”* [P6, primary care]

One participant emphasized the role of this philosophy in driving variability in individual providers’ approaches.

*“...there is a sort of a divide between...prescribers who really embrace a harm reduction philosophy and those who don’t...even within our group there are providers who feel more or less willing to continue prescribing if someone is using another substance.”* [P20, primary care]

For some participants, a desire to respect patients’ preferences was another driver of providing buprenorphine for these patients outside of an SUD specialty setting.

*“...there’s a good percentage of patients who would prefer to receive this care in primary care, and we wouldn’t be meeting the needs of those individuals if we mandate that they receive specialist treatment because they’re using other substances.”* [P1, primary care]

Alternately, participants perceived that many providers outside of SUD specialty settings do not prescribe buprenorphine to patients using other substances due to a belief that SUD specialty care is the only appropriate treatment setting for this patient population.

*“I think that...general practitioners are uncomfortable prescribing buprenorphine to people who don't look 'perfect,' right? So, if you're sort of a 'white collar' individual who has an opioid use disorder because of overuse of pain medication, then they're willing to prescribe buprenorphine. But if you're somebody with other co-occurring substances they think that you need to be in an addiction treatment center, or are unwilling to prescribe you buprenorphine, or both.”*

[P11, mental health]

Participants also described how lack of knowledge, skills and experience related to treating patients with polysubstance use among some providers could prevent or delay buprenorphine care.

*“I think it has to do with provider awareness and knowledge about how to treat patients that are more complex...Instead of doing...what they think might be the wrong thing, they may just say, 'sorry you've got to go through withdrawals, I can't prescribe because I'm not comfortable, you have to wait until this consult service calls.' So, it's like a delay in care.”* [P14, pharmacy]

### ***Providers' perceptions of patient factors***

Participants perceived that instability in patients' lives related to other substance use created barriers to engaging in MOUD care in both their clinic and SUD specialty settings. They described several sources of instability including intoxication and withdrawal, mental health conditions, strained relationships, unemployment, housing instability, and legal system involvement.

*“The danger is not necessarily the substance itself, but the chaos it creates in their life, physical and mental health, and socially as well...Their ability to come in for appointments is all over the place.”* [P5, primary care]

Participants also perceived that fear of disclosing other substance use may present a barrier to OUD care for patients with co-occurring substance use/SUDs.

*“[Patients] may be less likely to try and get [OUD] care if they know that they’re using illicit substances, they feel like they’ll be in trouble. So, they just don’t try to get care.”* [P14, pharmacy]

When discussing referring patients with co-occurring substance use/SUDs to SUD specialty care, participants discussed their perceptions of how stigma might impact some patients’ preferences around the setting in which they receive MOUD care. Some perceived that many patients see SUD specialty settings as stigmatizing and therefore prefer to receive treatment in other healthcare settings.

*“A lot of patients will do everything they can to avoid the [SUD specialty clinic]...Due to the stigmatization, they’d rather be treated outside of there if they can.”* [P7, pain]

However, one participant perceived that some patients experience less stigma in SUD specialty care compared to primary care.

*“I would imagine that they would prefer specialty care just because the people that are in specialty care have worked with patients similar to them. So that understanding is there. I hear a lot from patients that their primary care provider doesn’t understand, they’re treating them like an addict.”* [P26, pharmacy]

### ***Professional interactions***

Participants described a broad spectrum of cross-disciplinary collaboration and discussed how varying degrees of collaboration impacted their approach to MOUD care. Some participants had clinicians with SUD expertise integrated into their clinic or had regular close collaboration with them—for example, collaboration between clinicians prescribing buprenorphine outside of SUD specialty settings and SUD clinical pharmacy specialists who manage the care, or regular meetings including SUD specialty care, primary care, mental health, and/or pain providers to discuss complex cases. This type of collaboration was reported by participants from larger and smaller as well as urban and rural facilities. Some participants discussed how collaboration and access to SUD expertise facilitated buprenorphine provision for patients with co-occurring substance use/SUDs outside of SUD specialty settings.

*“It depends on how actively [providers are] engaged in kind of a collegial, collaborative process around care...Some people may have kind of a sharp line over which they don’t prescribe [buprenorphine] in circumstances. And then others who work more with the [SUD specialty clinic] in a collaborative fashion I think are willing to have more flexibility with their prescribing. I think having support for the individual provider from more experienced clinicians is pretty critical to create some more flexibility in that care.” [P4, primary care]*

Other participants described how cross-disciplinary collaboration led to improved handoffs to SUD specialty care rather than increased buprenorphine prescribing in their clinical setting.

*“I feel like one of the things that makes it easier is that we have kind of a whole system where we can do a warm handoff to addiction services...we can kind of work in concert. I know I did not have that when I worked in private, I would just*

*have to recommend the referral, and then ...I don't even know what would happen, if they went, or were getting the care they needed.” [P16, pain]*

Alternately, some participants at both larger and smaller as well as urban and rural facilities reported that care and expertise was siloed between disciplines, which made it more difficult to adequately support patients with co-occurring substance use/SUDs.

*“Having access and really being involved in the substance use clinic, and having a counselor, is what my goal would be [for patients with co-occurring substance use]. But I have to say that I don't have much of an awareness or a relationship with how that system runs. Mental health seems to be quite separate from primary care here.” [P19, primary care]*

Several primary care providers felt that the VA's Primary Care-Mental Health Integration model (PCMHI), a national effort to formally integrate mental health into primary care, did not adequately support substance use-related care.

*“...not every PCMHI person is also comfortable with opioid use disorder, or substance use disorder. So, if we're talking about obstacles, that would be another piece to improve...their knowledge of substance use disorder, since they're kind of connected in the realm of primary care.” [P3, primary care]*

Some participants providing care at smaller, more rural facilities reported that they were the only buprenorphine provider in their clinic. These participants were prescribing buprenorphine to patients with co-occurring substance use/SUDS, suggesting that this isolation was not necessarily a barrier to doing this. However, some noted they would like to have more information about what other providers are doing.

*“I think that maybe I’m not too far off what everybody else does. I would be curious to see how I pair up.”* [P25, primary care]

### ***Incentives and resources***

Participants reported a lack of resources within their clinic needed to provide MOUD to patients with co-occurring substance use/SUDs, including nursing staff, support personnel, and lack of adequate time to address more complex issues with patients. Some described how turnover contributed to lack of time and staff.

*“They want me to see patients every half hour, and some of these patients you need an hour with, because of the issues they have. You can’t deal with alcohol and opioid use disorder...in half an hour.”* [P7, pain]

Participants also discussed resources outside of their clinic. The accessibility of SUD specialty clinic services was described as an important barrier or facilitator to caring for patients with co-occurring substance use SUDs, with respect to referring patients there for MOUD and/or for additional services to address other SUDs. Many mentioned specific barriers including far distance, limited hours of availability, and wait times. Alternately, some described these services as more accessible when they were located at the same facility as their clinic and had same-day access.

*“...the VA serves a population in our [VA regional network] that resides in a very large geographic area. Yet we provide all of our specialty services in two cities that are very difficult for people to access...there are a lot of individuals who would like to receive [SUD specialty clinic] services and cannot because of their geographic location.”* [P1, primary care]

Some participants also described the low availability of other higher-level SUD services needed to support some patients with co-occurring substance use/SUDs, including detoxification services and residential treatment.

