Impact of Comorbid Chronic Pain or Mental Illness on Substance Use Treatment Among Cohort of Individuals at High Risk of Opioid Overdose

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Abstract

Background and Aims: The opioid and overdose epidemics have become an increasing concern across the United States, with over 100,000 people dying from overdose in 2021 alone. Chronic pain and/or serious mental illness (SMI) increases risk of opioid use, and opioid use disorder (OUD) can also exacerbate these conditions. Treatment for OUD can be lifesaving, but many lack access. We aimed to characterize how these comorbidities affect 90-day substance use treatment uptake after an emergency department (ED) visit among patients at risk of opioid overdose.

Methods: We conducted a cohort study using data from the Navigator Trial, wherein patients presenting to the ED at risk of opioid overdose received a behavioral health intervention. Baseline study data for 648 trial participants were linked to statewide administrative data on substance use disorder (SUD) treatment (including buprenorphine & methadone therapy, residential programs, and entry into other licensed SUD treatment facilities). Records accessed included initiation of a new treatment episode, transfer between programs, and re-enrollment in care. Risk ratios for each exposure of interest (chronic pain and SMI) were estimated with unadjusted and adjusted modified Poisson models (rather than logistic regression to account for the non-rare nature of the outcome). Adjusted models included potential confounders (gender, race/ethnicity, education, monthly income, housing status, childhood trauma, and current health insurance) that were selected a priori based on theoretical directed acyclic graphs (DAGs). In an exploratory post hoc analysis, results were further stratified by baseline treatment status.

Results: The mean age of participants was 37 (SD=11); 439 (68%) were male and 446 (69%) had been unhoused in the last six months. Overall, 43% of participants enrolled in treatment within 90 days of the ED visit. Those with SMI were more likely to enroll in treatment than those

without (adjusted risk ratio [ARR]=1.24, 95% confidence interval [CI]: 1.01-1.53), although this effect was only among those already accessing some form of treatment at baseline (ARR=1.58, 95% CI: 1.10-2.27). Chronic pain was not associated with 90-day treatment enrollment overall (ARR=1.12, 95% CI: 0.91-1.38) or within baseline treatment subgroups.

Conclusions: Among participants at high risk of opioid overdose who receive ED-based interventions for OUD, those with comorbid SMI (but not chronic pain) who were in treatment at baseline were more likely to switch treatment programs or newly enroll in additional programs following the ED visit. Further mixed methods research is needed to determine most common pathways for treatment engagement and risk factors for treatment interruption in this population. Touchpoints within the medical system should be leveraged to ensure that all persons, including those with comorbid SMI, can access integrated, high-quality SUD treatment at the desired intensity level.

Introduction

The opioid and overdose epidemics have become an increasing concern across the United States (US). In 2021 alone, over 106,000 people died from opioid overdose, a greater than 3-fold increase since 10 years prior.[1,2] Within the last decade, adults in the US are more likely to die from accidental opioid overdose than car accidents, and overdose is now the leading cause of accidental death.[3] High rates of fatal overdose drove a decrease in national life expectancy in 2017, and that year, the US Department of Health and Human Services declared the opioid epidemic a public health emergency.[4] However, fatal overdose rates only scratch the surface of the problem. Over three million US citizens misuse opioids, and there are over 1.5 million emergency department (ED) visits related to opioid use disorder (OUD) each year.[5,6]

States have dedicated significant resources to addressing the opioid and overdose epidemics. Evidence-based treatments, including medications for opioid use disorder (MOUD), have been shown to improve outcomes for people with OUD.[7,8] Over a million individuals are currently receiving MOUD in the US, a number that increased 142% from 2016 to 2018.[9] However, there is still significant unmet need and some populations (e.g., women, people living in high poverty areas) may have particular difficulty accessing lifesaving treatment. The present study focuses on populations living with mental illness (MI) and chronic pain, two conditions that frequently co-occur with opioid use.[10–14] Opioids have been commonly prescribed for chronic pain and evidence suggests that some people use opioids as self-medication for physical and mental pain. However, although opioids may lead to short term symptom alleviation, opioid use can in turn exacerbate both conditions, and increase risk of developing OUD.[10,15,16]

Comorbid MI with OUD can complicate the treatment process. In a study of nearly 400,000 records in a prescription opioid registry, the authors found that people with comorbid

MI and OUD had a higher risk of both overdose and overdose-related mortality than those with OUD only.[11] Further, withdrawal and opioid dependence can acutely exacerbate some MI symptoms.[16,17] Integrated care, in which both comorbidities are addressed simultaneously, leads to best outcomes.[10] However, access to integrated care is often lacking in the US across all levels of MI severity.[18] For example, among people with both substance use disorder (SUD) and a mild/moderate or severe MI, only 16% and 32%, respectively, are enrolled in treatment for both SUD and MI, according to a national survey.[19] Similarly, a Substance Abuse and Mental Health Services Agency (SAMHSA) report from 2020 found that among people with a SUD, only 6.5%, 8.0%, and 10.9% of adults with SUD alone, co-occurring any MI, or SMI, respectively, received substance use treatment at a specialized facility.[20] While these numbers highlight the large proportion of people with co-occurring conditions without adequate care, it is worth noting that rates of SUD treatment for those with SMI tend to be higher than rates of treatment for those with SUD alone or with more mild MI.

