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Associations between pharmacotherapy for opioid dependence and clinical and criminal justice outcomes among adults with co-occurring serious mental illness

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Abstract

Adults suffering from a serious mental illness (SMI) and a substance use disorder are at especially high risk for poor clinical outcomes and also arrest and incarceration. Pharmacotherapies for treating opioid dependence could be a particularly important mode of treatment for opioid-dependent adults with SMI to lower their risk for overdose, high-cost hospitalizations, repeated emergency department visits, and incarceration, given relapse rates are very high following detoxification in the absence of one of the three FDA-approved pharmacotherapies. This study estimates the effects of methadone, buprenorphine, and oral naltrexone on clinical and justice-related outcomes in a sample of justice-involved adults with SMI, opioid dependence, and criminal justice involvement. Administrative data were merged from several public agencies in Connecticut for 8,736 adults 18 years of age or older with schizophrenia spectrum disorder, bipolar disorder, or major depression; co-occurring moderate to severe opioid dependence; and who also had at least one night in jail during 2002–2009. Longitudinal multivariable regression models estimated the effect of opioid-dependence pharmacotherapy as compared to outpatient substance abuse treatment without opioid-dependence pharmacotherapy on inpatient substance abuse or mental health treatment, emergency department visits, criminal convictions, and incarcerations, analyzing instances of each 12 months before and after an index treatment episode. Several baseline differences between the study groups (opioid-dependence pharmacotherapy group versus outpatient treatment without opioid-dependence pharmacotherapy) were adjusted for in the regression models. All three opioid-dependence pharmacotherapies were associated with reductions in inpatient substance abuse treatment, and among the oral naltrexone subgroup, also reductions in inpatient mental health treatment, as well as improved adherence to SMI medications. Overall, the opioid-dependence pharmacotherapy group had higher rates of arrest and incarceration in the follow-up period than the comparison group; but those using oral naltrexone had lower rates of arrest (including felonies). The analysis of observational administrative data

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provides useful population-level estimates but also have important limitations that preclude conclusive causal inferences. Large reductions in crisis-driven service utilization associated with opioid-dependence pharmacotherapy in this study suggest that evidence-based medications for treating opioid dependence can be used successfully in adults with SMI and should be considered more systematically during assessments of treatment needs for this population.

Keywords

pharmacotherapy for opioid dependence; co-occurring mental health and substance use disorders; crisis-driven treatment utilization; arrest; incarceration

1. Introduction

Adults who suffer from a serious mental illness (SMI) combined with a substance use disorder are at especially high risk for poor clinical outcomes and also arrest and incarceration;^{1–7} and many, especially racial and ethnic minorities, have limited access to high quality treatment.^{8–12} Substance use disorders are about three times more prevalent among justice-involved SMI individuals than those who are not justice-involved (75% vs. 25%, respectively);^{13–16} and both types of disorders are approximately twice as prevalent among female inmates (30%) than their male counterparts (15%).^{17–18} Opioid dependence, while not as prevalent as alcohol dependence among this population, likely increases SMI adults' risk for high-cost hospitalizations, repeated emergency department visits, and incarceration. In theory, pharmacotherapy for treating opioid dependence could be a particularly important mode of treatment for opioid dependence among adults with SMI, perhaps by reducing drug-seeking behavior, helping patients focus more on psychiatric treatment, or even lessening some psychiatric symptoms. Sustained recovery from addiction may be a key to helping these patients benefit from psychiatric medications for their mental illness and psychosocial treatment as well, and thereby improving clinical outcomes and reduce risk of substance-related criminal recidivism. Empirical research is needed to examine the effectiveness of opioid-dependence pharmacotherapy in this special population with complex needs and barriers to care. This study estimates the effects of three types of opioid-dependence pharmacotherapy on clinical and justice-related outcomes in a sample of justice-involved adults with co-occurring opioid dependence and serious mental illness.

Many studies have demonstrated that pharmacotherapy can be effective for treating opioid dependence.^{19–22} The medications work quickly but it usually takes a long time to change a drug-related lifestyle that often develops over many years. That can be done with motivation, attending self-help groups, counseling, and psychotherapy, in any combination that is appropriate for the patient. The medications can help give them time to work their way out of the addiction. There is also evidence that methadone and buprenorphine are cost-effective, including when combined with psychosocial therapeutic approaches.²³ The literature examining the use of pharmacotherapy in people with opioid dependence and co-occurring mental illness demonstrates that opioid-dependence pharmacotherapy can also be used successfully in people with SMI,^{24–27} without additional side effects or major concerns about negative interactions with psychotropic medications. Finally, several studies have

demonstrated that pharmacotherapy for treating opioid dependence in drug court participants,²⁸ probationers,^{29–30} parolees,³¹ jail releasees,³¹ and a mixed population of individuals with recent criminal justice involvement³¹ was associated with reduced risk of relapse, overdose death, and/or re-offending.

