Chronic pain diagnoses and opioid dispensings among insured individuals with serious mental illness

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Ashli Owen-Smith
Georgia State University

Christine Stewart
Kaiser Permanente Washington Health Research Institute

Musu M. Sesay
Kaiser Permanente Georgia Center for Research and Evaluation

Sheryl M. Strasser
Georgia State University

Bobbi Jo Yarborough
Kaiser Permanente Northwest

Brian Ahmedani
Henry Ford Health System

Lisa R. Miller-Matero
Henry Ford Health System

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Essentia Institute of Rural Health

Irina V. Haller
Essentia Institute of Rural Health

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Central Western Massachusetts Healthcare

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Saint Louis University

Rebecca Rossom
HealthPartners Institute for Education and Research

Greg Simon
Kaiser Permanente Washington Health Research Institute

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Abstract
Background Individuals with major depressive disorder (MDD) and bipolar disorder (BD) have particularly high rates of chronic non-cancer pain (CNCP) and are also more likely to receive prescription opioids for their pain. However, there have been no known studies published to date that have examined opioid treatment patterns among individuals with schizophrenia.

Methods Using electronic medical record data across 13 Mental Health Research Network sites, individuals with diagnoses of MDD (N=65,750), BD (N=38,117) or schizophrenia or schizoaffective disorder (N=12,916) were identified and matched on age, sex and Medicare status to controls with no documented mental illness. CNCP diagnoses and prescription opioid medication dispensings were extracted for the matched samples. Multivariate analyses were conducted to evaluate (1) the odds of receiving a pain-related diagnosis and (2) the odds of receiving opioids, by separate mental illness diagnosis category compared with matched controls, controlling for age, sex, Medicare status, race/ethnicity, income, medical comorbidities, healthcare utilization and chronic pain diagnoses.

Results Multivariable models indicated that having a MDD (OR=1.90; 95% CI=1.85–1.95) or BD (OR=1.71; 95% CI=1.66–1.77) diagnosis was associated with increased odds of a CNCP diagnosis after controlling for age, sex, race, income, medical comorbidities and healthcare utilization. By contrast, having a schizophrenia diagnosis was associated with decreased odds of receiving a chronic pain diagnosis (OR=0.86; 95% CI=0.82–0.90). Having a MDD (OR=2.59; 95% CI=2.44–2.75) or BD (OR=2.12; 95% CI=1.97–2.28) diagnosis was associated with increased odds of receiving chronic opioid medications, even after controlling for age, sex, race, income, medical comorbidities, healthcare utilization and chronic pain diagnosis; having a schizophrenia diagnosis was not associated with receiving chronic opioid medications.

Conclusions Individuals with serious mental illness, who are most at risk for developing opioid-related problems, continue to be prescribed opioids more often than their peers without mental illness. Mental health clinicians may be particularly well-suited to lead pain assessment and management efforts for these patients. Future research is needed to evaluate the effectiveness of involving mental health clinicians in these efforts.
Background
Chronic non-cancer pain (CNCP) affects an estimated 25.3 million Americans (1) at a cost of $600 billion (2). The use of long-term opioid therapy as a treatment for CNCP has quadrupled in the last 15 years (3–5) despite little empirical evidence that opioids are effective for treating CNCP long-term (6, 7) and has instead resulted in dramatic increases in opioid abuse and overdose deaths (8, 9). In order to more effectively address this epidemic, we need to better understand which populations are most burdened by CNCP and which populations are at the greatest risk of opioid use/abuse in order to guide both clinical and policy-related decisions.

Evidence suggests that individuals with mental illness may be one population with particularly high rates of CNCP and may also be more likely to receive prescription opioids for their pain. Several studies have reported that individuals with depression and bipolar disorder, for example, have more frequent pain complaints, higher pain intensity and more pain chronicity (10–17) and are also significantly more likely to receive long-term opioids, at a higher daily dose, and with greater days supplied compared with patients without mental illness (19–25). By contrast, evidence suggests that CNCP is less prevalent among individuals with schizophrenia compared to individuals without mental illness (26); to our knowledge, there have been no studies published to date that have examined opioid treatment patterns specifically among individuals with schizophrenia compared to controls.