Affordability of care, alongside access, stigma, and lack of readiness to stop using are cited as the most common barriers to SUD treatment.[19] Providers often feel ill-equipped to treat SUD, which creates challenges for providing integrated care and leads to missed opportunities to engage patients already in MI treatment in SUD treatment as well.[12] Despite the increasing awareness of integrated care for those with SUD and MI, a recent review highlighted the dearth of research about evidence-based treatment for these populations and called for further investigation into how to best serve patients with co-occurring MI and SUD.[21]

Chronic pain is also a risk factor for SUD and can make SUD recovery more challenging by contributing to decreased quality of life and increased opioid use.[13,14] Opioid prescribing for chronic pain became common in the 1990s, peaking in the early 2010s.[22,23] For example, in 2011

alone, doctors prescribed a total of 219 million opioid prescriptions, a nearly 3-fold increase since 1991.[24] However, increased recognition of addictive properties of opioids and climbing opioid overdose rates rapidly changed prescribing guidelines, rules, and practices.[22] Chronic pain patients were caught in the middle of shifting national guidelines and reported feeling increasingly stigmatized with labels such as "drug-seeking" or "junkie."[25] Those with co-occurring chronic pain and SUD are particularly affected by structural stigma and drug-related discrimination. In a qualitative study of 34 patients with chronic pain and SUD, many participants reported frustration with doctors' lack of empathy for and ability to treat pain.[26] The study further concluded that alternative pain management methods must be an aspect of SUD treatment.[26] A 2022 systematic review suggests that methadone, buprenorphine, cognitive behavioral therapy and mindfulness are all promising methods of managing both chronic pain and OUD, but further research is necessary to confirm and compare efficacy.[27] A literature review by Speed et al. similarly emphasized the importance of continued research into the impact of and treatment for co-occurring chronic pain and OUD.[13]

Some recent research has investigated the effect of MI and chronic pain on access to and retention in OUD treatment, but findings are inconsistent. Among over 18,000 Medicaid recipients at risk of opioid overdose in Rhode Island (RI), patients were less likely to access MOUD after an opioid overdose or OUD diagnosis if they had comorbid mental illness or back pain (used as a proxy for chronic pain based on available medical records).[28] Conversely, a 2018 study found that anxiety and chronic pain were positively associated with OUD treatment retention, although no other psychiatric disorders were significantly associated with retention.[29]

The present study will expand upon the current evidence base by investigating whether co-occurring SMI or chronic pain is associated with SUD treatment engagement within 90 days,

among patients presenting to the emergency department (ED) and at high risk of a subsequent opioid overdose. We hypothesized that people with SMI may be more or less likely to initiate treatment than those without SMI due to multiple competing factors, while people with chronic pain would be less likely to initiate treatment than those without chronic pain. Understanding patterns of SUD treatment enrollment among people with SMI and chronic pain can inform the development of tailored, ED-based strategies and programs to increase access to treatment among these populations.

Methods

Sample

This study is an observational cohort study using data from 648 patients participating in a randomized controlled trial. Specifically, the Navigator Trial was designed to compare the efficacy of receiving a brief, ED-based behavioral intervention delivered by peer recovery support specialists versus licensed social workers for individuals presenting to EDs at risk of opioid overdose (clinicaltrials.gov identifier: NCT03684681).[30] The study recruited participants at two EDs in Rhode Island (RI) from November 2018 through May 2021. These EDs receive around half of all opioid-related ED visits in RI.[31] Participants consented to electronic health record review and linkage to statewide administrative SUD treatment data. This study was approved by the Lifespan, Brown University, and Rhode Island Department of Health institutional review boards. We followed STROBE guidelines throughout this report.

Trial inclusion criteria required that participants were: 1) being treated for an opioid overdose at the time of the ED visit, 2) were receiving treatment related to OUD (e.g., infectious complication or opioid withdrawal) at the time of the ED visit, or 3) were identified as having an

opioid overdose within the previous 12 months (determined either by self-report or electronic health records review). Additionally, participants were required to be at least 18 years old, speak English, not be in police custody at the time of the ED visit, not be critically ill or injured, not be pregnant, and live in RI. As detailed in the previously published trial protocol, baseline data were collected from all participants via a blinded, interviewer-administered survey in the ED.[32] Interviewers ensured that survey participation did not interfere with provision of care in the ED, so some participants did not complete the entire baseline survey (see statistical analysis section below).