The three FDA-approved medications for treating opioid dependence—methadone, buprenorphine, and naltrexone—are pharmacologically distinct, and may have varying effectiveness for adults with co-occurring SMI. Methadone, a full opioid agonist, is the oldest medication for treating opioid dependence and requires daily dosing in the early phase of treatment at a community-based opioid treatment program. Buprenorphine, a partial opioid agonist, can be prescribed in office-based clinical settings by clinicians who have undertaken special licensure requirements, and, like methadone, does not necessitate that the patient detoxify from opioids before beginning treatment. Oral naltrexone is an opioid antagonist, blocking the effects of opioids, and does require the patient to be fully detoxified and abstinent from opioids for a least one week. Oral naltrexone is also approved for treatment of alcohol dependence. A 2011 review concluded that oral naltrexone for treating opioid dependence is not superior to treatment with placebo or no medication.³² It is also noteworthy that the FDA label for oral naltrexone is for the blockade of the effects of exogenously administered opioids, given it was approved without clinical trials data demonstrating its superiority to placebo but rather based solely on its pharmacologic properties. It is possible that different types of patients are offered and accept these three medications—perhaps those with the most severe opioid dependence tend to use methadone treatment, and the least severe opt for naltrexone once detoxified—which could also influence effectiveness in this population. Other reasons for using oral naltrexone could be having co-occurring alcohol dependence, or initiating the medication during residential treatment after opioid withdrawal is completed and an adequate period of abstinence is obtained. It could also be that individuals who use opioid-dependence pharmacotherapy and are actively involved in the justice system are more likely to use naltrexone than methadone or buprenorphine given a tradition of resistance to the opioid-based medications, in particular, among criminal justice professionals.^{33–37}

A newer literature indicates that opioid-dependence pharmacotherapy is dramatically underutilized in treating substance use disorders, including opioid dependence, due in part to prescribers' reluctance to offer medications, and other barriers to access.^{38–39} However, public health leaders have recently made strong calls for more routine use of opioid-dependence pharmacotherapy,⁴⁰ and federal policy changes have signaled an important shift in collective thinking about addiction and the role that medications can play in recovery. A new 2016 Federal Rule {81 FR 44711} increased caseload limits for buprenorphine provision among eligible clinicians from 100 to 275 patients in 2016; and in a specific effort to improve opioid-dependence pharmacotherapy access and implementation, the Office of National Drug Control Policy instituted a new policy in 2015 requiring all federally-funded drug courts to lift medication-assisted treatment bans and allow eligible clients to use FDA-approved medications to treat their substance use disorders.

In short, more effective treatment of opioid dependence in adults with co-occurring SMI could improve not only their substance use outcomes but also contribute to better mental

health outcomes if they are more likely to achieve clinical stability, which together could yield corresponding gains in quality of life and diminished social burden of disease. Implementation of opioid-dependence pharmacotherapy in vulnerable populations with criminal justice involvement could be particularly important, given the justice system's traditional resistance to this medical treatment approach.^{33–37} This article reports new empirical evidence along these lines from a longitudinal analysis of merged multi-agency records in a large sample of Connecticut adults with co-occurring SMI and opioid dependence who are involved with the criminal justice system.

2. Materials and methods

Administrative records of treatment service utilization and criminal justice events were merged from several public agencies in Connecticut. The Department of Mental Health and Addiction Services (DMHAS) provided records with information on demographic characteristics, clinical diagnoses, outpatient treatment utilization, state psychiatric and substance abuse hospitalizations, and methadone treatment utilization. The Department of Social Services Medicaid program provided service claims for office-based opioid medication prescriptions, psychotropic medications for treating SMI, outpatient service utilization, emergency department (ED) and crisis center visits, and psychiatric and substance abuse hospitalizations in community hospitals. The Department of Correction provided records on periods of incarceration, the Department of Public Safety provided records of criminal offense convictions, and the Judicial Branch provided records on periods of time under probation. The data from these public agencies were matched, merged, and de-identified, originally for another study (NIH R01-MH086232).

Study inclusion criteria were being aged 18 years or older, having a recorded diagnosis of schizophrenia spectrum disorder, bipolar disorder, or major depression, a recorded diagnosis of moderate to severe opioid dependence, at least one night spent in a Connecticut jail or prison during 2002–2009, and having engaged in community-based treatment for opioid dependence sometime during 2003–2008. There were 8,736 adults who met all study criteria and were included in the analytic sample. The Duke University School of Medicine and DMHAS Institutional Review Boards approved this study.

Opioid-dependence pharmacotherapy utilization was identified from DMHAS service records for methadone maintenance treatment, and Medicaid-reimbursed pharmacy claims for buprenorphine or oral naltrexone (extended release naltrexone was not approved for treatment of opioid dependence until 2010). Methadone treatment was provided in community-based opioid treatment programs; buprenorphine was most commonly received during office-based treatment by physicians meeting federal buprenorphine licensure requirements; and oral naltrexone was likely received in specialty mental health or substance abuse programs, or in a federally qualified health centers. For the pharmacotherapy group ($n=4,800$), the index treatment episode was defined as the first observed outpatient opioid-dependence pharmacotherapy episode. The methadone treatment records from DMHAS are specifically for methadone maintenance treatment. (There is a separate level of care code for methadone treatment for detoxification.) In an effort to estimate a comparable starting point for individuals in their courses of treatment, we started counting the maintenance episode

from oral naltrexone and buprenorphine pharmacy claims on the 8th day, assuming that up to the first seven days may have been spent in detoxification or titration of the treatment regimen. For the comparison group (n=3,936), the index treatment episode was defined as the first observed episode of outpatient substance abuse treatment without pharmacotherapy for opioid dependence, or outpatient mental health treatment if accompanied by an opioid dependence diagnosis (to avoid missing cases of integrated mental health and substance abuse treatment, which, in Connecticut, are usually provided in mental health treatment settings).