This gap in the literature, in addition to other methodological limitations inherent in many prior studies—including small sample sizes (12, 22) and limited generalizability (e.g., examining only military veterans) (10, 20, 24)—prompted the present study. Specifically, we investigated (1) whether individuals with major depressive disorder (MDD), bipolar disorder (BD) and schizophrenia are more or less likely to receive a chronic pain diagnosis compared to individuals with no psychiatric diagnoses and (2) whether individuals with MDD, BD and schizophrenia are more or less likely to receive chronic prescription opioid medications compared to individuals with no psychiatric diagnoses using data from health care systems in the Mental Health Research Network (MHRN) that are representative of a large, geographically and racially/ethnically diverse population across the U.S.
Methods
Data Source
The MHRN is a consortium of research centers located within 13 large integrated health care systems, many of which also have affiliated health insurance plans and serve over 12.5 million individuals across 15 states with diverse populations in the United States. All MHRN sites maintain a Virtual Data Warehouse consisting of electronic health record (EHR) and insurance claim data for all enrolled members or patients. Data on encounters, pharmacy fills, diagnoses, laboratory tests and demographics are organized using standardized definitions across sites and are quality checked locally (27).

The current study involved 10 MHRN systems. These sites were 6 Kaiser Permanente sites (Georgia, Washington, Northwest, Hawaii, Northern California, Southern California), Henry Ford Health System, Essentia Health, Baylor Scott and White Healthcare and Health Partners. Institutional Review Boards at each site approved the study protocol for this project.

Study Population
Individuals were included if they met the following criteria: adults aged 18–70 years (as of January 1, 2016) with a diagnosis of MDD (ICD–9 296.2–296.39/ICD–10 F32-F33.9), BD (ICD–9 296.0x, 296.1x, 29.40-296.89/ICD–10 F30-F31.9) or schizophrenia including schizoaffective disorder (ICD–9 295.x/ICD–10 F20.x, F25.x) documented at least two times by mental healthcare provider in 2015 or 2016 (cases had to “start” 2016, the 12-month study period, with a diagnosis so at least 1 diagnosis had to occur in 2015). Patients who had diagnoses in more than 1 of these categories were categorized hierarchically: schizophrenia>BD>MDD. For example a patient with schizophrenia and MDD would be classified in the schizophrenia group and a patient with only MDD would be classified in the MDD group. This is an approach used in prior studies that have similarly employed a hierarchy of non-overlapping categories (28, 29). Eligible individuals had to have continuous health plan membership throughout 2015 and 2016 (but could have a gap in enrollment records of ≤30 days, as administrative gaps can occur as a result of delays in membership data processing and thus are not indicative of membership interruptions/disenrollment). Individuals with any cancer or metastatic cancer diagnoses (ICD–9 140–165, 170–172, 174–176, 179–199, 200–208, 238.6/ ICD–10 C00–26.9,
C30.x, C37-C41.9, C43.x, C45-C45.7, C45.9, C46-C58., C60-C76.8, C7A.x, C7B.x, C80.x, C81-C85.99, C86.x, C88.x, C90-C96.9, D03.x, D45, D47.Z9, during this same time period were excluded.

Controls were identified using the same criteria as described above except that they had no documented mental illness diagnoses during 2015 or 2016 (they could not “start” 2016, the 12-month study period, with a diagnosis nor receive one during 2016). Matching was done separately for each group (e.g., schizophrenia controls were selected and removed from the pool of controls, then BD controls, followed by MDD controls). Controls for each group were matched on age (in 4-year bands), sex and Medicare status using stratified random sampling. Matching cases to controls was 1:2 for schizophrenia diagnosis and 1:1 each for BP and MDD diagnoses. These ratios were based on what numbers were required to find an adequate number of controls for each group.