Measures

Exposures. The two primary exposures of interest were self-reported hospitalization for SMI and current chronic pain at the baseline ED visit. SMI was defined as any self-reported previous inpatient hospitalization for mental illness (i.e., endorsement of the following question: "Have you ever been hospitalized for a mental illness or depression?"). Hospitalization may have been voluntary or involuntary. This measure was a proxy for the National Institute of Mental Health definition of SMI and in alignment with the National Committee for Quality Assurance classification, which also incorporates inpatient hospitalization.[33–35] Current chronic pain was defined as a self-reported, current painful condition lasting three months or longer, in accordance with the International Association for the Study of Pain definition.[36] Participants who said yes to all three of the following questions were classified as having current chronic pain: 1) "Most of us have had pain from time to time (such as headaches, back pain, and toothaches). Have you had any pain in the past 7 days?", 2) "Have you had pain in any of the previously mentioned areas for 3 months or longer?", and 3) "Do you consider yourself to have a chronic pain condition?"

Outcome. The study outcome was engagement in SUD treatment within 90 days after the baseline ED visit. Treatment engagement was assessed through deterministic linkages to two statewide administrative databases on SUD treatment, including the Behavioral Health Online Database and the Prescription Drug Monitoring Program database.[37,38] The Behavioral Health Online Database includes data from all SUD treatment programs licensed by the state (e.g., methadone opioid treatment programs, residential detoxification, outpatient or residential SUD treatment). The Prescription Drug Monitoring Program database includes all buprenorphine prescriptions dispensed to RI residents by retail pharmacies. Treatment engagement included the following events: (1) new treatment episode in publicly licensed SUD treatment program or (2) fill of a buprenorphine within 90 days of the baseline ED visit. In other words, participants engaged in SUD treatment at baseline would have the outcome if they switched treatment types (e.g., counseling to MOUD, methadone to buprenorphine, unofficial treatment program to state licensed program), filled a buprenorphine prescription, or enrolled in an additional treatment type (e.g., adding MOUD to counseling).

Confounders. We selected *a priori* confounding variables that were hypothesized to be associated with the study exposures (SMI, chronic pain) and study outcome (90-day SUD treatment engagement), based on the data available and theoretical directed acyclic graphs (Supplemental Figure 1). Hypothesized confounders were measured at the baseline ED visit and included: age (<=30, 30-50, >=50) current gender identity (male, female and other, the latter includes participants who selected transgender or non-binary), race/ethnicity (operationalized as mutually exclusive categories including White non-Hispanic, Black non-Hispanic, Hispanic any race, “other” Non-Hispanic), education (did not complete high school, completed high school), monthly income from legal sources ($0-$1,500, >$1,500), housing status (housed, unhoused

within the past 6 months), childhood trauma history (experienced sexual, physical, and/or psychological trauma during childhood – yes, no), and current health insurance (yes, no). Other non-Hispanic race/ethnicity included mixed race, Native Hawaiian, Pacific Islander, and unspecified other race. For each measure, responses of "don't know or refuse to respond" were recoded as missing and included as an additional category. Of note, overdose as reason for the index ED visit was not considered a confounder because it could be in the causal pathway between SMI/chronic pain and 90-day SUD treatment engagement (i.e., a potential mediator).

Potential Effect Modifier. We also explored potential effect modification by current SUD treatment engagement at the baseline ED visit. Participants who responded yes to both of the following questions were categorized as currently in treatment: 1) "Have you ever been in any kind of alcohol or drug treatment program?" and 2) "Are you currently in an addiction treatment program?"

Statistical Analysis

We generated descriptive statistics characterizing the prevalence of each study exposure (SMI and current chronic pain) in the study population by sociodemographic characteristics and tested for differences across groups using chi-squared tests (categorical variables) and *t*-tests (continuous variables). In addition, we used a chi-squared test to examine the association between the two exposures. Due to high rates of missingness for each exposure variables, we compared the sociodemographic characteristics of participants with versus without missing exposure data using chi-squared tests.

For our primary analysis, we fit separate modified Poisson regression models to estimate the association between each study exposure (i.e., history of SMI and current chronic pain) and the

outcome of 90-day SUD treatment engagement, with and without adjustment for confounders. Each model excluded participants with missing exposure data but included "missing" as a separate category for each confounder. To understand the potential impact of missing exposure data on our findings, we then completed a best-case worst-case sensitivity analysis, categorizing all participants with missing exposure data as exposed and then unexposed and, thereby, generating the possible range of estimates. As a *post hoc* exploratory analysis, we also considered potential effect modification of the associations of interest by stratifying the model by current SUD treatment engagement at the baseline ED visit.

All statistical analyses were performed using SAS software version 9.4.[39] *A priori* alpha was set to 0.05, and we used two-sided tests.

Results

Recruitment for the Navigator Trial has been described in detail elsewhere.[30] Briefly, between November 2018 and May 2021, 2,665 patients at one of two EDs in RI completed an in-person screening for study eligibility. Of those, 648 patients at risk of opioid overdose ultimately provided informed consent and participated in the trial.