*“We need more support at the higher levels of care for people, like some of these really complex patients...I think if it was easier for them to access residential treatment that could go a long way. I think the front door is more open than it used to be, people can walk in and get linked to care, but if their trajectory is not successful...it’s almost like we don’t have enough care at the higher intensity level.”* [P20, primary care]

Finally, some participants described how the availability of other VA services, including mental health and social services, helped patients with co-occurring substance use/SUDs engage in MOUD care.

*“The VA makes it so much easier to care for patients as compared to the community...Our ability to provide housing, and potentially employment, probably has the biggest impacts on our ability to help someone manage their conditions...That’s the thing that sets the VA apart.”* [P5, primary care]

However, some mentioned barriers to accessing these services including distance and wait times for mental health services (particularly in smaller, more rural facilities) and complex processes for signing up for social services.

### ***Capacity for organizational change***

Participants discussed how policies in primary care, mental health and pain impacted MOUD care for patients with co-occurring substance use/SUDs. Some reported that their clinics

employed OUD treatment agreements that require or strongly recommend abstinence from other substances, but that the language and/or enforcement had become more “lenient” in recent years.

*“The old protocol said, ‘I will not abuse any substances.’ And it has a place for the patient to initial. I think the new one says that we recommend not abusing any of the other substances, the verbiage has just become more lenient.”* [P26, pharmacy]

Some linked changes in their clinic’s policy to broader policies encouraging expanded provision of buprenorphine.

*“Originally [no substance use] was part of the contract for treatment. I think it has to do with the changes that have been happening on a bigger scale. It seems like everything that’s coming through, whether it’s local policy, or national policy, there’s just a lot of encouragement for [buprenorphine] to be more widely available, to be available in a variety of different settings, and to get it to people because it seems to really work.”* [P17, mental health]

Participants also discussed the impact of clinic leadership. One participant felt that leadership in their clinic did not support buprenorphine provision for people with co-occurring substance use/SUDs.

*“I feel pressured sometimes, ‘Dr. [name], what are you doing prescribing buprenorphine to this person when they have this urine drug screen for amphetamines?’”* [P24, pain]

Alternately, another participant described how their current VA clinic was more supportive of treating patients with co-occurring substance use compared to the lack of support from leadership in a non-VA setting they had previously worked in.

*“The last place I worked at before coming here...one of the reasons I left was because the administration was saying if they use meth you have to cut them off, if they use benzos, you have to cut them off...frankly, the reason I’m at the VA is because I refused to stop treating patients with polysubstance use.”* [P23, primary care]

Several participants reported that some SUD specialty clinics have restrictive policies around other substance use such as requiring negative urine drug screen results to receive MOUD, or generally require more structured care (e.g., more frequent visits). Some discussed how these restrictions might result in patients with more complex needs who have “stepped up” to receive care in an SUD specialty setting care being lost to follow-up or “stepping off” (i.e., ending up in a lower-level setting for MOUD care).

*“In the VA we have the ‘stepped care’ model for opioid use disorder...we’re like when people just ‘step off.’ That’s some of our patients...I wonder if that’s because in other settings they tend to be more regulated...and more restricted. So, I wonder if [more regulated SUD specialty care] just doesn’t work for some people, and so that’s why we end up seeing them in our sort of catch-all clinic.”*

[P20, primary care]

### ***Social, political and legal factors***

Finally, participants described factors external to the VA healthcare system impacting MOUD care for patients with co-occurring substance use/SUDs. Many participants were providing buprenorphine via telehealth due to the COVID-19 pandemic and reported that telehealth generally did not change their approach to treating patients with co-occurring

substance use/SUDs. However, some reported that it was more challenging to assess for other substance use via telehealth.

*“[Telehealth] doesn’t really impact too much the decision to prescribe buprenorphine [to patients with other substance use], we just have to...ask more questions, ask the same questions in different ways, to try to make sure that you’re getting...as full of an assessment as you can get via phone or via video.”* [P14, pharmacy]

Some participants said that telehealth had increased access to specialty SUD services for patients in rural areas but noted limitations including some patients’ lack of internet/phone access or preference for in-person care. However, some reported that the pandemic had negatively impacted availability of SUD services (e.g., reduced provision of SUD specialty clinic services and residential treatment).

Participants also described how changes in the substance use landscape had impacted MOUD care for patients with co-occurring substance use/SUDs. Some discussed how the legalization and normalization of cannabis use had made them more willing to prescribe buprenorphine for patients who use cannabis, but this change was challenging for some.

*“I was trained in a world where cannabis was an illegal substance...if I were to use the standards that I was trained under, then I would have to kick out...the majority of my patients. So it is, that is a challenge. I feel like I’ve had to be flexible to explain the risks to their long-term goals in their life. And balance that with the stability that they’re getting with [buprenorphine].”* [P18, mental health]

Participants also reported that a sharp increase in fentanyl use, and other opioids being contaminated with fentanyl, had increased risk of overdose for their patients with OUD. They

discussed how this made a harm reduction approach to buprenorphine provision in the presence of co-occurring substance use more urgent.

*“[Prescribing buprenorphine is] definitely safer than having them continue to use opioids that they’re getting off of the street, especially with the increase in the amount of opioids on the street that...are contaminated with fentanyl.” [P6, primary care]*

### **Support needed to increase MOUD receipt among patients with co-occurring substance use/SUDs**

Participants were asked what support they felt was needed to support MOUD provision for patients with co-occurring substance use/SUDs. Support recommended by participants is summarized in Table 4.3.

Participants recommended providing education/training to providers outside of SUD specialty settings related to treating OUD among patients with co-occurring substance use/SUDs. Some suggested specific content including monitoring, buprenorphine dosing, providing injectable vs. oral/sublingual buprenorphine, referral, and motivational interviewing. They also suggested providing data on the risk of death associated with providing vs. not providing buprenorphine when patients are using other substances, and education on harm reduction principles.

*“Maybe some data for data-driven folks, this is the risk of death off buprenorphine for these folks, this is the risk of death with buprenorphine... Because I think people are just so scared to cause harm. And some of the*

*decisions are just about weighing pros and cons, and I think people just do it incorrectly sometimes.” [P23, primary care]*

Participants also recommended increasing collaboration between clinicians providing buprenorphine care outside of SUD specialty settings and SUD specialists. Suggestions included having experts available for consultation and regular meetings to discuss cases.

*“We have wonderful conferences that anybody can pop into to discuss a case...a group of colleagues meeting regularly where you can just be like, ‘Hey, what do you do with this situation that I’ve never encountered before?’ Everyone should have that.” [P8, mental health]*

Participants recommended giving clinicians providing buprenorphine care outside of SUD specialty settings more time to spend with each patient, increasing nursing and other staff in their clinic, and increasing same-day access in their clinic. They also recommended increasing the availability of SUD specialty services and improving linkage to these services through integrating more SUD care into other care settings, locating SUD clinics at the same physical location as other clinics, and improving referral and warm hand-off processes.