2.1 Measures

2.1.1 Outcomes—Crisis-driven healthcare utilization and criminal reoffending were measured using dichotomous variables (any versus none) during each month of a two-year observation period. Three separate indicators of crisis-driven healthcare were created: any inpatient mental health treatment, any inpatient substance abuse treatment, and any visits to the ED or other crisis-care provider. An additional treatment outcome variable was constructed to measure the effect of MAT on adherence to psychotropic medications for treating SMI, calculated as the proportion of days in a month in which an individual had a supply of psychotropic medication appropriate for his or her primary psychiatric diagnosis—i.e., the medication possession ratio (MPR). We created a dichotomous indicator of whether the MPR was at least 80% within each given month. This approach is consistent with existing research that also used MPR as a proxy for medication adherence.^{41–44} We did not construct MPR for the opioid-dependence pharmacotherapies given large variability in average length of utilization across medication types; however, we did conduct sensitivity analyses including length of index episode in all outcome models to understand the influence of medication treatment retention on the study findings. Criminal offending was measured as (1) any days in jail or prison, (2) any criminal arrest conviction (felony, misdemeanor, infraction, or violation), and (3) any felony arrest conviction.

2.1.2 Explanatory variables—Two dichotomous main effects variables indicated time-period, the 12-month post-period following initiation of index treatment episode (reference: pre-period); and study group membership, pharmacotherapy group (reference: comparison group). An interaction term of time X study group measured the difference in change over time on model outcomes between the two study groups (pharmacotherapy vs outpatient treatment without pharmacotherapy).

2.1.3. Covariates—Multivariate regression models adjusted for age at time of index treatment; gender; race/ethnicity (non-Hispanic white, African-American, Hispanic/Latino, and other); educational need, measured by DOC on a scale of 1 (lowest) to 5 (highest); primary SMI diagnosis (schizophrenia spectrum disorder, bipolar disorder, or major depressive disorder); and substance dependence type (opioid only or co-occurring opioid with alcohol dependence).

Time-varying covariates that were measured during each month of the observation period included: any days on probation, enrollment in Medicaid (≥ 15 days), any Supplemental Security Income, any outpatient treatment utilization (mental health, substance abuse,

Assertive Community Treatment, residential care), a dichotomous indicator of at least 80% SMI medication possession ratio (included in all models except MPR outcome model, and lagged by one month to minimize reverse causation bias in measuring and interpreting the association between MPR and outcomes of interest), and secular time (measured as twenty-four 30-day periods). We also adjusted our models for time-at-risk in the community, by including as covariates the number of jail days (for inpatient treatment outcome models), inpatient days (for jail outcome model), and total community days (for arrest and ED/crisis outcome models).

2.2 Analysis

A series of Generalized Estimating Equations (GEE)⁴⁵ was carried out to determine if there were group differences in the odds of crisis-driven healthcare utilization and criminal reoffending before and after the index treatment episode. A dataset was constructed with 24 repeated person-month observations, where each individual had 12 months of observations before and after the initiation of the index treatment event (pharmacotherapy or other outpatient substance abuse treatment without pharmacotherapy). Each outcome model included the two dichotomous main effect variables, their interaction terms, and time-fixed and time-varying covariates listed in the measurement section.

We also conducted a set of subgroup analyses stratified by medication type to determine if methadone, buprenorphine, or oral naltrexone specifically were associated with differential effects on the crisis-driven service utilization and criminal justice outcomes measured in the full-sample models.

Finally, we compared service utilization and criminal justice outcomes between two of the pharmacotherapy groups – those using methadone for their index treatment and those using buprenorphine, given these two medications were the most commonly used and relatively comparable.

All analyses were carried out using SAS 9.4 PROC GENMOD procedure.

3. Results

The pharmacotherapy group was more likely than the comparison group to be of non-Hispanic white racial/ethnic background and considerably less likely to be African American; less likely to have schizophrenia and more likely to have a major depression as a co-occurring mental health diagnosis (Table 1). For both study groups, major depression was the most prevalent diagnosis, followed by bipolar disorder, and then schizophrenia. The comparison group was more likely than the pharmacotherapy group to have co-occurring alcohol dependence, but alcohol dependence was high across both groups. The relatively high rates of co-occurring alcohol dependence in the comparison group may be explained by cautious use of methadone maintenance treatment among individuals with severe alcohol dependence.

Among the pharmacotherapy group, those using methadone (n=4,031) in their index treatment episode were less likely to be non-Hispanic white and more likely to be Hispanic/

Latino; more likely to have major depression than those using the other two medications; and less likely to have co-occurring alcohol dependence than those using the other two medications (Table 1). Those using buprenorphine (n=502) were least likely to be female or African-American as compared to those using the other medications. The average age among methadone clients was higher than among individuals using buprenorphine. Individuals using oral naltrexone (n=267) were most likely to be female and far more likely to have co-occurring alcohol dependence.

Notable differences in treatment service utilization between the two study groups in the 12 months preceding their index treatment episode include the pharmacotherapy group having used significantly more outpatient and inpatient substance abuse treatment, but no significant differences in mental health outpatient or inpatient mental health treatment utilization (Table 2). The pharmacotherapy group was also somewhat more likely to have visited the ED and to have no SMI medication claims covered by Medicaid in those 12 months. The service use characteristics suggest that the pharmacotherapy group may have had more severe substance use disorders than the comparison group during the pre-period and perhaps “stepped up” to pharmacotherapy from psychosocial treatment alone. The comparison group was more likely than the pharmacotherapy group to have been arrested or incarcerated in the 12 months prior to index treatment, but the pharmacotherapy group was somewhat more likely to have been on probation (Table 2).