**Measures**

Non-cancer chronic pain diagnoses documented on at least 2 dates in 2016 were extracted for the matched samples. The chronic pain conditions extracted included: back pain, neck pain, limb/extremity pain, arthritis, fibromyalgia/widespread muscle pain, headache, orofacial/ear/temporomandibular pain, abdominal/bowel pain, chest pain, urogenital/pelvic/menstrual pain, fractures/contusions/sprains/strains and other painful conditions [which included sickle cell disease, complex regional pain syndrome, systemic lupus erythematosus, acquired deformities (excluding spinal disorders), spinal cord injury and neuropathic pain]. The list of ICD codes used for identifying pain conditions are available online (https://github.com/MHResearchNetwork/MHRN-Central/blob/master/WP_MHRN_SMI_painOpioids.zip).

Prescription opioid medication dispensings were also extracted for the matched samples. We were specifically interested in *chronic* opioid use, defined by prescriptions dispensed that covered at least 70 days in any 90-day period or 6+ dispensings in 2016. This definition was based on prior studies conducted at one of the MHRN sites (30, 31). The list of NDC codes used for identifying opioid medication dispensings are also available online (https://github.com/MHResearchNetwork/MHRN-Central/blob/master/WP_MHRN_SMI_painOpioids.zip).

We also examined sociodemographic (age, sex, race/ethnicity, neighborhood socioeconomic status)
and clinical characteristics of the study population using data from 2016. Overall medical comorbidity burden was calculated using the Charlson Comorbidity Index Score (CCIS). This score contains 19 categories of comorbidity, with each category weighted based on the adjusted risk of 1-year post-discharge mortality. The overall comorbidity score reflects the cumulative increased likelihood of 1-year post-discharge mortality; the higher the score, the more severe the burden of comorbidity (32).

Total health care utilization (hospitalizations, ED visits and other in-person outpatient encounters) was based on summarized data from the last 6 months of 2015. This timeframe was selected so that we had a baseline measure of recent utilization history prior to the study period (which was 2016). Because we were interested in counting utilization days, multiple outpatient encounters documented on the same day counted as one encounter. Preliminary data comparisons across sites were made by the study team to investigate site variation and to ensure accuracy of the data before creating aggregated estimates. This preliminary comparison found very little site variation, supporting the stability of the aggregated estimates.

Analyses
The primary goals of our analyses were to examine whether having a diagnosis of MDD, BD or schizophrenia/schizoaffective disorder was associated with receipt of a chronic pain diagnosis and then subsequent chronic opioid prescription dispenses. For initial bivariate models, we used t-tests for continuous variables and Pearson $\chi^2$-tests for categorical data. Multivariate analyses were conducted to evaluate (1) the odds of receiving a chronic pain-related diagnosis and (2) the odds of receiving opioids, by separate mental illness diagnosis category compared with matched controls, controlling for age, sex, Medicare status, race/ethnicity, income, medical comorbidities, healthcare utilization and chronic pain diagnoses. Results of the models were reported as adjusted odds ratios (ORs) with 95% confidence intervals (CIs).

Results
The total number of patients identified was 377,927 (248,283 cases, 129,644 controls); however, only one-third of the available MDD cases were included in the final dataset (selected randomly) because there were not a sufficient number of controls available. The sample of persons with MDD and
matched controls (total n = 131,488) included 72% women, 86% with a neighborhood income > $40,000 per year, was 57% White, 9% Black/African-American, 22% Hispanic/Latino, and between the ages of 18 and 70 (mean: 43.5, SD: 13.8). Individuals with MDD (N = 65,750) were more likely to have higher Charlson comorbidity scores and greater healthcare utilization than matched controls without psychiatric illness (N = 65,738); they were also more likely to have any CNCP diagnosis (62.4% compared to 39.8% of controls) and to receive chronic opioid medications (10.1% compared to 2.4% of controls; see Table 1).

The sample of persons with BP and matched controls (total n = 76,232) included 67% women, 85% with a neighborhood income > $40,000 per year, was 60% White, 9% Black/African-American, 18% Hispanic/Latino, and between the ages of 18 and 70 (mean: 42.7, SD: 13.3). Individuals with BP (N = 38,117) were similarly more likely to have a higher Charlson comorbidity score and a greater healthcare utilization than matched controls without any psychiatric illness (N = 38,115); they were also more likely to have any CNCP diagnosis (61.5% compared to 40.3% of controls) and receive chronic opioid medications (10.4% compared to 3.0% of controls; see Table 2).