*“Maybe co-locating [SUD specialty] treatment programs within primary care. So that stigma goes away, it’s more normalized again.” [P3, primary care]*

Finally, a few participants recommended creating clear institutional policies or guidelines related to providing buprenorphine to patients with co-occurring substance use/SUDs. They discussed how this would help providers feel more supported in taking a harm reduction-informed and patient-centered approach to care.

*“Maybe it would be policy. It would be encouraging to know that, as a provider, if you’re taking this harm reduction approach, that you’re supported. Because it’s*

*scary and it's risky. But we're essentially meeting patients where they are, as opposed to demanding that they meet our requirements in order to have access to a life-saving treatment...just knowing that's a decision, that's an approach that would be supported."* [P17, mental health]

## **DISCUSSION**

This qualitative study examined the experiences and perspectives of VA clinicians providing buprenorphine care in primary care, mental health, and pain clinics related to addressing OUD among patients with co-occurring substance use/SUDs. Although they reported that this topic was not clearly addressed in clinical guidelines or training, participants generally felt that patients should receive MOUD in the presence of other substance use/SUDs. Some viewed their primary role as providing this care, while others viewed their primary role as facilitating linkage to OUD care in SUD specialty settings. Participants described multiple barriers and facilitators to providing buprenorphine to patients with co-occurring substance use/SUDs, as well as barriers and facilitators to linking them to SUD specialty care.

Consistent with the concept of stepped care, patients with OUD who have co-occurring substance use/SUDs may benefit from receiving MOUD in higher-level (e.g., SUD specialty care) rather than lower-level (e.g., primary care) settings.<sup>27,85</sup> However, participants in this study pointed out multiple reasons why many of these patients may not initiate or be retained in care in SUD specialty settings. Therefore, it is important that clinicians providing OUD care outside of SUD specialty settings are supported in caring for patients with co-occurring substance use/SUDs. Although many participants in this study prescribed buprenorphine for this patient

population, they often perceived that most providers outside of SUD specialty settings did not and described multiple barriers.

Participants in this study reported varied approaches to assessing polysubstance use and co-occurring SUDs among patients with OUD. Using validated screening tools to assess for other substance use is recommended for office-based MOUD care,<sup>86</sup> and ongoing work to validate and implement symptom checklists to assess SUDs offers valuable tools for MOUD providers that would help support recommendations.<sup>87-89</sup> SUDs are substantially under-diagnosed in the VA,<sup>74,90</sup> and more consistent screening for other substance use and assessment of other SUDs may help improve the quality of MOUD care provided outside of SUD specialty settings and increase linkage to additional care for other SUDs.

Findings suggest that clinical guidelines related to providing buprenorphine to patients with co-occurring substance use/SUDs should be made more visible to clinicians providing this care outside of SUD specialty settings, and that these clinicians may benefit from more detailed and directive guidance. Clinical guidelines for OUD treatment state that other substance use is not a contraindication for buprenorphine, but mention potential risks (particularly for alcohol and benzodiazepines which may increase risk of respiratory depression) and suggest that some patients using other substances may benefit from receiving OUD treatment in an SUD specialty care setting rather than other settings.<sup>6,18</sup> VA's SUD clinical practice guidelines state that MOUD "should not automatically be discontinued due to a patients' use of another substance," and promote the provision of patient-centered OUD care across multiple care settings.<sup>5</sup> However, many providers may not be familiar with national guidelines or may find them vague. More specific and consistent guidelines/policies communicated at the clinic or facility level may help

providers feel more comfortable and supported in caring for patients with co-occurring substance use/SUDs.

Participants also noted the need for more specific training on how to most effectively treat OUD in patients with co-occurring substance use (e.g., monitoring, dosing), and suggested that providers outside of SUD specialty settings may benefit from education on the relative harms of providing vs. not providing buprenorphine and harm reduction principles. This information could be more systematically included in buprenorphine waiver trainings and continuing education materials. As some providers may gain more information from interactions with colleagues and experience treating patients compared to reading clinical guidelines or attending trainings, these concepts could also be integrated into multiple care improvement activities such as cross-disciplinary meetings or clinical decision-support tools. Efforts are needed to improve integration of SUD care and expertise outside of SUD specialty settings, such as increasing capacity to provide SUD care in PCMH clinics,<sup>91</sup> and creating opportunities for providers in these settings to collaborate with SUD specialists. Additionally, lack of adequate provider time and staffing, consistently reported as barriers in expanding MOUD care,<sup>92,93</sup> remain important problems to be addressed.

Simultaneously, efforts are needed to improve access to SUD specialty clinics and other higher-level SUD care (such as supervised detoxification and residential treatment) for patients who would benefit from and are willing to receive this care. These efforts may include devoting funding and resources to provide these services in more locations and during expanded hours, as well as clarifying referral pathways and creating warm handoff processes. Increased telehealth provision of SUD specialty treatment may increase access for patients living far from VA facilities, and work is needed to continue assessing the effectiveness and improving the quality

of this care.<sup>94,95</sup> Co-locating SUD specialty services with other clinics and use of warm handoffs may facilitate linkage and reduce stigma for patients. Finally, SUD specialty clinics should adopt flexible policies around providing MOUD to patients with ongoing substance use (e.g., not requiring negative urine drug screens to receive MOUD) and may consider other ways to increase flexibility in care for patients who struggle to meet clinic requirements.

This study has strengths and limitations. While a qualitative approach allowed us to obtain rich, detailed information and discover unanticipated factors affecting this care, findings cannot be considered representative of all buprenorphine providers in the regional network. Specifically, providers who agreed to participate may have been more willing to provide buprenorphine care to patients with co-occurring substance use/SUDs than those who did not participate, a possibility supported by the finding that many participants perceived that most other providers outside of SUD specialty settings were not willing to prescribe for these patients. These findings can inform future quantitative surveys of providers that can better assess the prevalence of different barriers and facilitators overall and across different VA facilities and clinic types. Additionally, findings represent provider perspectives which may or may not align with experiences and perspectives of patients—research that quantitatively assesses patient-related barriers is needed, as well as research that includes the perspectives of patients with co-occurring substance use/SUDs. Finally, findings may have limited generalizability in other VA regional networks and in non-VA healthcare settings.

## **CONCLUSIONS**

In this qualitative study of 27 VA clinicians providing buprenorphine care in primary care, mental health and pain clinics, participants reported varied approaches to assessing other

substance use/SUDs and varied approaches to treating OUD for these patients. Participants reported multi-level barriers and facilitators to providing buprenorphine care to patients with co-occurring substance use/SUDs, as well as barriers and facilitators to linking these patients to care in SUD specialty settings. Specifically, they reported a lack of clear recommendations in guidelines and training, and discussed their perceptions of how provider factors (e.g., knowledge and attitudes), patient factors (e.g., life instability related to other substance use and preferences around treatment setting), organizational factors (e.g., cross-disciplinary collaboration, resources, and clinic policies/leadership), and external factors (e.g., the COVID-19 pandemic and changes in the substance use landscape) impacted MOUD receipt for these patients. A growing majority of people with OUD use other substances and/or have co-occurring non-opioid SUDs, and the VA and other healthcare systems need to address barriers to MOUD for these patients. Efforts are needed to support clinicians outside of SUD specialty settings in providing buprenorphine care to patients with co-occurring substance use/SUDs, as well as to improve linkage to SUD specialty clinics and other higher-level SUD care. These efforts may increase MOUD receipt and improve OUD care quality for patients with co-occurring substance use/SUDs.