Participant Characteristics

Among the 648 participants, the mean age was 37 years (standard deviation=11, see Table 1). Most participants (n=439, 68%) were male. There were 424 White non-Hispanic (65%), 38 Black non-Hispanic (6%), 107 Hispanic any race (17%), and 79 other non-Hispanic (12%) participants. Most participants were high school graduates (n=453, 70%), had a monthly income $1,500 or less (n=439, 68%), had experienced childhood trauma (n=414, 64%) and were

unhoused within the last six months (n=446, 69%). Nearly half of participants (n=293, 45%) were attending the ED due to an opioid overdose.

At baseline, 569 participants (88%) had data on history of SMI, while 558 (86%) had data on current chronic pain. Participants with missing versus complete data on SMI and chronic pain were similar, with the only exception being that those with missing SMI data were slightly older (mean 39 vs. 37 years, $p = 0.033$) (Table S1). Among 569 participants with data on SMI, about half (n=294, 52%) had a history of SMI (i.e., had a history of hospitalization for mental illness). Compared to participants without SMI, those with SMI were more likely to have a monthly income of $1500 or less (79% vs. 67%, $p = 0.001$), were more often unhoused (82% vs. 56%, $p < 0.0001$), were insured at higher rates (95% vs. 90%, $p = 0.039$), were more likely to have experienced childhood trauma (82% vs. 61%, $p = <0.0001$), and were less likely to have attended the ED visit for an overdose (40% vs 49% $p = 0.021$).

In contrast, participants with and without chronic pain were generally similar, except those with chronic pain were older (mean 41 vs. 35 years, $p < .0001$) and more often had experienced childhood trauma (79% vs. 70%, $p = 0.046$).

SUD Treatment Engagement

Overall, 278 participants (43%) initiated SUD treatment within 90 days of the index ED visit. Among those with complete data for SMI and chronic pain, 247 participants (43%) and 242 participants (43%), respectively, initiated treatment within 90 days.

In unadjusted and adjusted models, participants with SMI were more likely to initiate SUD treatment within the 90 days following the ED visit compared to those without SMI (Table 2). After adjustment for gender identity, race/ethnicity, education, monthly income, housing,

current health insurance, and childhood trauma, participants with SMI had 1.24 times the likelihood of treatment engagement compared to those without SMI (95% confidence interval [CI]: 1.01-1.53). Results did not meaningfully change in the best-case-worst-case sensitivity analysis, suggesting that missingness was unlikely to be influencing these results (Table S2). In exploratory analyses stratified by baseline treatment status, SMI was *only* associated with 90-day SUD treatment engagement among those who reported being in some form of treatment at baseline (Table 3).

Current chronic pain at baseline was not associated with subsequent 90-day treatment engagement in unadjusted or adjusted models. The results were similar in best-case worst-case sensitivity analyses and when stratifying by baseline treatment status (see Tables 3 and S2).

Discussion

A nuanced understanding of barriers to treatment engagement and retention can inform targeted and tailored supports to reduce substance use-related harms among high-risk populations, such as those with SMI and chronic pain. Over half of study participants had been hospitalized for a MI and nearly one-in-three had current chronic pain. The prevalence of these comorbid conditions in individuals presenting to the ED at risk of opioid overdose underscores the importance of studying the unique healthcare needs of these populations, particularly given that SUD may exacerbate SMI and chronic pain.[10,15,16] In addition, the high prevalence of housing instability, low income, and childhood trauma among the study population, all of which are correlated with SMI and some of which are correlated with chronic pain, suggests that social determinants of health must also be taken into account in understanding and addressing disparities in patterns of treatment enrollment.

In the present study, those with a history of SMI who were engaged in some form of treatment at baseline were more likely than those without SMI to transfer or add a treatment program. This may be due to more frequent contact with the medical system or because current treatment programs are not adequately meeting their needs. Prior literature supports the notion that some psychiatric comorbidities can negatively impact treatment retention among people who use substances, although results are inconsistent and rarely focus specifically on people who use opioids.[40–42] Further, Medicaid claims studies have found that comorbid psychiatric diagnoses with SUD predict lower odds of engagement in substance use treatment, a result not found in our study population, but that lends further support to the possibility that this population has specific needs that some treatment programs may not address.[28,43] Some of the differences in results may be due to differing populations, as unlike prior literature, the present study focused only on patients attending the ED and included both those in treatment and not in treatment at baseline. Additionally, all individuals in our study were randomized to receive a behavioral intervention from either a licensed social worker or peer recovery support specialist, which would not necessarily have been the standard of care in prior studies. Other data suggest that while treatment rates are low among people with SUD, those with co-occurring mental illness of increasing severity are increasingly likely to be enrolled in substance use treatment, although in the present study *baseline* rates of treatment engagement did not differ by SMI.[19] Overall, results align with prior literature that the population with comorbid substance use and SMI has unique patterns of engagement with SUD treatment, and suggests that current treatment for these comorbidities may have some inadequacies. Still, there is some heterogeneity in types of disparities observed and further research will be necessary to confirm reasons for increased turnover between treatment programs among participants with SMI.