The sample of persons with schizophrenia and matched controls (total n = 38,707) included 44% women, 83% with a neighborhood income > $40,000 per year, was 51% White, 13% Black/African-American, 22% Hispanic/Latino, and between the ages of 18 and 70 (mean: 42.3, SD: 13.8). Individuals with schizophrenia (N = 12,916) had lower neighborhood-level incomes, higher Charlson comorbidity scores, and greater healthcare utilization than matched controls without any psychiatric illness (N = 25,791); they were also slightly more likely to have any CNCP diagnosis (47.2% compared to 42.0% of controls) and receive chronic opioid medications (6.5% compared to 5.0% of controls; see Table 3).

Multivariable models indicated that having a MDD (OR = 1.90; 95% CI = 1.85—1.95) or BD (OR = 1.71; 95% CI = 1.66—1.77) diagnosis was associated with increased odds of receiving a comorbid chronic pain diagnosis after controlling for age, sex, race, income, medical comorbidities and healthcare utilization. By contrast, having a schizophrenia diagnosis (OR = 0.86; 95% CI = 0.82—0.90) was associated with decreased odds of receiving a chronic pain diagnosis (see Table 4).
Having a MDD (OR = 2.59; 95% CI = 2.44—2.75) or BD (OR = 2.12; 95% CI = 1.97—2.28) diagnosis was associated with increased odds of receiving chronic opioid medications, even after controlling for age, sex, race, income, medical comorbidities, healthcare utilization and having a chronic pain diagnosis; having a schizophrenia diagnosis was not associated with receiving chronic opioid medications (see Table 4).

Discussion
The present study found that individuals with MDD and BD diagnoses were significantly more likely to receive CNCP-related diagnoses compared to matched controls; by contrast, individuals with schizophrenia or schizoaffective disorder were significantly less likely to receive CNCP-related diagnoses compared to matched controls. These findings confirm and extend those from previous studies (16, 17, 26) and suggest that the pattern of CNCP-related diagnoses may be different for individuals with MDD or BD than for individuals with schizophrenia or schizoaffective disorder. This finding is not surprising given that symptoms of MDD and BD overlap more with each other than with symptoms of schizophrenia and schizoaffective disorder (10).

Compared to the general population, individuals with schizophrenia have increased risk of experiencing multiple physical comorbidities warranting pain control (33–36) and thus it seems counterintuitive that they were less likely to receive CNCP diagnoses than controls in the present study. There are several possible explanations for the lower prevalence of CNCP diagnoses among individuals with schizophrenia. First, there is some evidence that individuals with schizophrenia have reduced sensitivity to pain compared to individuals without psychiatric illness (37–40). Further, antipsychotics have been shown to have analgesic qualities (41); therefore, this decreased likelihood of receiving a pain diagnosis could reflect lower levels of pain. However, results from a recent meta-analysis indicate that antipsychotic-free patients with schizophrenia also had elevated pain thresholds compared to controls (40). Therefore, this decreased likelihood of receiving a pain diagnosis could reflect lower levels of pain. An alternative explanation may be that individuals with schizophrenia are less likely to express pain rather than actually experiencing less pain, either because they are unable to adequately describe the physical symptoms due to social communication impairments (42) or they
withhold this information because of concerns about how they will be treated by healthcare providers. For example, Kuritzky and colleagues reported that a large percentage of people (~40%) with schizophrenia who had pain-related complaints indicated that they never reported these complaints in order to avoid being perceived a burden to providers and/or to avoid hospitalization (26, 43). However, another study with Veterans Health Administration patients found that patients with schizophrenia were twice more likely to report chronic pain in comparison to those without schizophrenia (10). Therefore, given these conflicting findings, authors of recent systematic review suggest that it is likely more appropriate to state that pain experience in schizophrenia is disturbed or distorted rather than decreased or absent (42).

