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Medication-based treatment among rural, primary care patients diagnosed with opioid use disorder and alcohol use disorder

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1. Introduction

In 2020, 2.7 million individuals aged 12 or older in the United States had an opioid use disorder (OUD), and 28.3 million had an alcohol use disorder (AUD) (SAMHSA, 2020). These disorders increase mortality risk, with 68,630 overdose deaths involving opioids and 99,017 deaths involving alcohol in 2020 (NIDA, 2020; White et al., 2022). A subset of individuals suffer from co-occurring OUD and AUD (OUD+AUD), with consequences over and above each disorder alone (Mintz et al., 2021). Several FDA-approved pharmacotherapies have been recommended to treat these disorders (APA, 2018; Comer et al., 2015). Medications for OUD (MOUD) such as buprenorphine and medications specific for AUD (MAUD) such as acamprosate and disulfiram reduce use and overdose prevalence (Kranzler & Soyka, 2018; Wakeman et al., 2020). Extended-release naltrexone has been approved and found to be safe and effective in treating both OUD and AUD (Korthuis et al., 2017). Although combinations such as buprenorphine together with acamprosate or disulfiram are being used in practice to treat co-occurring OUD and AUD, to date, there are no clinical studies that have examined use of these combinations in practice (Hood, Leyrer-Jackson, & Olive, 2020). Despite their effectiveness, buprenorphine, naltrexone, and MAUD have been underutilized within primary care, with studies finding that only 21% of U.S. primary care patients with OUD were prescribed buprenorphine, and 3.3% of patients with AUD were prescribed acamprosate, disulfiram, or naltrexone (Lapham et al., 2020; Rittenberg et al., 2020).

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Problematically, prescription rates are also low in rural communities despite having similar OUD and AUD rates as non-rural areas (Hallgren et al., 2020). In a study of primary care organizations mostly serving rural patients, 26.1% of patients with documented OUD received buprenorphine, and 1.0% received naltrexone; 3.3% of patients with documented AUD received MAUD and 4.1% received naltrexone (Hallgren et al., 2020). Differences in prescribing patterns between individuals with OUD only, AUD only, and OUD+AUD in rural settings have not been previously studied. The present study used electronic health record (EHR) data from six rural primary care sites to determine the prevalence, types, and duration of buprenorphine, MAUD, naltrexone, and a combination of buprenorphine and MAUD prescription among patients in three substance use disorder (SUD) groups: those diagnosed with OUD only, those with AUD only, and those with OUD+AUD.

2. Material and methods

2.1 Data

We conducted a secondary analysis of EHR data gathered as part of a prospective, single-arm, multisite study conducted by the Clinical Trials Network (CTN-0102) that examined the feasibility of implementing a care coordination model between primary care and external telemedicine providers to expand MOUD access for patients in rural settings (Hser et al., 2023). The overall study sample included 36,762 adult patients who visited one of six rural primary care sites in the Northeastern and Northwestern United States at least once from October 2019 to January 2021. Our study identified 1,874 patients diagnosed with OUD only, AUD only, or OUD+AUD during that timeframe. The clinics' EHR data included information on patients' demographics, diagnoses, and medication prescriptions. Study procedures were approved by the single Institutional Review Board (IRB) – BRANY, and the study was registered at Clinicaltrials.gov (NCT04418453). Measures descriptions are detailed in eMethods in the Supplement.

2.2 Measures

2.2.1 OUD only, AUD only, and OUD+AUD diagnoses.—Patients who had at least one diagnosis code (International Classification of Diseases, 10th revision, Clinical Modification (ICD-10) or SNOMED, see Supplemental Tables 1 and 2) associated with opioid dependence or abuse in the EHR during the 15-month observational period were defined as having OUD. Patients were placed in the OUD only group if they did not also have a diagnosis code associated with alcohol dependence or abuse. Next, patients who had at least one diagnosis code associated with alcohol dependence or abuse were defined as having AUD. Patients were placed in the AUD only diagnosis group if they did not also have a diagnosis code associated with opioid dependence or abuse. Lastly, patients who had both a diagnosis code associated with opioid dependence or abuse *and* a diagnosis code associated with alcohol dependence or abuse were defined as having both disorders and placed in the OUD+AUD group.