Our findings that chronic pain was not associated with 90-day SUD treatment engagement differs from some prior studies. Quantitative and qualitative literature has found that chronic pain can negatively impact treatment enrollment.[26,28,43,44] Chronic pain may decrease quality of life among patients with SUD, which can complicate the recovery process.[13] These previous studies had slightly higher rates of chronic pain (30-54% vs 28%) and older populations (where age data were available). Thus, those with more severe chronic pain may have been less likely to enroll in a randomized trial (such as this one) due to mobility issues, which could bias present findings towards the null.[45] Results may also differ as a result of varying measurement of chronic pain (the current study uses self-reported chronic pain, while prior claims studies use other conditions such as back pain as a proxy for chronic pain) and different source populations (previous studies limited enrollment by type of insurance). In addition, the potential effect of the study intervention itself on minimizing disparities in access to substance use treatment cannot be dismissed.

Strengths and Limitations

This study had several important limitations. First, while the use of statewide administrative data to measure SUD treatment engagement throughout the study leads to almost no loss to follow-up and is generally a strength of this study, some treatment engagement events that occur outside of RI or in programs not licensed by the state may not be captured. Still, prior Medicaid claims studies only captured enrollment events through Medicaid, while the present study captures all enrollment events in RI regardless of insurance status. Second, there were relatively high rates of missingness for both exposures. However, participants with missing and complete exposure data did not differ meaningfully by baseline characteristics, and best-case-

worst-case sensitivity analyses were consistent with the primary results, so it is unlikely that results were biased by missing exposure data. Third, the self-reported nature of the survey data may lead to some exposure and confounder misclassification due to social desirability biases (e.g., under-reporting prior hospitalization for MI). However, there is no reason to believe misclassification would be differential (i.e., associated with the outcome). Additionally, self-reported exposure history is also a strength as it may be more complete than what could be obtained through medical records, particularly for chronic pain and confounders. Fourth, while survey data allowed for consideration of multiple confounders, there is potential for residual confounding. Some confounding variables were also collapsed into binary categories out of analytic necessity due to sample size, but this may leave some residual confounding. In addition, while authors are unaware of any specific unmeasured confounding, it is always possible there are unknown confounders, particularly when studying complex exposures such as SMI and chronic pain that interact with many social determinants of health. Fifth, results may not be generalizable to: a) populations at risk of overdose who have not recently attended the ED, and b) populations who have not received an ED-based behavioral intervention with a peer recovery support specialist or clinical social worker.

Future Directions

Future studies should continue to examine pathways of initiation, retention, interruption, and re-engagement in SUD treatment among patients with SMI, as well as patterns of treatment engagement across SUD treatment types. Further, it may be optimal to continue to characterize the effects of comorbid SMI and chronic pain on treatment engagement through *mixed* methods research. With such complex and sensitive topics, it is critical to have patient input regarding

preferences, barriers, and facilitators for treatment engagement. Additionally, overdose outcomes should be examined among people with SMI and chronic pain, because if treatment engagement is similar but risk of overdose is greater, it could indicate that populations with comorbidities have additional unmet needs. Finally, future work should examine the impact of *severe* chronic pain compared to mild or no chronic pain, as chronic pain is likely more of a barrier to treatment for those whose chronic pain severely limits their daily activities.

Individuals with co-occurring conditions likely have more touchpoints with the medical system. These other touchpoints, such as ED, psychiatric, and primary care visits should continue to be leveraged to provide direct access to SUD treatment programs and other supportive services that meet patients' needs. Integrated care is recommended as best practice for those with OUD and MI or chronic pain, so for many integrated care may be the optimal form of treatment.[18,26] Nonetheless, based on symptom severity, personal preference, or time limitations, others may prefer less intensive treatment options (e.g., MOUD alone), and programs such as on-demand, low-threshold buprenorphine (a less burdensome type of treatment) induction should be readily available across medical system touchpoints.[46–49] In addition, programs must take into account the multiple social determinants (e.g., housing, childhood trauma, low socio-economic status) that are prevalent in populations with OUD, SMI and/or chronic pain, and contribute to some barriers to treatment. In order to implement both better integrated and low-barrier trauma-informed programs, states should continue working on capacity-building of mental health and other medical professionals to provide SUD treatment.[28]

Table 1. Baseline characteristics of Navigator Trial participants, stratified by hospitalization for mental illness and chronic pain, number (row %, unless otherwise specified)