Behavioral health clinicians may be less likely to assign pain-related diagnoses for individuals with schizophrenia because many have limited training in physical symptom management (44) and are more focused on treating psychiatric than medical concerns (45-47); primary care clinicians may be less likely to assign pain-related diagnoses because their short consultation times make it difficult to both assess mental symptoms and conduct physical assessments. Additionally, less experienced providers may be uncomfortable with serious mental illness and may avoid intensifying their interaction with a patient by asking probing questions about physical symptoms and performing a physical exam (44). Indeed, there is ample evidence that individuals with schizophrenia are less likely than their peers without any psychiatric illnesses to receive medical procedures and treatments for a range of conditions including cancer screening and treatment (48), use of antihypertensive and lipid-lowering drugs (49) and appropriate diabetes care (including A1C and cholesterol testing, eye and feet exams, etc.) (50, 51). Future studies are needed to better understand providers’ decision-making with respect to diagnosing and treating pain among patients with schizophrenia.

This lack of expression and/or disclosure of pain-related complaints by patients or under-diagnosis by providers may lead to the under-detection and under-treatment of CNCP among individuals with schizophrenia. This is problematic given that CNCP among individuals with mental illness is associated with worsening of psychiatric symptoms, impaired recovery/poor therapeutic response (10, 52), greater functional incapacitation (53, 54), lower quality of life (55, 56) and increased risk of suicide.
Therefore, it is essential to systematically assess and monitor CNCP-related conditions among individuals with schizophrenia. Psychiatrists may be particularly well-suited to oversee pain management in this population and thus need adequate education and training to equip them to do so (59).

The present study also found that individuals with MDD and BD diagnoses were over two times more likely to receive chronic opioid medication prescriptions compared to matched controls. This finding is consistent with prior literature which has similarly reported that opioids are more commonly prescribed (and prescribed at higher doses) in these populations compared to those without these mental health conditions, even after controlling for a wide array of other demographic and clinical risk factors (19, 22, 24, 25). One explanation for this is that these individuals may present with greater pain severity (60), thereby increasing the likelihood that clinicians will prescribe an opioid and at a higher dose (61). However, the relationship between depressive symptoms and opioid use is complex and likely bidirectional in nature, as prior research indicates that chronic opioid use can increase the risk of new-onset depression (62) as well as depression recurrence (63). Regardless of the nature of the causal relationship, there is evidence that mental illness is associated with diminished opioid analgesia (64) and, more importantly, mental illness is a known risk factor for a range of adverse opioid-related outcomes including opioid use disorder (65–69). Therefore, individuals most at risk for developing opioid-related problems are also more likely to be prescribed opioids (20). Healthcare providers should be especially conservative in prescribing opioids for individuals with mental illness—or avoid opioid therapy altogether for this population, consistent with the current Canadian Medical Association recommendation (70)—and instead, favor non-pharmacological alternatives (25) such as behavioral/psychosocial approaches.

The present study has several limitations. First, opioid prescription data is based on dispensings, and thus may not accurately represent patients’ actual medication use. Second, we categorized patients who had more than 1 mental health diagnosis hierarchically; therefore, a patient with schizophrenia could also have had depression but he/she would not have been included in the analyses on individuals with depression. Thus our findings should be interpreted accordingly—e.g., depression is
associated with an increased odds of a pain diagnosis and receipt of opioid prescriptions when not comorbid with schizophrenia. However, consistent with diagnostic criteria (71), we applied a hierarchy with diagnosis of schizophrenia superseding a diagnosis of mood disorder and bipolar disorder superseding a diagnosis of unipolar depression. Third, study results were derived from a sample of members of integrated payer-provider systems. There is some evidence to suggest that individuals who are more economically and socially disadvantaged may be more severely ill (72). Therefore, our largely insured sample may underrepresent the most impaired patients. Thus, caution is urged in generalizing the findings to uninsured populations. This study’s strengths include a large, geographically and racially/ethnically diverse study population, the comparison of 3 populations with serious mental illness to matched controls, and the inclusion of important statistical confounders such as healthcare utilization in multivariate models.