**Table 4.1. Interview participant characteristics (N=27)**

	<b>N</b>	<b>%</b>
VA workplace type(s) <sup>a</sup>		
VA medical center (VAMC)	14	52%
Community-based outpatient clinic (CBOC)	7	26%
Both VAMC and CBOC	6	22%
VA workplace location(s) <sup>a</sup>		
Urban	17	63%
Rural	6	22%
Both urban and rural	4	15%
Clinic type		
Primary care	12	44%
Mental health	7	26%
Pain	4	15%
Pharmacist (multiple clinic types)	4	15%
Clinical training		
Physician	16	59%
Nurse practitioner/physician assistant	7	26%
Pharmacist	4	15%
Buprenorphine waiver training <sup>b</sup>		
Completed outside of VA	21	78%
Completed through VA	5	19%
Did not complete	1	4%
Received other MOUD education <sup>c</sup>		
Yes	22	81%
No	5	19%
	<b>Mean (SD)</b>	<b>Range</b>
Years in current position	3.5 (2.6)	8 months – 10 years
Years at VA	6.9 (5.7)	8 months – 24 years
Years providing buprenorphine <sup>d</sup>	4.9 (3.3)	8 months – 16 years
Estimated # of patients currently prescribing buprenorphine for <sup>d</sup>	20.4 (22.6)	0 – 80 patients

MOUD = medications for opioid use disorder; VA = Veterans Health Administration

<sup>a</sup>Some participants provided buprenorphine care at multiple VA facilities

<sup>b</sup>Pharmacists cannot obtain a waiver or prescribe buprenorphine, but some had completed the waiver training

<sup>c</sup>Types of other MOUD training included residency training; addiction certification; grand rounds and case review meetings; continuing education courses; VA conferences, trainings, and implementation interventions

<sup>d</sup>Missing for n=1 participant

**Table 4.2. Summary of factors impacting MOUD receipt for patients with co-occurring substance use/SUDs, organized by TICD Checklist domains**

<b>Individual health professional factors</b>
<i>Providers' awareness of recommendations</i>
<ul style="list-style-type: none"> <li>• In general, participants reported that there are not clear recommendations around buprenorphine care for patients with co-occurring substance use/SUDs in guidelines or training.</li> <li>• Other information sources may shape providers' approaches (e.g., colleagues, doing research)</li> <li>• Providers may generally agree that patients using other substances should receive MOUD, but vary in how they view their primary role (i.e., providing the care vs. facilitating linkage to higher-level care)</li> </ul>
<i>Other individual health professional factors</i>
<ul style="list-style-type: none"> <li>• Some providers may lack relevant knowledge/skills/experience</li> <li>• Providers have a range of perceptions/attitudes (safety/other concerns; beliefs about appropriateness of non-SUD care setting; harm reduction philosophy; patient-centered approach)</li> </ul>
<b>Providers' perceptions of patient factors</b>
<ul style="list-style-type: none"> <li>• Life instability related to other substance use may create barriers to receiving MOUD care</li> <li>• Fear of disclosing other substance use may be a barrier to receiving MOUD care</li> <li>• Patients may or may not prefer to receive MOUD in an SUD specialty setting, which may be impacted by addiction-related stigma</li> </ul>
<b>Professional interactions</b>
<ul style="list-style-type: none"> <li>• Collaboration with SUD experts may facilitate buprenorphine provision for patients with co-occurring use/SUDs outside of SUD specialty settings, or facilitate linkage to SUD specialty care</li> <li>• Siloed care/expertise may make it more difficult to adequately support these patients</li> <li>• Existing VA efforts to integrate primary care and mental health may not adequately address SUD care</li> </ul>
<b>Incentives and resources</b>
<i>Within participants' clinics</i>
<ul style="list-style-type: none"> <li>• Lack of adequate time with patients to address complex issues may be a barrier</li> <li>• Lack of nursing and other staff may be a barrier</li> </ul>
<i>Outside participants' clinics</i>
<ul style="list-style-type: none"> <li>• Low accessibility of SUD specialty clinics may be a barrier to linking patients to higher-level MOUD care and/or additional care for other SUDs</li> <li>• Availability of other higher-level SUD care (e.g., detox, residential treatment) may be too low</li> <li>• Mental health and social services provided through the VA may help patients with co-occurring use/SUDs engage in MOUD care, but there may be barriers to accessing these services</li> </ul>
<b>Capacity for organizational change</b>
<ul style="list-style-type: none"> <li>• Clinic policies/treatment agreements banning other substance use may have become more flexible in recent years to encourage increased provision of buprenorphine</li> <li>• Some SUD specialty clinics may still have strict rules around other substance use or generally require more structured care, which may present barriers for some patients with co-occurring use/SUDs</li> <li>• Leadership in primary care, mental health and pain clinics may vary in their support of buprenorphine provision for this population</li> </ul>
<b>Social, political and legal factors</b>
<ul style="list-style-type: none"> <li>• Telehealth does not seem to greatly impact providers' approach to treating OUD among patients with co-occurring use/SUDs, but may make it more difficult to assess other substance use</li> <li>• Telehealth may have increased access to SUD specialty services for some patients in rural areas, however the COVID-19 pandemic may have also decreased provision of these services</li> <li>• Cannabis legalization/normalization may have made some providers more willing to provide buprenorphine care to patients who use cannabis</li> <li>• Concerns about overdose risk related to a rise in fentanyl use may increase the urgency of providing buprenorphine regardless of other substance use</li> </ul>

MOUD = medications for opioid use disorder; OUD = opioid use disorder; SUD = substance use disorder; TICD = Tailored Implementation for Chronic Diseases; VA = Veterans Health Administration

**Table 4.3. Summary of support recommended by participants to increase MOUD receipt among patients with co-occurring substance use/SUDs**

- Create clear institutional policies/guidelines related to providing buprenorphine to patients with co-occurring substance use/SUDs
- Provide more specific education/training to providers outside of SUD specialty settings related to treating OUD among patients with co-occurring substance use/SUDs
- Increase collaboration between providers outside of SUD specialty settings and SUD specialists
- Give buprenorphine providers outside of SUD specialty settings more time to spend with each patient
- Increase nursing and other staff
- Increase same-day availability
- Increase availability of SUD specialty services
- Improve linkage to SUD services (integrate SUD care into other settings, co-locate SUD clinics with other clinics, improve referral and warm hand-off processes)

MOUD = medications for opioid use disorder; OUD = opioid use disorder; SUD = substance use disorder

## **Chapter 5: Conclusions**

Efforts to increase and improve MOUD care should explicitly address the role of co-occurring substance use/SUDs, which are common among people with OUD and have been found to be negatively associated with MOUD receipt.<sup>10-13,15-17</sup> However, more information is needed to effectively address this issue. This dissertation involved three aims: 1) examine associations between distinct types of co-occurring SUDs and either initiation or continuation of MOUD among outpatients with OUD in the national VA healthcare system; 2) assess whether the VA SCOUTT initiative's effectiveness in increasing MOUD receipt was modified by the presence of co-occurring SUDs; and 3) qualitatively assess the perspectives of VA clinicians providing buprenorphine care in primary care, mental health, and pain settings to understand their approach to addressing OUD in patients with co-occurring substance use/SUDs, barriers and facilitators to MOUD receipt for this patient population, and support needed to increase MOUD receipt in this patient population.