Characteristic	Total N (col %)	Serious Mental Illness Yes N (%)	No N (%)	*p*	Current chronic pain Yes N (%)	No N (%)	*p*
Total	648	294 (52)	275 (48)		154 (28)	404 (72)	
Age, years				0.652			<0.0001*
mean (SD)	37 (11)	36 (10)	37 (11)		41 (11)	35 (10)	
Current Gender Identity				0.075			0.163
Female or other	203 (31)	105 (57)	79 (43)		56 (31)	122 (69)	
Male	439 (68)	189 (49)	196 (51)		98 (26)	282 (74)	
Race/ Ethnicity				0.963			0.973
White, non-Hispanic	424 (65)	194 (52)	177 (48)		102 (28)	264 (72)	
Black, non-Hispanic	38 (6)	17 (50)	17 (50)		8 (24)	25 (76)	
Hispanic any race	107 (17)	47 (49)	48 (51)		25 (27)	67 (73)	
Other non-Hispanic	79 (12)	36 (52)	33 (48)		19 (28)	48 (72)	
Education				0.876			0.134
Did not complete High School	185 (29)	89 (52)	81 (48)		39 (23)	128 (77)	
Completed High School	453 (70)	205 (52)	192 (48)		115 (30)	274 (70)	
Missing	10 (2)	0 (0)	2 (100)		0 (0)	2 (100)	
Monthly Income				0.001*			0.110
$0-1,500	439 (68)	218 (56)	171 (44)		116 (31)	264 (69)	
>$1,500	154 (24)	57 (40)	85 (60)		33 (23)	108 (77)	
Missing	55 (8)	19 (50)	19 (50)		5 (14)	32 (86)	
Housing				<0.0001*			0.411
Housed	192 (30)	53 (30)	121 (70)		44 (25)	130 (75)	
Unhoused	446 (69)	241 (61)	154 (39)		110 (29)	274 (71)	
Health insurance				0.039*			0.090
Yes	576 (89)	275 (54)	238 (46)		145 (29)	357 (71)	
No	48 (7)	16 (37)	27 (63)		7 (17)	35 (83)	
Missing	24 (4)	3 (23)	10 (77)		2 (14)	12 (86)	

Childhood Trauma History				<0.0001*		0.046
Yes	414 (64)	237 (59)	163 (41)		117 (30)	272 (70)
No	160 (25)	51 (33)	105 (67)		32 (21)	117 (79)
Missing	74 (11)	6 (46)	7 (54)		5 (25)	15 (75)
Baseline SUD Treatment				0.482		0.887
Currently in treatment	178 (27)	84 (54)	71 (46)		42 (27)	112 (73)
Not currently in treatment	447 (69)	204 (51)	197 (49)		109 (28)	282 (72)
Missing	23 (4)	7 (54)	6 (46)		3 (23)	10 (77)
Overdose as reason for index ED visit				0.021*		0.207
Yes	293 (45)	117 (46)	135 (54)		63 (25)	190 (75)
No	353 (55)	177 (56)	138 (44)		90 (30)	213 (70)
Serious Mental Illness				NA		0.170
Yes		NA	NA		84 (30)	194 (70)
No		NA	NA		64 (25)	193 (75)
Missing		NA	NA		6 (26)	17 (74)
Chronic pain				0.170		NA
Yes		84 (57)	64 (43)		NA	NA
No		194 (50)	193 (50)		NA	NA
Missing		16 (47)	18 (53)		NA	NA

*P<.05

Note: Total number column includes all study participants. Breakdowns by exposure status only include individuals in that sub-analysis (those with complete data for the exposure of interest – 569 for hospitalization for mental illness, and 558 for chronic pain). Rows by exposure status may not add to column total.

Note: P-values are chi-square tests for all variables besides age (t-test). Test statistics do not include covariate missing values.

Note: Serious mental illness was defined as self-reported prior hospitalization for mental illness

Note: Participants were asked their current gender identity, other includes respondents who selected transgender or non-binary

Table 2. Bivariate and multivariable associations between history of hospitalization for a mental illness, chronic pain, and engagement in substance use disorder treatment within 90 days of the index ED visit among patients in the Navigator Trial

Exposure	Total N	90-day treatment enrollment No N (%)	Yes N (%)	Unadjusted Risk Ratio	Adjusted Risk Ratio**
Serious Mental Illness					
Total	569	322 (57)	247 (43)		
No	275	172 (63)	103 (37)	1 [reference]	1 [reference]
Yes	294	150 (51)	144 (49)	1.31* (1.08 – 1.58)	1.24* (1.01– 1.53)
Current Chronic Pain					
Total	558	316 (57)	242 (43)		
No	404	234 (58)	170 (42)	1 [reference]	1 [reference]
Yes	154	82 (53)	72 (47)	1.11 (0.91 – 1.36)	1.12 (0.91 – 1.38)

*P<.05

**Models adjusted for age, current gender identity, race/ethnicity, education, monthly income, housing, current health insurance, and childhood trauma history.