Marked subgroup differences in service utilization were noted during the 12-month pre-period. The oral naltrexone subgroup, in particular, showed relatively high levels of utilization across treatment sectors and types, including outpatient mental health treatment, inpatient mental health and substance abuse treatment, and psychotropic medication for treating SMI (relatively more patients with a high MPR and fewer with no SMI medication use, compared to the other medication subgroups), as well as receipt of SSI (Table 2). The methadone subgroup used less outpatient mental health care than the other two medication subgroups and had more ED/crisis visits. More than 80% had no utilization of SMI medication during the pre-period. The buprenorphine group also had significantly less treatment utilization compared to the oral naltrexone group, including less outpatient and inpatient mental health care, and were more likely to have used no SMI medication during the pre-period.

Criminal justice involvement also varied by index-medication type among the pharmacotherapy group, including relatively few arrests among the methadone subgroup, relatively high prevalence of probation among the buprenorphine subgroup, and relatively high levels of arrest among the oral naltrexone group (Table 2).

The large majority of individuals in the pharmacotherapy group used methadone during their index treatment episode (Table 3) and any subsequent pharmacotherapy episodes during the follow-up period. Methadone was also associated with significantly longer treatment duration (mean number of days 206.92, SD: 122.05) than either buprenorphine (mean days 110.48, SD: 111.32) or especially oral naltrexone (mean days 45.75, SD: 60.81).

In the full sample regression models, (Table 4), MAT was associated with increased odds of incarceration (OR: 1.35, 95% CI: 1.24 – 1.07) and arrest (OR: 1.23, 95% CI: 1.13 – 1.33) over time versus the comparison group. MAT was, however, associated with sizable relative reductions in both inpatient substance abuse treatment (OR: 0.38, 95% CI: 0.34 – 0.43) and ED/crisis visits (OR: 0.81, 95% CI: 0.73 – 0.91) after initiating the index treatment episode. No significant differences were found in the full sample between study groups in inpatient mental health treatment and adherence to SMI medication after index treatment began.

The analyses that stratified by medication type revealed significant differences in the extent to which the opioid-dependence medications were associated with the range of criminal justice and service utilization outcomes, with the subgroup using oral naltrexone having the most favorable outcomes across medication types (Table 5). In the methadone subgroup, both the methadone and comparison groups had reductions in odds of incarceration after initiating their index treatment episode, but the pharmacotherapy group's reduction was significantly smaller (OR: 1.39, 95% CI: 1.27 – 1.52). The odds of arrest after initiating treatment were higher among the methadone group than the comparison group. (OR: 1.28; 95% CI: 1.17 – 1.40). Regarding service utilization, the methadone group had large relative reductions in both inpatient substance abuse treatment (OR: 0.35, 95% CI: 0.31 – 0.39) and ED visits (OR: 0.79, 95% CI: (0.70 – 0.89).

Among the subgroup using buprenorphine, there were no significant differences from the comparison group for criminal justice outcomes (Table 5). Like the methadone group, they also had substantial relative reductions in inpatient substance abuse treatment (OR: 0.54, 95% CI: 0.43 – 0.67).

The subgroup using oral naltrexone had increased odds of incarceration as compared to the comparison group (OR: 1.62, 95% CI: 1.28 – 2.05), but had a relative reduction in odds of any type of arrest (OR: 0.80, 95% CI: 0.64 – 0.99) and also, specifically, felony convictions (OR: 0.68, 95% CI: 0.46 – 1.00) (Table 5). The oral naltrexone group also had consistently favorable service utilization outcomes, with significant reductions in both inpatient mental health treatment (OR: 0.61, 95% CI: 0.43 – 0.89) and inpatient substance abuse treatment (OR: 0.61, 95% CI: 0.47 – 0.79), as well as significant improvements in adherence to SMI medication (OR: 1.56, 95% CI: 1.13 – 2.16).

The analyses comparing the subgroups of individuals using either methadone or buprenorphine for their index treatment indicated that buprenorphine was favorable as compared to methadone on some outcomes but not others (Table 6). Specifically, the buprenorphine subgroup had lower odds of incarceration than the methadone subgroup (OR: 0.67, 95% CI: 0.55 – 0.82), and better odds of good adherence to SMI medications (OR: 1.43, 95% CI: 1.05 – 1.93). The buprenorphine group, however, had significantly higher odds of inpatient substance abuse treatment than the methadone group (OR: 1.52, 95% CI: 1.23 – 1.87).

Outcomes from the sensitivity analyses that included length of index treatment episode for the pharmacotherapy group were consistent with our model results presented here.

4. Discussion

The results of these analyses suggest that opioid-dependence pharmacotherapy was associated with substantial reductions in crisis-driven service utilization among justice-involved, opioid-dependent adults with SMI, including reductions for all pharmacotherapy subgroups in inpatient substance abuse treatment, and especially for the oral naltrexone subgroup, which had reductions in both inpatient substance abuse and mental health treatment, as well as improved adherence to SMI medications. It is possible that lower rates of crisis care among the pharmacotherapy group versus comparison group were related to the lower prevalence of schizophrenia and bipolar disorder in pharmacotherapy group; but any average differences between study groups that were driven specifically by psychiatric diagnoses would be relatively stable over time, and in this sample the pharmacotherapy group had reductions in crisis care after initiating opioid-dependence medications. Reductions in inpatient treatment for all three pharmacotherapies may mean that they experienced fewer opioid relapses and/or fewer mental health crises. If so, reductions in inpatient care among this population could yield substantial savings for the public behavioral healthcare system given the high cost of hospitalization.