2.2.2 Medications.—Medications prescribed for OUD or AUD were pulled from the clinics' EHR using prescription orders from primary care physicians or from the telehealth provider, Bright Heart Health. Medication types fell into five categories: 1) buprenorphine;

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2) oral naltrexone; 3) injectable naltrexone; 4) MAUD (acamprosate, disulfiram); and 5) medication for OUD+AUD (buprenorphine together with acamprosate or disulfiram). We also calculated the number of days that each patient was prescribed a medication appropriate to their diagnosis/diagnoses during the 15-month observational period. The number of days on medication was calculated by summing the total number of days that patients were prescribed medication, with any overlapping days counting as one day and any gaps between medications counting as zero days.

2.2.3 Demographics.—Demographics including age, gender, race, and ethnicity were collected during each patient's first clinic encounter. Lastly, race/ethnicity was specified as a single categorical variable: Black/African American, Hispanic/Latinx, other race/ethnicity, and White. Since the sample was predominantly comprised of patients identifying as White, the present study focused on two main categories, White and non-White, when examining race differences across diagnosis groups.

2.3 Analytic Plan

Group differences (i.e., OUD only, AUD only, OUD+AUD) were tested using the Kruskal-Wallis Test for continuous, non-normally distributed measures (age, days on medication), and chi-square tests for categorical measures (gender, race and ethnicity), with omnibus tests for overall differences followed by Dunn's tests for pair-wise comparisons. Given small sample sizes, Fisher's exact test was used to determine whether there were group differences in the type of medication that was prescribed for patients in the different SUD diagnosis groups. All statistical analyses were conducted using Stata 16 (kwallis; dunntest; tabchi; tab *vars*, e).

3. Results

3.1 Demographic differences

The present study's sample of 1,874 patients ranged in age from 18 to 81 (M=46.1, SD=15.0), with 41.5% of patients being male and 58.5% female. Approximately 54.2% were diagnosed with OUD only, 37.9% with AUD only, and 7.9% with OUD+AUD (Table 1). Patients with AUD only were oldest and had the highest proportion of females. Further, patients with AUD only and those with OUD+AUD had a higher proportion of White individuals compared to patients with OUD only.

3.2 Medications

Approximately 45.1% (n=846) of the study sample were prescribed at least one type of medication, with 88.3% being prescribed buprenorphine, 7.9% oral naltrexone, 0.6% injectable naltrexone, 2.2% MAUD, and 0.9% medication for OUD+AUD. Patients with OUD+AUD were most likely to be prescribed some form of FDA-approved medication to treat at least one of their disorders (p<.001, Table 1). Specifically, patients with OUD+AUD were more likely to be prescribed buprenorphine compared to other medications. Patients with AUD only, however, were the least likely to receive pharmacological treatment, with only 7.8% being prescribed naltrexone, and 2.5% being prescribed other MAUD. Further, patients with OUD+AUD were less likely to receive oral naltrexone than patients with AUD

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only. Lastly, patients with AUD only were more likely to be prescribed oral naltrexone compared to those with OUD only. Prevalence of injectable naltrexone was low for all groups (0.3% or less).

Patients with OUD+AUD (*median*=294.5, *IQR*=279) had significantly more days on medication than patients with OUD only (*median*=223.0, *IQR*=296), and both groups had more days on medication than patients with AUD only (*median*=45.0, *IQR*=60) during the 15-month study period. Of note, among 747 patients receiving buprenorphine, only 30 (4.0%) received injectable buprenorphine during the 15-month study period; most patients were prescribed sublingual buprenorphine. Similarly, most patients prescribed naltrexone received oral tablets (n=67, 93.1%); only 5 patients (6.9%) received injectable naltrexone.