Conclusion
The presence of pain significantly impacts individuals’ engagement in and adherence to their mental health treatment and is an important moderator of treatment-related outcomes with respect to both pharmacotherapy and psychotherapy (73, 74). Therefore, the systematic assessment and treatment of pain among individuals with mental illness is critical to short- and long-term improvements in quality of life. Given the lack of evidence about efficacy of long-term opioid treatment for CNCP and risks of drug interactions and/or use disorders, specifically among individuals with serious mental illness, non-pharmacological (e.g., behavioral/psychosocial) treatments are needed for this population. Unfortunately, barriers to accessing these types of interventions exist, such as limited patient and clinician awareness, stigma, limited capacity and reimbursement issues (73). Consequently, there have been recent calls for engaging mental health clinicians in pain treatment for this population, as they may be particularly well-suited to assess pain symptoms, incorporate pain into treatment plans and encourage self-management activities and participation in behavioral/psychosocial treatments for pain (73). Future research is needed to evaluate the effectiveness of involving mental health clinicians in pain management.

Abbreviations
CNCP: Chronic non-cancer pain
MDD: major depressive disorder
BD: bipolar disorder
MHRN: Mental Health Research Network

Declarations

Ethics approval and consent to participate: We have included the required statement in the body of the manuscript.

Consent for publication: Not applicable.

Availability of data and material: All SAS code is provided on the MHRN GitHub site: see https://github.com/MHResearchNetwork/MHRN-Central/blob/master/WP_MHRN_SMI_painOpioids.zip

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Authors’ contributions: AOS, CS and MS had full access to all of the data and take responsibility for the integrity of the data and accuracy of the data analysis. All authors have contributed to and have approved the final submitted manuscript.

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Tables

Table 1: Patients with Major Depressive Disorder (MDD) compared to Matched Controls

| Characteristic  | Patients with MDD (N=65,750) n(%)/Mean±SD | Matched Controls (N=65,738) n(%)/Mean±SD | Test Statistic | p-value |
|-----------------|---------------------------------------------|-------------------------------------------|----------------|---------|
| Total           | 65750                                       | 65738                                     |                |         |
| Age             | 43.5± 13.8                                  | 43.5± 13.8                                | \( t = -0.14 \) | 0.89    |
| Sex             |                                             |                                           |                |         |
| Male            | 18733 (28.5%)                               | 18731 (28.5%)                             | \( \chi^2 = 0 \) | 0.99    |
| Female          | 47013 (71.5%)                               | 47005 (71.5%)                             |                |         |
| Medicare        | 6329 (9.6%)                                 | 6322 (9.6%)                               | \( \chi^2 = 0 \) | 0.96    |
| Race            |                                             |                                           | \( \chi^2 = 5891.77 \) | <0.0001 |
| White/Caucasian | 43647 (66.3%)                               | 31328 (47.7%)                             |                |         |
| Black/African-American | 5894 (9.0%) | 5940 (9.0%) |            |         |
| Asian           | 3850 (5.9%)                                 | 8846 (13.5%)                              |                |         |
| Pacific Islander| 540 (0.8%)                                  | 791 (1.2%)                                |                |         |
| Native American | 672 (1.0%)                                  | 462 (0.7%)                                |                |         |
| Other           | 180 (0.3%)                                  | 165 (0.3%)                                |                |         |
### Table 2: Patients with Bipolar Disorder compared to Matched Controls

| Characteristic                      | Patients with Bipolar Disorder (N=38,117) n(%)/Mean±SD | Matched Controls (N=38,115) n(%)/Mean±SD | Test Statistic | p-value |
|-------------------------------------|--------------------------------------------------------|------------------------------------------|----------------|---------|
| Age                                 | 42.7± 13.2                                             | 42.7± 13.3                                | t=-0.20        | 0.84    |
| Sex                                 |                                                         |                                          |                |         |
| Male                                | 12530(32.9%)                                           | 12530(32.9%)                             | χ²=0           | 0.99    |
| Female                              | 25585 (67.1%)                                          | 25583 (67.1%)                            |                |         |
| Medicare                            | 6386 (16.8%)                                           | 6383 (16.8%)                             | χ²=0           | 0.98    |
| Race                                |                                                         |                                          |                |         |
| White/Caucasian                     | 27348(71.8%)                                           | 18408 (48.3%)                            | χ²=5450.33     | <0.0001 |
| Black/African-American              | 3410 (9.0%)                                            | 3594 (9.4%)                              |                |         |