The associations between pharmacotherapy and criminal justice outcomes were more mixed. In the full-sample models and the models for the methadone and oral naltrexone strata, pharmacotherapy was associated with smaller reductions in the rate of incarceration than the comparison group. More individuals in the pharmacotherapy group were on probation in the follow-up period than their counterparts in the comparison group (data not shown), and it is known that greater legal scrutiny can result in more incarceration, especially for individuals with co-occurring substance use and mental health disorder.⁴⁶ It is possible, then, that the pharmacotherapy group's probation status, with correspondingly heightened oversight, contributed to their higher rate of incarceration. It may also be that other legal involvement (e.g., statewide jail diversion program participation) was part of their initiation of pharmacotherapy, and that other outstanding criminal charges emerged at that time and had to be resolved, resulting in jail time in some cases. Such an interpretation could be consistent as well with the criminal justice outcome findings for the oral naltrexone subgroup, for whom pharmacotherapy was associated with smaller improvements in incarceration than the comparison group, but significant reductions in new arrests, including felonies (which included new felony drug charges).

Clearly, pharmacotherapy alone cannot provide a “vaccine” against future criminal involvement in some individuals who offend for reasons other than those directly related to their mental illness or opioid dependence. This would be generally consistent with examples in the literature of interventions for mentally ill adults at risk for criminal justice involvement that are associated with improved clinical engagement and functioning, but not reductions in offending risk.^{47–50} The social environments that surround many in the study population expose them regularly to criminal activity and increase their own risk of involvement;^{51–52} for those with strong criminogenic risk factors, treatment that does not address them is likely to have a limited impact on future criminal behavior.

The subgroup that used oral naltrexone in its index treatment episode had the strongest associations with improvements in treatment-related outcomes and reductions in convicted arrests, including felonies. One possible explanation for this differential association is that this subgroup was different to begin with, given the necessity to fully detoxify from opioids before beginning oral naltrexone treatment. As a result of this selection factor, perhaps the oral naltrexone subgroup had less severe opioid dependence on average, were generally more treatable, and/or motivated to succeed in treatment. This medication subgroup had the highest representation of women among the three pharmacotherapies, and also substantially more women than the comparison group. The significant reduction in felony convictions for this medication group only could be attributed to some extent to the medication if oral naltrexone was effective in treating their opioid dependence and if prior offending among the group's women had been driven largely by their opioid use. It could also be that, among the 82% of this subgroup that was also alcohol dependent, oral naltrexone worked simultaneously to treat both opioid and alcohol dependence, thereby more fully addressing their substance use problems and leading to better outcomes. The findings for this group should be interpreted with caution, however, given the potential for unmeasured selection factors affecting medication choice, evidence that oral naltrexone has not been found to be more effective than treatment without medication or placebo,³² and also short average length of treatment as compared to those who used methadone and buprenorphine.

The study has important limitations. Administrative records of SMI diagnoses are not as reliable as direct concurrent assessments using structured diagnostic tools. DMHAS does, however, conduct diagnostic assessments at intake for both outpatient and inpatient treatment, and reviews those diagnoses every six months or more frequently to help ensure their validity. A randomized controlled trial would have yielded more definitive findings than our quasi-experimental design, since some differences between the groups may not be captured by the administrative data. Moreover, our study groups were non-equivalent on several dimensions that could not be completely controlled by means of multivariable adjustment. Specifically, the pharmacotherapy group had significantly more crisis-driven service utilization and inpatient and outpatient treatment for substance use in the 12 months preceding index treatment, suggesting they had more severe disorders than their counterparts in the comparison group. A propensity scores analysis⁵³ was attempted to adjust for confounding in this observational sample, but it performed poorly in generating matched sample, and gave imprecise estimates of treatment effect. We found that conventional covariate adjustment approach applied in this study outperformed the propensity score approach and provide less biased treatment effect estimates.

In addition, it is possible that having counted buprenorphine and oral naltrexone utilization starting on the 8th day, in an effort to estimate a comparable starting point of observation for the three different medications, introduced a selection effect by only including those who complete the earliest stage of treatment, and possibly to a greater extent for oral naltrexone given its relatively low average duration of index treatment and high dropout rates early in treatment. That should be considered during interpretation of medication-specific findings, especially for the oral naltrexone subgroup analyses, but that selection effect likely does not have a significant influence on analyses for the overall sample given the small size of the oral naltrexone group and that methadone treatment predominated. Also, concurrent cocaine

dependence was not captured in these analyses, so the extent to which it may predict treatment dropout⁵⁴ is not reflected here. Also, the pharmacotherapy programs may have differed in the quality and nature of their psychosocial programs.