Note: Serious mental illness was defined as self-reported prior hospitalization for mental illness

Table 3. Bivariate and multivariable associations between history of hospitalization for a mental illness, chronic pain, and the engagement in substance use disorder treatment within 90 days of the index ED visit among patients in the Navigator Trial, stratified by baseline treatment status (row %)

Exposure		Total N	90-day treatment enrollment No N (%)	Yes N (%)	Unadjusted Risk Ratio	Adjusted Risk Ratio
Currently in Treatment	**Serious Mental Illness**					
No	No	197	124 (63)	73 (37)	1 [reference]	1 [reference]
	Yes	204	110 (54)	94 (46)	1.24 (0.98 – 1.57)	1.17 (0.91 – 1.50)
Yes	No	71	44 (62)	27 (38)	1 [reference]	1 [reference]
	Yes	81	36 (43)	48 (57)	1.50* (1.06 –2.13)	1.58* (1.10 – 2.27)
Missing	Yes	7	4 (57)	3 (43)		
	No	6	4 (67)	2 (33)		
Currently in Treatment	**Current Chronic Pain**					
No	No	282	168 (60)	114 (40)	1 [reference]	1 [reference]
	Yes	109	64 (60)	45 (41)	1.02 (0.78 – 1.33)	1.08 (0.82 – 1.42)
Yes	No	112	59 (53)	53 (47)	1 [reference]	1 [reference]
	Yes	42	17 (40)	25 (60)	1.26 (0.92 – 1.73)	1.24 (0.89 – 1.74)
Missing	Yes	10	7 (70)	3 (30)		
	No	3	1 (33)	2 (67)		

Note: Serious mental illness was defined as self-reported prior hospitalization for mental illness

Supplementary Table 1. Baseline characteristics of Navigator Trial participants, stratified by missingness for hospitalization for mental illness and chronic pain, number (row %)

Characteristic	Total N	Serious Mental Illness			Current chronic pain		
		Missing N (%)	Not missing N (%)	*p*	Missing N (%)	Not missing N (%)	*p*
No.	548	79 (12)	569 (88)		90 (14)	558 (86)	
Age, years				0.033*			0.232
mean (SD)	37 (11)	39 (11)	37 (11)		38 (11)	37 (11)	
Gender				0.275			0.694
Female or other	203	19 (9)	184 (91)		25 (12)	178 (88)	
Male	439	54 (12)	385 (88)		59 (13)	380 (87)	
Missing	6	6 (100)	0 (0)		6 (100)	0 (0)	
Race Ethnicity				0.970			0.986
White, non-Hispanic	424	53 (13)	371 (88)		58 (14)	366 (86)	
Black, non-Hispanic	38	4 (11)	34 (89)		5 (13)	33 (87)	
Hispanic any race	107	12 (11)	95 (89)		15 (14)	92 (86)	
Other non-Hispanic	79	10 (13)	69 (87)		12 (15)	67 (85)	
Education				0.121			0.132
Did not complete High School	185	15 (8)	170 (92)		18 (10)	167 (90)	
Completed High School	453	56 (12)	397 (88)		64 (14)	389 (86)	
Missing	10	8 (80)	2 (20)		8 (80)	2 (20)	
Monthly Income				0.209			0.102
$0-1,500	439	50 (11)	389 (89)		59 (13)	380 (87)	
>$1,501	154	12 (8)	142 (92)		13 (8)	141 (92)	
Missing	55	18 (33)	37 (67)		17 (31)	38 (69)	
Housing				0.442			0.113
Housed	192	18 (9)	174 (91)		18 (9)	174 (91)	
Unhoused	446	51 (11)	395 (89)		62 (14)	384 (86)	
Missing	10	10 (100)	0 (0)		10 (100)	0 (0)	
Current health insurance				0.911			0.945
Yes	576	63 (11)	513 (89)		74 (13)	502 (87)	
No	48	5 (10)	43 (90)		6 (13)	42 (88)	

Missing	24	10 (42)	14 (58)		11 (46)	13 (54)	
Childhood Trauma History				0.587			0.711
Yes	160	14 (3)	400 (97)		25 (6)	389 (94)	
No	414	4 (3)	156 (98)		11 (7)	149 (93)	
Missing	74	54 (73)	20 (27)		61 (82)	13 (18)	
Baseline SUD Treatment				0.344			0.747
Currently in treatment	178	23 (13)	155 (87)		24 (13)	154 (87)	
Not currently in treatment	447	46 (10)	401 (90)		56 (13)	391 (87)	
Missing	23	10 (43)	13 (57)		10 (43)	13 (57)	
Overdose as reason for index ED visit				0.213			0.852
Yes	293	41 (14)	252 (86)		40 (14)	253 (86)	
No	353	38 (11)	315 (89)		50 (14)	303 (86)	
Missing	2	0 (0)	2 (100)		0 (0)	2 (100)	

*P<.05

Note: Chi-square tests do not include covariate missing values

Note: P-values are chi-square tests for all variables besides age (t-test). Test statistics do not include covariate missing values.