*Includes sickle cell disease, complex regional pain syndrome, systemic lupus erythematosus, acquired deformities (excluding spinal disorders), spinal cord injury, lyme disease, neuropathic pain

**Chronic use defined by 70+ days supply in a 90-day period, receiving 6+ dispenses in a year
| Ethnicity                          | Patients with Schizophrenia (N=12,916) n(%) | Matched Controls (N=25,791) n(%) | Test Statistic | p-value |
|----------------------------------|----------------------------------------------|----------------------------------|----------------|---------|
| Asian                            | 1782 (4.7%)                                  | 4993 (13.1%)                    |                |         |
| Pacific Islander                 | 281 (0.7%)                                   | 453 (1.2%)                      |                |         |
| Native American                  | 499 (1.3%)                                   | 281 (0.7%)                      |                |         |
| Other                            | 94 (0.3%)                                    | 117 (0.3%)                      |                |         |
| Unknown                          | 4694 (12.3%)                                 | 10262 (27.0%)                   |                |         |
| Ethnicity (Hispanic)             | 5473 (14.4%)                                 | 8307 (21.8%)                    | $\chi^2=711.63$ | <0.0001 |
| Neighborhood Income              |                                              |                                 |                |         |
| <$40,000 per year                | 4985 (13.1%)                                 | 4835 (12.7%)                    | $\chi^2=0.41$  | 0.52    |
| >$40,000 per year                | 32544 (85.4%)                                | 32006 (84.0%)                   |                |         |
| Charlson Comorbidity Index       | 0.55± 1.10                                   | 0.28± 0.81                      | $t=39.21$      | <0.0001 |
| Total healthcare utilization in last 6 mo | 8.6± 11.3                                   | 2.4± 4.8                        | $t=99.04$      | <0.0001 |
| Pain conditions                  |                                              |                                 |                |         |
| Any Pain                         | 23423(61.5%)                                 | 15342 (40.3%)                   | $\chi^2=3426.65$ | <0.0001 |
| Back pain                        | 7756 (20.4%)                                 | 3650 (9.6%)                     | $\chi^2=1737.92$ | <0.0001 |
| Neck pain                        | 3713 (9.7%)                                  | 1805 (4.7%)                     | $\chi^2=711.12$ | <0.0001 |
| Limb/extremity pain, arthritis   | 12052(31.6%)                                 | 7401 (19.4%)                    | $\chi^2=1492.66$ | <0.0001 |
| Fibromyalgia/widespread muscle   | 2384 (6.3%)                                  | 663 (1.7%)                      | $\chi^2=1012.43$ | <0.0001 |
| Headache                         | 5000 (13.1%)                                 | 1845 (4.8%)                     | $\chi^2=1597.48$ | <0.0001 |
| Orofacial/ear/temporomandibular  | 477 (1.3%)                                   | 237 (0.6%)                      | $\chi^2=81.42$  | <0.0001 |
| Abdominal/bowel pain             | 5777 (15.2%)                                 | 2821 (7.4%)                     | $\chi^2=1145.30$ | <0.0001 |
| Chest pain                       | 3009 (7.9%)                                  | 1348 (3.5%)                     | $\chi^2=671.51$  | <0.0001 |
| Urogenital/pelvic/menstrual pain | 1925 (5.1%)                                  | 959 (2.5%)                      | $\chi^2=336.23$  | <0.0001 |
| Fractures/contusions/sprains/strains | 5567 (14.6%)                               | 2743 (7.2%)                     | $\chi^2=1076.93$ | <0.0001 |
| Other painful conditions*        | 4137 (10.9%)                                 | 2034 (5.3%)                     | $\chi^2=779.68$  | <0.0001 |
| Chronic opioid use**             | 3961 (10.4%)                                 | 1156 (3.0%)                     | $\chi^2=1648.10$ | <0.0001 |