### **Summary of findings**

In Aim 1 (Chapter 2), we found that only certain co-occurring SUDs were negatively associated with initiation and/or continuation of MOUD. Alcohol use disorder and cannabis use disorder were negatively associated with initiating any MOUD, and specifically with initiating buprenorphine in secondary analyses examining separate types of MOUD. Among those with prior-year MOUD receipt, alcohol use disorder, cannabis use disorder, and amphetamine/other stimulant use disorder were negatively associated with continuing any MOUD. In secondary analyses, amphetamine/other stimulant use disorder and sedative use disorder were negatively

associated with buprenorphine continuation, while alcohol use disorder was negatively associated with methadone continuation.

In Aim 2 (Chapter 3), we did not find that the effectiveness of the SCOUTT initiative was significantly modified by the presence of co-occurring SUDs. However, results from analyses stratified by the presence of co-occurring SUDs suggest that the initiative may have contributed to a steeper increase over time in MOUD receipt in SCOUTT clinics and an immediate increase in MOUD receipt in SUD clinics among patients without co-occurring SUDs, but not in patients with co-occurring SUDs.

In Aim 3 (Chapter 4), we found that VA buprenorphine providers in primary care, mental health and pain clinics reported varied approaches to assessing other substance use/SUDs and varied approaches to addressing OUD among patients with co-occurring substance use/SUDs. Although they reported that this topic was not clearly addressed in clinical guidelines or training, participants generally felt that patients with co-occurring substance use should receive MOUD. Some viewed their primary role as providing this care, while others viewed their primary role as facilitating linkage to OUD care in SUD specialty settings. Participants reported multi-level barriers and facilitators to providing buprenorphine care to patients with co-occurring substance use/SUDs, as well as barriers and facilitators to linking these patients to care in SUD specialty settings. Specifically, they reported a lack of clear recommendations in guidelines and training, and discussed their perceptions of how provider factors (e.g., knowledge and attitudes), patient factors (e.g., life instability related to other substance use and preferences around treatment setting), organizational factors (e.g., cross-disciplinary collaboration, resources, and clinic policies/leadership), and external factors (e.g., the COVID-19 pandemic and changes in the substance use landscape) impacted MOUD receipt for these patients.

## **Implications and future directions**

Aim 2 findings suggest that focusing on increasing MOUD receipt among patients with co-occurring SUDs could improve the overall effectiveness of ongoing and future MOUD implementation efforts. SCOUTT was implemented in facilities where this patient population was initially less likely to receive MOUD in SCOUTT clinics, but more likely to receive MOUD overall (including in SUD clinics). Therefore, more research is needed to test whether similar interventions may have a greater impact on patients with co-occurring SUDs in facilities that reflect patterns in the national VA (i.e., where patients with co-occurring SUDs are less likely to receive MOUD overall).<sup>12</sup> However, findings from Aim 3 highlight several barriers that can be addressed and facilitators that can be leveraged in MOUD implementation efforts. These could include incorporating validated substance use/SUD screening tools, providing more specific training around MOUD provision for patients with co-occurring substance use/SUDs, promoting principles of harm reduction principles and patient-centered care, and creating opportunities for collaboration with SUD specialists.

Aim 3 also highlighted other important areas for improvement outside of MOUD implementation efforts. Clinical guidelines related to providing buprenorphine to patients with co-occurring substance use/SUDs could be made more detailed and more visible to clinicians providing this care outside of SUD specialty settings. More specific and consistent guidelines and policies communicated at the clinic or facility level may help providers feel more comfortable and supported in caring for patients with co-occurring substance use/SUDs. Additionally, efforts are needed to improve access to SUD specialty clinics and other higher-level SUD care for patients who would benefit from and are willing to receive this care,

including increasing service availability, improving referral processes, and ensuring clinic policies do not prevent OUD access for patients with co-occurring substance use.

Based on findings from Aim 1, the efforts described above should consider that barriers specifically related to co-occurring alcohol, cannabis and amphetamine use disorder may need particular attention. Providers in Aim 3 interviews described safety concerns about providing buprenorphine in the presence of alcohol use specifically, and some were specifically concerned about illicit substances (which would include methamphetamine). They also described how life instability related to other substance use can create barriers to MOUD care, and methamphetamine use in particular may be linked to serious health and social problems for some patients.<sup>58</sup> Interestingly, some providers in Aim 3 interviews noted they were less concerned about providing buprenorphine to patients with cannabis use compared to other substance use. There may be unknown barriers to MOUD for patients with co-occurring cannabis use disorder that are unrelated to provider decision-making. More research is needed to understand the mechanisms underlying negative associations between these specific co-occurring SUDs and MOUD receipt, particularly cannabis use disorder.

In summary, findings from this dissertation suggest that VA patients with alcohol or cannabis use disorders may be most likely to face barriers to MOUD initiation, while those with alcohol, cannabis or amphetamine use disorders may be most likely to face barriers to MOUD continuation. Current efforts to implement MOUD outside of SUD specialty settings may be primarily increasing MOUD receipt (in both SUD and non-SUD settings) for patients without co-occurring SUDs. Providers in these settings report multiple barriers to as well as facilitators of providing MOUD to this patient population and linking them to SUD specialty care. Ongoing and future MOUD implementation efforts can work to address these barriers and leverage these

facilitators to improve MOUD care for patients with co-occurring substance use/SUDs, keeping in mind that barriers specifically related to co-occurring alcohol, cannabis and amphetamine use disorder may need particular focus. This dissertation has limitations. Notably, more research is needed that examines the perspectives of patients with OUD who have co-occurring substance use/SUDs. While this research may have limited generalizability outside of the VA healthcare system, findings may have implications outside of the VA – for example, qualitative findings regarding strengths of the VA system that support MOUD care for patients with co-occurring SUDs (e.g., evolving policies and opportunities for cross-disciplinary collaboration) may provide helpful examples for other healthcare systems. In summary, findings from this dissertation provide a foundation for future work to increase and improve MOUD care for patients with co-occurring substance use/SUDs.