4. Discussion

Overall, the present results indicate that rural patients with AUD were the least likely to receive medication to treat their SUD. Further, while there are currently no clear guidelines on the ideal duration of MAUD prescription, findings of the present study show that, on average, patients with AUD only receive prescriptions for two months. While the National Institute of Alcohol Abuse and Alcoholism (NIAAA) has not established an optimal duration for prescription of medications to treat AUD, a minimum of an initial three months of pharmacotherapy is recommended, with recommendations for continuation if medication is beneficial to the patient (NIAAA, 2007). We also found that patients with OUD+AUD were most likely to be prescribed medication, but when treated tended to be prescribed buprenorphine, which only treats OUD and not AUD. Prevalence of MAUD and naltrexone prescription was very low among patients with OUD+AUD. The low rates of naltrexone prescription are concerning given current evidence of the effectiveness of extended release-naltrexone in treating both disorders (Korthuis et al., 2017). However, low rates of MAUD prescription among patients with OUD+AUD may be due to current lack of evidence from clinical studies on the safety and effectiveness of these combined therapies (Hood et al., 2020).

Our findings update and confirm that medications to treat AUD are likely being underutilized in rural primary care clinics (Hallgren et al., 2020). In rural areas, where behavioral therapies that are commonly used to treat patients with AUD are limited (Rehm et al., 2016), pharmacotherapies may be an important tool in addressing AUD, and efforts should be made to increase awareness and training to support their use in primary care (Poorman, McQuade, & Messmer, 2024). Additionally, greater support for rural primary care clinics including integrating specialty expertise in OUD and AUD in assessing and treating these disorders either on-site or through Project ECHO-like initiatives and implementing telemedicine to remotely deliver treatment for OUD and AUD could be practical next steps for addressing low rates of pharmacological treatment of OUD and AUD in rural communities.

There are some limitations to be considered. This study found an unusually high prevalence of patients with OUD as well as buprenorphine prescription for patients with OUD only or those with OUD+AUD when compared to the prevalence found in prior urban and

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rural samples (Boudreau et al., 2020; Hallgren et al., 2020). This may be related to the current sample being patients in study clinics that were highly motivated to provide MOUD to treat their patients with OUD. As such, the present study may be limited in its generalizability to patients in rural settings overall as well as to patients in non-rural settings. However, given that medications are the most effective form of treatment for OUD, it remains concerning that more than one-third of patients with OUD may not be receiving recommended prescriptions. Another limitation of the current study is that there were low rates of medication prescription for AUD, especially for naltrexone and MAUD. As such, we were unable to assess whether there were significant differences in the types of medications prescribed for patients with OUD only, AUD only, or OUD+AUD. Further research on types of SUD medication treatment with larger sample sizes could shed additional light on treatment patterns and gaps for patients with OUD and AUD in rural areas.

5. Conclusions

Increasing emphasis is being placed on SUDs being treated in primary care, especially in rural areas (Rotenstein et al., 2023). The present study reinforces the gaps in treatment for patients with OUD and/or AUD who live in rural areas and calls for a better understanding of these gaps as well as additional support for rural clinicians in providing pharmacological treatment. Further, the current work highlights the need to better understand rural clinician perspectives on treating OUD+AUD and to provide support for physicians to initiate MAUD in addition to buprenorphine among patients with OUD+AUD.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Group differences by SUD diagnosis group.

	OUD only (n = 1,015)	AUD only (n = 710)	OUD+AUD (n = 149)
Age (years), mean (SD) ***	41.7 (14.0)[a]	52.9 (13.7)[b]	39.2 (11.3)[a]
Female, no. (%) ***	548 (54.0)[a]	459 (64.6)[b]	88 (59.1)[ab]
White, no. (%) *	951 (93.7)[a]	685 (96.5)[b]	144 (96.5)[ab]
Any medication for OUD and/or AUD, no. (%) ***	646 (63.7)[a]	73 (10.3)[b]	127 (85.3)[c]
Medication type, no. (%) ***			
Buprenorphine	634 (62.5)	-	113 (75.8)
Naltrexone (oral)	9 (0.9)	53 (7.5)	5 (3.4)
Naltrexone (injectable)	3 (0.3)	2 (0.3)	-
MAUD	-	18 (2.5)	1 (0.7)
Medication for OUD+AUD	-	-	8 (5.4)
Days on medication, mean (SD) ***	220.5 (152.4)[a]	62.5 (48.3)[b]	264.7 (149.2)[c]

Note: Groups that do not share a common superscripted letter are significantly different at $p < 0.05$.

* $p < 0.05$

*** $p < 0.001$ indicate significant omnibus tests.