Generalizability of the findings to other populations and regions may be limited somewhat by sample selection factors that produced baseline differences in opioid-dependence pharmacotherapy access in Connecticut. Specifically, adults with co-occurring SMI and opioid dependence had relatively good access to pharmacotherapy treatment given their high rate of Medicaid enrollment (80 – 90 percent of this study sample was eligible and enrolled in Medicaid at some time during the two-year study window), as compared to justice-involved adults with substance use disorders only—most of whom are uninsured and not Medicaid-eligible. The study window closed before Medicaid expansion under the Affordable Care Act (ACA), but Connecticut had a General Assistance program in place prior to 2010, where low-income childless adults were eligible for medical assistance including for medications.⁵⁵ Furthermore, many states' Medicaid formularies cover opioid-dependence pharmacotherapy at minimal out-of-pocket expense. As of 2013, for treatment of opioid dependence, 31 states' Medicaid programs covered methadone maintenance treatment, all 50 states covered buprenorphine, 42 states covered naltrexone, and 28 states covered all three medications.⁵⁶ Conversely, in states that have not expanded Medicaid or among individuals in expansion states that continue to be ineligible and uninsured, opioid-dependent adults rely on free behavioral healthcare for indigent populations and have very limited access to pharmacotherapy, if any. Adults with co-occurring SMI may also be more likely to have established treatment regimens, which could have facilitated the addition of pharmacotherapy for treating their substance use disorder. Nationally, ACA Medicaid expansion has played an important role in expanding access to pharmacotherapy for treating opioid dependence in the states that have adopted the policy.

5. Conclusions

There were significant associations between opioid-dependence pharmacotherapy and reductions in crisis-driven service utilization—in particular, inpatient hospitalization—demonstrated in these analyses. Reductions in inpatient treatment for this population with complex and challenging behavioral health disorders could result in important cost savings for public treatment systems. Oral naltrexone, in particular, was associated with reduced risk of new arrests—including felonies. Next steps in this line of research would include studies to better understand how to ameliorate barriers to opioid-dependence pharmacotherapy for this population and improve prescribing rates. Large reductions in crisis-driven service utilization associated with pharmacotherapy in this study suggest that evidence-based medications for treating opioid dependence can be used successfully in adults with SMI—substantially reducing both the individual burden and social cost of these complex problems—and should be considered routinely as an important treatment option.

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Availability without accessibility? State Medicaid coverage and authorization requirements for opioid dependence medications.

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Highlights

- Opioid-dependence pharmacotherapy is effective for adults with severe mental illness and opioid dependence.
- Opioid-dependence pharmacotherapy substantially reduces this population's risk for hospitalization.
- Naltrexone appears to reduce risk for convicted arrests, including felonies.
- Opioid-dependence pharmacotherapy was not superior to other treatment in reducing incarceration risk.
- Opioid-dependence pharmacotherapy should be routinely considered as a treatment option for this population.

Table 1

Demographic and clinical characteristics of sample of opioid-dependent adults with severe mental illness in CT during 12 months before index treatment episode, by opioid pharmacotherapy type and study group (n=8,736)

	Opioid pharmacotherapy group (n=4,800)				Comp group (n=3,936)			
	Methadone (n=4,031)	Buprenorphine (n=502)	Naltrexone (n=267)	%	All pharmacotherapy types	N	%	
<i>Demographic and clinical characteristics</i>								
Age (Mean, SD)	36.22 (8.94)	34.27 (10.13)	35.29 (9.77)		35.96 (9.13)	35.71 (9.58)		
Gender								*
Female	1,453 36.05 %	155 30.88 %	109 40.82 %		1,717 35.77 %	1,296 32.93 %		
Male	2,578 63.95 %	347 69.12 %	158 59.18 %		3,083 64.23 %	2,640 67.07 %		
Race/ethnicity								***
White	2,420 60.03 %	374 74.50 %	198 74.16 %		2,992 62.33 %	2,077 52.77 %		
Black/African-American	439 10.89 %	37 7.37 %	37 13.86 %		513 10.69 %	944 23.98 %		
Hispanic/Latino	1,162 28.83 %	90 17.93 %	29 10.86 %		1,281 26.69 %	897 22.79 %		
Other (Native American, Asian)	10 0.25 %	1 0.20 %	3 1.12 %		14 0.29 %	18 0.46 %		
SMI diagnosis								***
Schizophrenia spectrum	669 16.60 %	75 14.94 %	54 20.22 %		798 16.63 %	827 21.01 %		
Bipolar disorder	1,071 26.57 %	174 34.66 %	98 36.70 %		1,343 27.98 %	1,034 26.27 %		
Major depressive disorder	2,291 56.83 %	253 50.40 %	115 43.07 %		2,659 55.4 %	2,075 52.72 %		
Substance dependence disorder								***
Opioid and alcohol	1,735 43.04 %	281 55.98 %	220 82.40 %		2,236 46.58 %	2,484 63.11 %		
Opioid only	2,296 56.96 %	221 44.02 %	47 17.60 %		2,564 53.42 %	1,452 36.89 %		

* Significant at 5% level;

** significant at 1% level;

*** significant at 0.1 %

Asterisks beside Comp Group column indicate comparison between All MAT group and Comp group; within-group MAT type comparisons: a=methadone vs. buprenorphine; b=methadone vs. naltrexone; c=buprenorphine vs. naltrexone.