## References

1. Substance Abuse and Mental Health Services Administration. Key Substance Use and Mental Health Indicators in the United States: Results from the 2020 National Survey on Drug Use and Health. (HHS Publication No. PEP21-07-01-003, NSDUH Series H-56). Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration. Accessed March 17, 2022 at <https://www.samhsa.gov/data/sites/default/files/reports/rpt35325/NSDUHFFRPDFWHTMLFiles2020/2020NSDUHFFR1PDFW102121.pdf>. 2021.
2. Hedegaard H, Miniño A, Spencer M, Warner M. Drug Overdose Deaths in the United States, 1999–2020. NCHS Data Brief No. 428. Centers for Disease Control and Prevention. Accessed January 7, 2022 from: <https://www.cdc.gov/nchs/products/databriefs/db428.htm>. 2021.
3. Ahmad F, Rossen L, Sutton P. Provisional drug overdose death counts. National Center for Health Statistics. Accessed January 18, 2022 at: <https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm>. 2022.
4. Volkow ND, Jones EB, Einstein EB, Wargo EM. Prevention and Treatment of Opioid Misuse and Addiction: A Review. *JAMA psychiatry*. 2019;76(2):208-216.
5. Department of Veterans Affairs. VA/DoD Clinical Practice Guideline for the Management of Substance Use Disorders. Accessed January 7, 2022 from: <https://www.healthquality.va.gov/guidelines/MH/sud/VADoDSUDCPG.pdf>. 2021.
6. Substance Abuse and Mental Health Services Administration. Medications for Opioid Use Disorder. Treatment Improvement Protocol (TIP) Series 63 Publication No. PEP21-

02-01-002. Rockville, MD: Substance Abuse and Mental Health Services Administration.  
Accessed January 7, 2022 from:

[https://store.samhsa.gov/sites/default/files/SAMHSA\\_Digital\\_Download/PEP21-02-01-002.pdf](https://store.samhsa.gov/sites/default/files/SAMHSA_Digital_Download/PEP21-02-01-002.pdf). 2021.

7. Wakeman SE, Laroche MR, Ameli O, et al. Comparative Effectiveness of Different Treatment Pathways for Opioid Use Disorder. *JAMA Netw Open*. 2020;3(2):e1920622.
8. Pierce M, Bird SM, Hickman M, et al. Impact of treatment for opioid dependence on fatal drug-related poisoning: a national cohort study in England. *Addiction*. 2016;111(2):298-308.
9. Krawczyk N, Mojtabai R, Stuart EA, et al. Opioid agonist treatment and fatal overdose risk in a state-wide US population receiving opioid use disorder services. *Addiction*. 2020;115(9):1683-1694.
10. Cicero TJ, Ellis MS, Kasper ZA. Polysubstance Use: A Broader Understanding of Substance Use During the Opioid Crisis. *Am J Public Health*. 2020;110(2):244-250.
11. Hassan AN, Le Foll B. Polydrug use disorders in individuals with opioid use disorder. *Drug Alcohol Depend*. 2019;198:28-33.
12. Lin LA, Bohnert ASB, Blow FC, et al. Polysubstance use and association with opioid use disorder treatment in the US Veterans Health Administration. *Addiction*. 2021;116(1):96-104.
13. Bhalla IP, Stefanovics EA, Rosenheck RA. Clinical Epidemiology of Single Versus Multiple Substance Use Disorders: Polysubstance Use Disorder. *Med Care*. 2017;55 Suppl 9 Suppl 2:S24-s32.

14. Lin LA, Bohnert ASB, Blow FC, et al. Polysubstance use and association with opioid use disorder treatment in the US Veterans Health Administration. *Addiction*. 2020.
15. Rhee TG, Rosenheck RA. Buprenorphine prescribing for opioid use disorder in medical practices: can office-based out-patient care address the opiate crisis in the United States? *Addiction*. 2019;114(11):1992-1999.
16. Murphy SM, Fishman PA, McPherson S, Dyck DG, Roll JR. Determinants of buprenorphine treatment for opioid dependence. *J Subst Abuse Treat*. 2014;46(3):315-319.
17. Mackey K, Veazie S, Anderson J, Bourne D, Peterson K. Evidence Brief: Barriers and Facilitators to Use of Medications for Opioid Use Disorder. In: *VA Evidence-based Synthesis Program Reports*. Washington (DC): Department of Veterans Affairs (US); 2019.
18. American Society of Addiction Medicine. The ASAM National Practice Guideline for the Treatment of Opioid Use Disorder: 2020 Focused Update. Accessed March 25, 2022 at: <https://www.asam.org/quality-care/clinical-guidelines/national-practice-guideline>. 2020.
19. Manhapra A, Rosenheck R. Commentary on Lin et al.: Saving lives during the opioid crisis-widening the focus from opioid use disorder to polysubstance use disorder and to multimorbidity. *Addiction*. 2021;116(1):105-106.
20. Knudsen HK, Lofwall MR, Walsh SL, Havens JR, Studts JL. Physicians' Decision-making When Implementing Buprenorphine With New Patients: Conjoint Analyses of Data From a Cohort of Current Prescribers. *J Addict Med*. 2018;12(1):31-39.
21. Green CA, McCarty D, Mertens J, et al. A qualitative study of the adoption of buprenorphine for opioid addiction treatment. *J Subst Abuse Treat*. 2014;46(3):390-401.

22. Payne BE, Klein JW, Simon CB, et al. Effect of lowering initiation thresholds in a primary care-based buprenorphine treatment program. *Drug Alcohol Depend.* 2019;200:71-77.
23. Shiner B, Leonard Westgate C, Bernardy NC, Schnurr PP, Watts BV. Trends in Opioid Use Disorder Diagnoses and Medication Treatment Among Veterans With Posttraumatic Stress Disorder. *J Dual Diagn.* 2017;13(3):201-212.
24. Wyse JJ, Robbins JL, McGinnis KA, et al. Predictors of timely opioid agonist treatment initiation among veterans with and without HIV. *Drug Alcohol Depend.* 2019;198:70-75.
25. Manhapra A, Stefanovics E, Rosenheck R. Initiating opioid agonist treatment for opioid use disorder nationally in the Veterans Health Administration: Who gets what? *Subst Abuse.* 2020;41(1):110-120.
26. Timko C, Schultz NR, Britt J, Cucciare MA. Transitioning From Detoxification to Substance Use Disorder Treatment: Facilitators and Barriers. *J Subst Abuse Treat.* 2016;70:64-72.
27. Gordon AJ, Drexler K, Hawkins EJ, et al. Stepped Care for Opioid Use Disorder Train the Trainer (SCOUTT) initiative: Expanding access to medication treatment for opioid use disorder within Veterans Health Administration facilities. *Subst Abuse.* 2020;41(3):275-282.
28. Campbell CI, Saxon AJ, Boudreau DM, et al. Primary Care Opioid Use Disorders treatment (PROUD) trial protocol: a pragmatic, cluster-randomized implementation trial in primary care for opioid use disorder treatment. *Addict Sci Clin Pract.* 2021;16(1):9.