Note: Serious mental illness was defined as self-reported prior hospitalization for mental illness

Supplementary Table 2: Best-Case-Worst-Case Analysis: Bivariate and multivariable associations between history of hospitalization for a mental illness, chronic pain, and the engagement in substance use disorder treatment within 90 days of the index ED visit among patients in the Navigator Trial when all participants with missing exposure data are categorized as exposed and unexposed

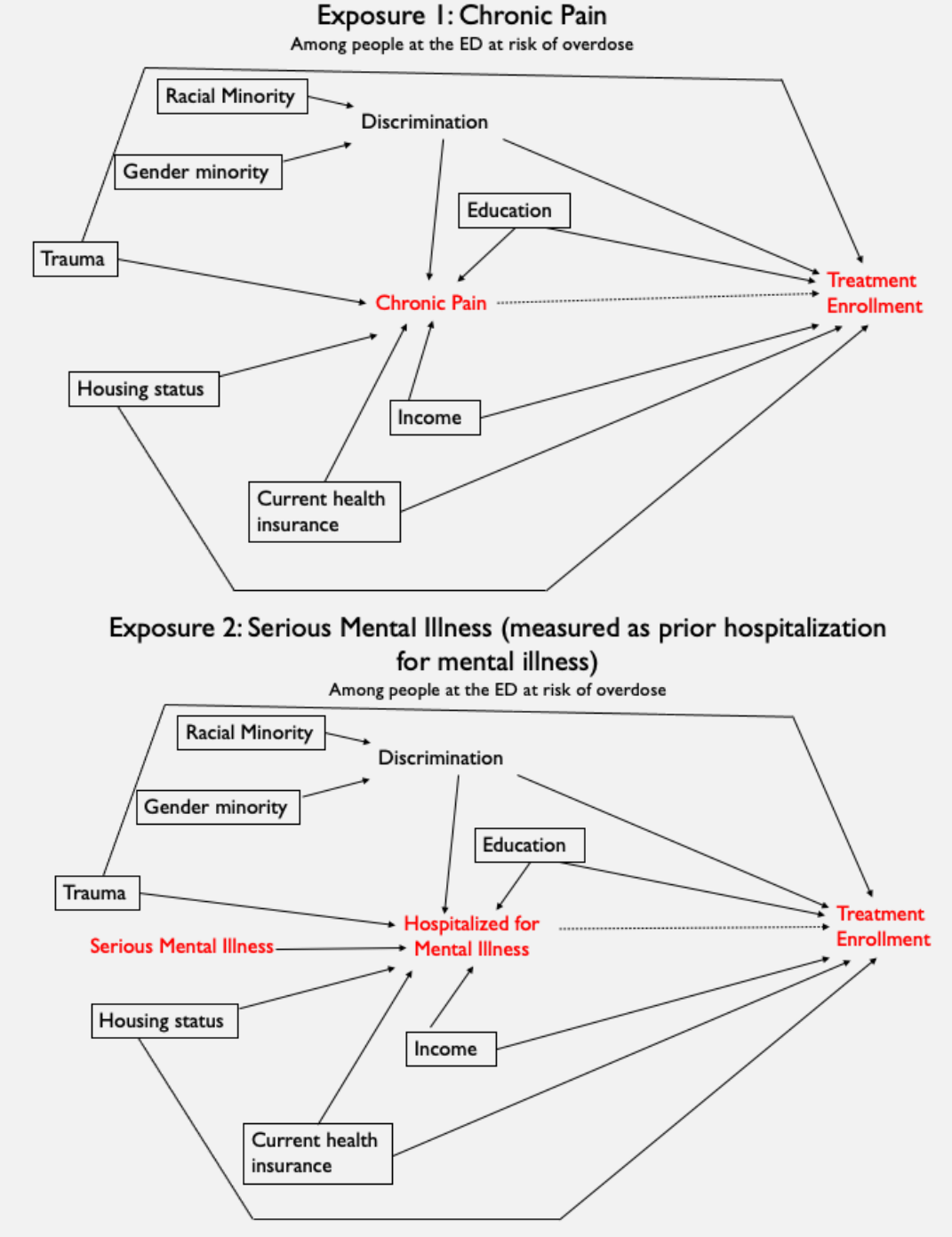
	Unadjusted Risk Ratio	Adjusted Risk Ratio**
Hospitalization for Mental Illness		
If Missing Were Hospitalized (Exposed)	1.25* (1.04 – 1.51)	1.23* (1.01 – 1.50)
If Missing Were Not Hospitalized (Unexposed)	1.29* (1.08 – 1.54)	1.23* (1.01 – 1.50)
Current Chronic Pain		
If Missing Have Current Chronic Pain (Exposed)	1.05 (0.88 – 1.26)	1.09 (0.90 – 1.32)
If Missing Do Not Have Current Chronic Pain (Unexposed)	1.12 (0.92 – 1.37)	1.12 (0.91 – 1.39)

*P<.05

**Models adjusted for age, current gender identity, race/ethnicity, education, monthly income, housing, current health insurance, at least one type of childhood trauma (sexual, physical, or psychological trauma)

Note: Serious mental illness was defined as self-reported prior hospitalization for mental illness

Supplementary Figure 1.



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