SMI=Serious mental illness

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Table 2

Service utilization and justice involvement among opioid-dependent adults with severe mental illness in CT during 12 months before index treatment episode, by opioid pharmacotherapy type and study group (n=8,736)

	Opioid pharmacotherapy group (n=4,800)				Comp group (n=3,936)			
	<u>Methadone (n=4,031)</u> N %	<u>Buprenorphine (n=502)</u> N %	<u>Naltrexone (n=267)</u> N %	<u>All pharmacotherapy types</u> N %	<u>Methadone (n=4,031)</u> N %	<u>Buprenorphine (n=502)</u> N %	<u>Naltrexone (n=267)</u> N %	<u>All pharmacotherapy types</u> N %
<i>Treatment service utilization</i>								
Mental health outpatient (mean number, SD)	6.22 (21.18)	8.25 (21.63)	19.76 (41.55)	7.18 (22.76)	7.20 (25.63)			
Substance abuse outpatient (mean number, SD)	20.48 (42.72)	21.63 (41.30)	25.46 (41.30)	20.88 (42.47)	5.92 (21.94)			***
Any MH inpatient days	398 9.87 %	68 13.55 %	86 32.21 %	552 11.50 %	505 12.83 %			
Any SA inpatient days	1,834 45.50 %	247 49.20 %	140 52.43 %	2,221 46.27 %	882 22.41 %			***
Any ER/crisis visits	1,092 27.09 %	128 25.50 %	128 47.56 %	1,355 28.23 %	958 24.34 %			***
Pre-index SMI MPR average								***
No recorded MPR	3,339 82.83 %	351 69.92 %	144 53.93 %	3,834 78.88 %	3,346 85.01 %			
Low MPR (<0.8)	469 11.63 %	103 20.52 %	74 27.72 %	282 7.16 %	646 13.46 %			
High MPR (≥ 0.8)	223 5.53 %	48 9.56 %	49 18.35 %	308 7.83 %	320 6.67 %			
<i>Criminal justice involvement</i>								
Any jail	1,628 40.39 %	200 39.84 %	107 40.07 %	1,935 40.31 %	1,888 47.97 %			***
Any probation	587 14.56 %	150 29.88 %	60 22.47 %	797 16.6 %	462 11.74 %			***
Any arrest	1,538 38.15 %	212 42.23 %	142 53.18 %	1,892 39.42 %	1,781 45.25 %			***
<i>Insurance</i>								
SSI (any)	680 16.87 %	115 22.91 %	77 28.84 %	872 18.17 %	767 19.49 %			
Medicaid enrollment (any)	3,503 86.90 %	502 100.00 %	267 100.00 %	4,272 89.00 %	3,141 79.80 %			***

* Significant at 5% level;

** significant at 1% level;

*** significant at 0.1%

Asterisks beside Naltrexone column indicate comparisons across 3 MAT medications; Asterisks beside Comp Group column indicate comparison between All MAT group and Comp group.

SMI=Serious mental illness; MPR= Medication Possession Ratio. Number of days of medication appropriate to diagnosis during 12 pre-index months divided by number of pre-index days in community. SSI=Supplemental Security Income. MPR average includes only person-months when individuals were enrolled in Medicaid, and is restricted to individuals with any record of medication who were diagnosed with schizophrenia spectrum or bipolar disorder.

Table 3

Types of opioid pharmacotherapy among opioid-dependent adults with serious mental illness in CT public behavioral health system (n=4,800)

	N	%	Median
<i>Index treatment episode</i>			
Methadone	4,031	83.98 %	
Number of days (if any: Mean, SD)	(206.92, 122.05)		183
Buprenorphine	502	10.46 %	
Number of days (if any: Mean, SD)	(110.48, 111.32)		61.5
Naltrexone	267	5.56 %	
Number of days (if any: Mean, SD)	(45.75, 60.81)		23
<i>Full 12-month follow-up period (includes index and any subsequent</i>			
Methadone	4,117	85.77 %	
Number of days (if any: Mean, SD)	(230.81, 116.14)		237
Buprenorphine	591	12.31 %	
Number of days (if any: Mean, SD)	(146.73, 121.25)		112
Naltrexone	285	5.94 %	
Number of days (if any: Mean, SD)	(57.83, 73.60)		22

* Total percentage exceeds 100% because individuals could receive more than one type of MAT during post-index observation period.

Criminal justice and crisis-driven service utilization outcomes among opioid-dependent adults with co-occurring serious mental illnesses, opioid pharmacotherapy group versus comparison group (n=8,736)

Table 4

Independent variables	Incarceration		Arrest		Felony		SA Inpatient		MH Inpatient		ER/Crisis		SMI Medication Adherence							
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI						
Study group X time interaction	1.35	1.24 - 1.07	***	1.23	1.13 - 1.33	***	1.11	0.96 - 1.27	0.38	0.34 - 0.43	***	.97	.82 - 1.15	0.81	0.73 - 0.91	***	1.03	0.87 - 1.23		
Main effects																				
Study group	0.71	0.66 0.77	***	0.90	0.84 - 0.96	**	0.91	0.82 - 1.01	2.68	2.46 - 2.93	***	0.90	0.77 - 1.04	1.12	1.01 - 1.23	*	0.66	0.56 - 0.78	***	
Time period	0.58	0.53 0.62	***	0.98	0.88 - 1.08		1.21	1.02 - 1.43	*	0.17	0.14 - 0.19	***	0.47	0.39 - 0.57	0.52	0.46 - 0.60	***	0.68	0.58 - .81	***

* Significant at 5% level;
** significant at 1% level;
*** significant at 0.1%

Table 5

Criminal justice and crisis-driven service utilization outcomes among opioid-dependent adults with co-occurring serious mental illnesses, by opioid pharmacotherapy type