29. Connock M, Juarez-Garcia A, Jowett S, et al. Methadone and buprenorphine for the management of opioid dependence: a systematic review and economic evaluation. *Health Technol Assess.* 2007;11(9):1-171, iii-iv.
30. Lagisetty P, Klasa K, Bush C, Heisler M, Chopra V, Bohnert A. Primary care models for treating opioid use disorders: What actually works? A systematic review. *PloS one.* 2017;12(10):e0186315.
31. Louie DL, Assefa MT, McGovern MP. Attitudes of primary care physicians toward prescribing buprenorphine: a narrative review. *BMC Fam Pract.* 2019;20(1):157.
32. Lin LA, Knudsen HK. Comparing Buprenorphine-Prescribing Physicians Across Nonmetropolitan and Metropolitan Areas in the United States. *Ann Fam Med.* 2019;17(3):212-220.
33. Lin L, Powell V, Macleod C, Bohnert AS, Lagisetty P. Factors associated with clinician treatment recommendations for patients with a new diagnosis of opioid use disorder. *J Subst Abuse Treat.* 2022:108827.
34. Brooks EM, Tong S. Implementing Office-Based Opioid Treatment Models in Primary Care. *J Am Board Fam Med.* 2020;33(4):512-520.
35. Wyse JJ, Gordon AJ, Dobscha SK, et al. Medications for opioid use disorder in the Department of Veterans Affairs (VA) health care system: Historical perspective, lessons learned, and next steps. *Subst Abus.* 2018;39(2):139-144.
36. Becker WC, Krebs EE, Edmond SN, et al. A Research Agenda for Advancing Strategies to Improve Opioid Safety: Findings from a VHA State of the Art Conference. *J Gen Intern Med.* 2020;35(Suppl 3):978-982.

37. Compton WM, Wiley T, Blanco C. The Importance of Learning Health Systems in Addressing the Opioid Crisis. *J Gen Intern Med.* 2020;35(Suppl 3):891-894.
38. Andersen RM, Davidson PL, Baumeister SE. Improving access to care in America. *Changing the US health care system: key issues in health services policy and management 3a edición San Francisco: Jossey-Bass.* 2007:3-31.
39. Ellis MS, Kasper ZA, Cicero TJ. Twin epidemics: The surging rise of methamphetamine use in chronic opioid users. *Drug Alcohol Depend.* 2018;193:14-20.
40. Kelly MM, Reilly E, Quinones T, Desai N, Rosenheck R. Long-acting intramuscular naltrexone for opioid use disorder: Utilization and association with multi-morbidity nationally in the Veterans Health Administration. *Drug Alcohol Depend.* 2018;183:111-117.
41. Manhapra A, Petrakis I, Rosenheck R. Three-year retention in buprenorphine treatment for opioid use disorder nationally in the Veterans Health Administration. *Am J Addict.* 2017.
42. Vakkalanka JP, Lund BC, Ward MM, et al. Telehealth Utilization Is Associated with Lower Risk of Discontinuation of Buprenorphine: a Retrospective Cohort Study of US Veterans. *J Gen Intern Med.* 2021:1-9.
43. Wyse JJ, McGinnis KA, Edelman EJ, et al. Twelve-Month Retention in Opioid Agonist Treatment for Opioid Use Disorder Among Patients With and Without HIV. *AIDS Behav.* 2022;26(3):975-985.
44. Rogal S, Youk A, Agbalajobi O, et al. Medication Treatment of Active Opioid Use Disorder in Veterans With Cirrhosis. *Am J Gastroenterol.* 2021;116(7):1406-1413.

45. Williams EC, Frost MC, Rubinsky AD, et al. Patterns of Alcohol Use Among Transgender Patients Receiving Care at the Veterans Health Administration: Overall and Relative to Nontransgender Patients. *J Stud Alcohol Drugs*. 2021;82(1):132-141.
46. Bradley KA, Williams EC, Achtmeyer CE, Volpp B, Collins BJ, Kivlahan DR. Implementation of evidence-based alcohol screening in the Veterans Health Administration. *The American journal of managed care*. 2006;12(10):597-606.
47. Finlay AK, Harris AH, Rosenthal J, et al. Receipt of pharmacotherapy for opioid use disorder by justice-involved U.S. Veterans Health Administration patients. *Drug Alcohol Depend*. 2016;160:222-226.
48. Grant BF, Saha TD, Ruan WJ, et al. Epidemiology of DSM-5 Drug Use Disorder: Results From the National Epidemiologic Survey on Alcohol and Related Conditions-III. *JAMA psychiatry*. 2016;73(1):39-47.
49. VHA Office of Rural Health. Chapter 3: Veteran Population, Enrollees, and Patients. A Rural Veterans Health Care Atlas Series -- 2nd edition. Accessed September 9, 2021 at [https://www.ruralhealth.va.gov/docs/atlas/CHAPTER\\_03\\_Vets\\_Enrollees\\_Pts.pdf](https://www.ruralhealth.va.gov/docs/atlas/CHAPTER_03_Vets_Enrollees_Pts.pdf). 2015.
50. Young BA, Maynard C, Boyko EJ. Racial differences in diabetic nephropathy, cardiovascular disease, and mortality in a national population of veterans. *Diabetes Care*. 2003;26(8):2392-2399.
51. Blosnich JR, Montgomery AE, Dichter ME, et al. Social Determinants and Military Veterans' Suicide Ideation and Attempt: a Cross-sectional Analysis of Electronic Health Record Data. *J Gen Intern Med*. 2020;35(6):1759-1767.

52. D'Hoore W, Bouckaert A, Tilquin C. Practical considerations on the use of the Charlson comorbidity index with administrative data bases. *J Clin Epidemiol*. 1996;49(12):1429-1433.
53. Fultz SL, Skanderson M, Mole LA, et al. Development and verification of a "virtual" cohort using the National VA Health Information System. *Med Care*. 2006;44(8 Suppl 2):S25-30.
54. Zou G. A modified poisson regression approach to prospective studies with binary data. *Am J Epidemiol*. 2004;159(7):702-706.
55. Holm S. A Simple Sequentially Rejective Multiple Test Procedure. *Scandinavian Journal of Statistics*. 1979;6(2):65-70.
56. StataCorp. Stata Statistical Software: Release 17, College Station, TX: StataCorp LLC. 2021.
57. Metrik J, Bassett SS, Aston ER, Jackson KM, Borsari B. Medicinal versus Recreational Cannabis Use among Returning Veterans. *Transl Issues Psychol Sci*. 2018;4(1):6-20.
58. Gonzales R, Mooney L, Rawson RA. The methamphetamine problem in the United States. *Annu Rev Public Health*. 2010;31:385-398.
59. Frost MC, Glass JE, Bradley KA, Williams EC. Documented brief intervention associated with reduced linkage to specialty addictions treatment in a national sample of VA patients with unhealthy alcohol use with and without alcohol use disorders. *Addiction*. 2020;115(4):668-678.
60. Witkiewitz K, Vowles KE. Alcohol and Opioid Use, Co-Use, and Chronic Pain in the Context of the Opioid Epidemic: A Critical Review. *Alcohol Clin Exp Res*. 2018;42(3):478-488.