	Incarceration			Arrest			Felony			SA Inpatient			MH Inpatient			ER/Crisis			SMI Medication Adherence		
	O.R.	95% C.I.	p	O.R.	95% C.I.	p	O.R.	95% C.I.	p	O.R.	95% C.I.	p	O.R.	95% C.I.	p	O.R.	95% C.I.	p	O.R.	95% C.I.	p
Methadone (n=7,967)																					
Study group X time interaction	1.39	(1.27–1.52)	***	1.28	(1.17–1.40)	***	1.14	(0.98–1.32)		0.35	(0.31–0.39)		1.10	(0.91–1.32)		0.79	(0.70–0.89)	***	0.93	(0.77–1.12)	
Main effects																					
Methadone study group	0.72	(0.66–0.77)	***	0.88	(0.82–0.94)	***	0.89	(0.79–0.99)	*	2.79	(2.54–3.06)		0.79	(0.68–0.93)	**	1.13	(1.02–1.25)	*	0.59	(0.50–0.71)	***
Time period	0.56	(0.52–0.61)	***	0.98	(0.88–1.08)		1.22	(1.02–1.45)	*	0.15	(0.13–0.18)		0.47	(0.39–0.57)	***	0.52	(0.46–0.60)	***	0.66	(0.55–0.79)	***
Buprenorphine (n=4,438)																					
Study group X time interaction	1.03	(0.84–1.25)		1.14	(0.96–1.35)		1.24	(0.92–1.66)		0.54	(0.43–0.67)		0.86	(0.61–1.22)		1.00	(0.77–1.30)		1.37	(1.00–1.87)	
Main effects																					
Buprenorphine study group	0.66	(0.55–0.80)	***	0.93	(0.81–1.08)		0.90	(0.71–1.13)		2.20	(1.88–2.56)		0.74	(0.56–0.98)	*	0.79	(0.65–0.97)	*	0.72	(0.54–0.96)	*
Time period	0.51	(0.47–0.56)	***	0.99	(0.87–1.13)		1.28	(1.04–1.59)	*	0.21	(0.17–0.26)		0.48	(0.38–0.61)	***	0.48	(0.40–0.57)	***	0.66	(0.53–0.81)	***
Naltrexone (n=4,203)																					
Study group X time interaction	1.62	(1.28–2.05)	***	0.80	(0.64–0.99)	*	0.68	(0.46–1.00)	*	0.61	(0.47–0.79)		0.61	(0.43–0.89)	**	0.86	(0.68–1.08)		1.56	(1.13–2.16)	**
Main effects																					
Naltrexone study group	0.64	(0.50–0.80)	***	1.18	(1.01–1.37)	*	1.23	(0.94–1.61)		2.67	(2.20–3.24)		2.00	(1.51–2.65)	***	1.54	(1.24–1.90)	***	0.91	(0.67–1.24)	
Time period	0.50	(0.45–0.55)	***	1.01	(0.88–1.14)		1.25	(1.01–1.56)	*	0.19	(0.15–0.24)		0.46	(0.36–0.57)	***	0.51	(0.43–0.61)	***	0.70	(0.57–0.87)	**

* Significant at 5% level;

** significant at 1% level;

*** significant at 0.1%

Models control for age, educational need, gender, primary SMI diagnosis, race/ethnicity, insurance (SSI, Medicaid), probation, service participation (residential, ACT, OP MH, OP SA), MPR (prior month MPR of 80% or higher), time, and community tenure. MPR model excludes MPR covariate. MPR models exclude MPR covariate, include only person-months when individuals were enrolled in Medicaid, and are restricted to individuals with any record of medication who were diagnosed with schizophrenia spectrum or bipolar disorder. (MPR model ns: Methadone 2,069, Buprenorphine 1,282, Naltrexone 1,229)

Table 6

Criminal justice and crisis-driven service utilization outcomes among opioid-dependent adults with co-occurring serious mental illnesses, methadone versus buprenorphine (n=4,533)

	Incarceration		Arrest		Felony		SA Inpatient		MH Inpatient		ER/Crisis		SMI medication adherence					
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI				
Medication type × time interaction	0.67	(0.55–0.82)	***	0.92	(0.78–1.10)	1.11	(0.83–1.49)	1.52	(1.23–1.87)	***	0.80	(0.56–1.14)	1.28	(0.99–1.67)	1.43	(1.05–1.93)	*	
Main effects																		
Buprenorphine (ref: Methadone)	1.00	(0.83–1.19)		1.03	(0.89–1.19)	1.02	(0.81–1.29)	0.78	(0.68–0.90)	**	0.93	(0.70–1.24)	0.67	(0.54–0.82)	***	1.27	(0.96–1.68)	
Time period	0.97	(0.89–1.06)		1.22	(1.08–1.38)	**	1.31	(1.05–1.64)	*	0.05	(0.05–0.06)	***	0.58	(0.45–0.74)	***	0.61	(0.50–0.73)	***

* Significant at 5% level;
** significant at 1% level;
*** significant at 0.1%

Models control for age, educational need, gender, primary SMI diagnosis, race/ethnicity, insurance (SSI, Medicaid), probation, service participation (residential, ACT, OP MH, OP SA), MPR (prior month MPR of 80% or higher), time, and community tenure. MPR model excludes MPR covariate. MPR models exclude MPR covariate, include only person-months when individuals were enrolled in Medicaid, and are restricted to individuals with any record of medication who were diagnosed with schizophrenia spectrum or bipolar disorder. (MPR model N=1,175)