61. Miele GM, Caton L, Freese TE, et al. Implementation of the hub and spoke model for opioid use disorders in California: Rationale, design and anticipated impact. *J Subst Abuse Treat.* 2020;108:20-25.
62. Korthuis PT, McCarty D, Weimer M, et al. Primary Care-Based Models for the Treatment of Opioid Use Disorder: A Scoping Review. *Ann Intern Med.* 2017;166(4):268-278.
63. Hagedorn H, Kenny M, Gordon AJ, et al. Advancing pharmacological treatments for opioid use disorder (ADaPT-OUD): protocol for testing a novel strategy to improve implementation of medication-assisted treatment for veterans with opioid use disorders in low-performing facilities. *Addict Sci Clin Pract.* 2018;13(1):25.
64. Hawkins EJ, Malte CA, Gordon AJ, et al. Accessibility to Medication for Opioid Use Disorder After Interventions to Improve Prescribing Among Nonaddiction Clinics in the US Veterans Health Care System. *JAMA Netw Open.* 2021;4(12):e2137238.
65. Lopez Bernal J, Cummins S, Gasparrini A. The use of controls in interrupted time series studies of public health interventions. *Int J Epidemiol.* 2018;47(6):2082-2093.
66. Grant BF, Goldstein RB, Saha TD, et al. Epidemiology of DSM-5 Alcohol Use Disorder: Results From the National Epidemiologic Survey on Alcohol and Related Conditions III. *JAMA psychiatry.* 2015;72(8):757-766.
67. Stein BD, Gordon AJ, Sorbero M, Dick AW, Schuster J, Farmer C. The impact of buprenorphine on treatment of opioid dependence in a Medicaid population: recent service utilization trends in the use of buprenorphine and methadone. *Drug Alcohol Depend.* 2012;123(1-3):72-78.

68. Finlay AK, Harris AHS, Timko C, et al. Disparities in Access to Medications for Opioid Use Disorder in the Veterans Health Administration. *J Addict Med.* 2020.
69. Lapham G, Boudreau DM, Johnson EA, et al. Prevalence and treatment of opioid use disorders among primary care patients in six health systems. *Drug Alcohol Depend.* 2020;207:107732.
70. Oliva EM, Harris AH, Trafton JA, Gordon AJ. Receipt of opioid agonist treatment in the Veterans Health Administration: facility and patient factors. *Drug Alcohol Depend.* 2012;122(3):241-246.
71. Charlson M, Szatrowski TP, Peterson J, Gold J. Validation of a combined comorbidity index. *J Clin Epidemiol.* 1994;47(11):1245-1251.
72. Wagner AK, Soumerai SB, Zhang F, Ross-Degnan D. Segmented regression analysis of interrupted time series studies in medication use research. *J Clin Pharm Ther.* 2002;27(4):299-309.
73. Kunins HV. Structural Racism and the Opioid Overdose Epidemic: The Need for Antiracist Public Health Practice. *J Public Health Manag Pract.* 2020;26(3):201-205.
74. Hoggatt KJ, Harris AHS, Washington DL, Williams EC. Prevalence of substance use and substance-related disorders among US Veterans Health Administration patients. *Drug Alcohol Depend.* 2021;225:108791.
75. Department of Veterans Affairs. VISN 20: Northwest Network. Accessed June 14, 2022 at <https://www.va.gov/directory/guide/region.asp?ID=1020>. 2021.
76. Pals H, Bratberg J. Improving access to care via psychiatric clinical pharmacist practitioner collaborative management of buprenorphine for opioid use disorder. *J Am Pharm Assoc.* 2022;62(4):1422-1429.

77. Substance Abuse and Mental Health Services Administration. Become a Buprenorphine Waivered Practitioner. Accessed June 6, 2022 at <https://www.samhsa.gov/medication-assisted-treatment/become-buprenorphine-waivered-practitioner>. 2022.
78. Parker C, Scott S, Geddes A. Snowball sampling. *SAGE research methods foundations*. 2019.
79. Flottorp SA, Oxman AD, Krause J, et al. A checklist for identifying determinants of practice: a systematic review and synthesis of frameworks and taxonomies of factors that prevent or enable improvements in healthcare professional practice. *Implement Sci*. 2013;8:35.
80. Wensing M, Oxman A, Baker R, et al. Tailored Implementation For Chronic Diseases (TICD): a project protocol. *Implement Sci*. 2011;6:103.
81. Elo S, Kyngas H. The qualitative content analysis process. *J Adv Nurs*. 2008;62(1):107-115.
82. ATLAS.ti. ATLAS.ti Scientific Software Development GmbH [ATLAS.ti 22 Windows]. Retrieved from <https://atlasti.com>. 2022.
83. Department of Veterans Affairs. About VHA. Accessed June 29, 2022 at: <https://www.va.gov/health/aboutVHA.asp>. 2022.
84. Department of Veterans Affairs. VHA Rurality Map. Accessed June 14, 2022 at <https://vha.maps.arcgis.com/home/webmap/viewer.html?useExisting=1>. 2022.
85. Spelman JF, Edens EL, Maya S, et al. A Facility-Wide Plan to Increase Access to Medication for Opioid Use Disorder in Primary Care and General Mental Health Settings. *Federal practitioner : for the health care professionals of the VA, DoD, and PHS*. 2021;38(10):460-464.

86. Donroe JH, Bhatraju EP, Tsui JI, Edelman EJ. Identification and Management of Opioid Use Disorder in Primary Care: an Update. *Curr Psychiatry Rep.* 2020;22(5):23.
87. Sayre M, Lapham GT, Lee AK, et al. Routine Assessment of Symptoms of Substance Use Disorders in Primary Care: Prevalence and Severity of Reported Symptoms. *J Gen Intern Med.* 2020;35(4):1111-1119.
88. Hallgren KA, Matson TE, Oliver M, Caldeiro RM, Kivlahan DR, Bradley KA. Practical assessment of DSM-5 alcohol use disorder criteria in routine care: High test-retest reliability of an Alcohol Symptom Checklist. *Alcohol Clin Exp Res.* 2022;46(3):458-467.
89. Hallgren KA, Matson TE, Oliver M, et al. Practical Assessment of Alcohol Use Disorder in Routine Primary Care: Performance of an Alcohol Symptom Checklist. *J Gen Intern Med.* 2022;37:1885–1893.
90. Williams EC, Fletcher OV, Frost MC, Harris AHS, Washington DL, Hoggatt KJ. Comparison of Substance Use Disorder Diagnosis Rates From Electronic Health Record Data With Substance Use Disorder Prevalence Rates Reported in Surveys Across Sociodemographic Groups in the Veterans Health Administration. *JAMA Netw Open.* 2022;5(6):e2219651-e2219651.
91. Zubkoff L, Shiner B, Watts BV. Staff Perceptions of Substance Use Disorder Treatment in VA Primary Care-Mental Health Integrated Clinics. *J Subst Abuse Treat.* 2016;70:44-49.
92. Hawkins EJ, Danner AN, Malte CA, et al. Clinical leaders and providers' perspectives on delivering medications for the treatment of opioid use disorder in Veteran Affairs' facilities. *Addict Sci Clin Pract.* 2021;16(1):55.

93. Gordon AJ, Kenny M, Dungan M, et al. Are x-waiver trainings enough? Facilitators and barriers to buprenorphine prescribing after x-waiver trainings. *Am J Addict.* 2022;31(2):152-158.
94. Uhl S, Bloschichak A, Moran A, et al. Telehealth for Substance Use Disorders: A Rapid Review for the 2021 U.S. Department of Veterans Affairs and U.S. Department of Defense Guidelines for Management of Substance Use Disorders. *Ann Intern Med.* 2022;175(5):691-700.
95. Lin LA, Fernandez AC, Bonar EE. Telehealth for Substance-Using Populations in the Age of Coronavirus Disease 2019: Recommendations to Enhance Adoption. *JAMA psychiatry.* 2020;77(12):1209-1210.