* Includes sickle cell disease, complex regional pain syndrome, systemic lupus erythematosus, acquired deformities (excluding spinal disorders), spinal cord injury, lyme disease, neuropathic pain
** Chronic use defined by 70+ days supply in a 90-day period, receiving 6+ dispenses in a year

Table 3: Patients with Schizophrenia compared to Matched Controls
| Category                                | Male       | Female      | Chi-Squared | p-value |
|----------------------------------------|------------|-------------|-------------|---------|
| **Gender**                             | 5144 (39.8%)| 10247 (39.7%)| 0.03        | 0.86    |
| **Medicare**                           | 5666 (43.9%)| 11332 (43.9%)|             |         |
| **Race**                               |            |             | 1021.2      | <0.0001 |
| White/Caucasian                        | 6889 (53.3%)| 12770 (49.5%)|             |         |
| Black/African-American                 | 2476 (19.2%)| 2724 (10.6%) |             |         |
| **Asian**                              | 1317 (10.2%)| 3008 (11.7%) |             |         |
| **Pacific Islander**                   | 153 (1.2%)  | 343 (1.3%)  |             |         |
| **Native American**                    | 138 (1.1%)  | 204 (0.8%)  |             |         |
| **Other**                              | 28 (0.2%)   | 44 (0.2%)   |             |         |
| **Unknown**                            | 1907 (14.8%)| 6696 (26.0%) |             |         |
| **Ethnicity (Hispanic)**               |            |             | 79.87       | <0.0001 |
| **Neighborhood Income**                |            |             | 170.42      | <0.0001 |
| <$40,000 per year                      | 2404 (18.6%)| 3444 (13.4%) |             |         |
| >$40,000 per year                      | 10345 (80.1%)| 21650 (83.9%)|             |         |
| **Charlson Comorbidity Index**         | 0.63± 1.18 | 0.43+ 1.07  | -16.58      | <0.0001 |
| **Total healthcare utilization in last 6mo** | 7.9± 10.9 | 2.6± 5.6 | -63.60 | <0.0001 |
| **Pain conditions**                    |            |             |             |         |
| Any Pain                               | 6092 (47.2%)| 10835(42.0%)| 92.96       | <0.0001 |
| Back pain                              | 1855 (14.4%)| 2687 (10.4%) | 129.23      | <0.0001 |
| Neck pain                              | 754 (5.8%)  | 1228 (4.8%) | 20.52       | <0.0001 |
| Limb/extremity pain, arthritis         | 2942 (22.8%)| 5312 (20.6%) | 24.41       | <0.0001 |
| Fibromyalgia/widespread muscle         | 386 (3.0%)  | 463 (1.8%)  | 57.13       | <0.0001 |
| Headache                               | 973 (7.5%)  | 1264 (4.9%) | 109.52      | <0.0001 |
| Orofacial/ear/temporomandibular        | 112 (0.9%)  | 150 (0.6%)  | 10.44       | 0.0012  |
| Abdominal/bowel pain                   | 1497 (11.6%)| 1907 (7.4%)  | 188.93      | <0.0001 |
| Pain Condition                                      | Adjusted OR (CI) | Adjusted OR (CI) | Chi-square |
|----------------------------------------------------|------------------|------------------|------------|
| Chest pain                                         | 1.90 (1.85 - 1.95)* | 2.59 (2.44 - 2)  | <0.001     |
| Urogenital/pelvic/menstrual pain                   | 1.71 (1.66 - 1.77)* | 2.12 (1.97 - 2)  | <0.001     |
| Fractures/contusions/sprains/strains               | 0.86 (0.82 - 0.90)* | 1.00 (0.91 - 1)  | <0.001     |

* Includes sickle cell disease, Complex Regional Pain Syndrome, systemic lupus erythematosus, acquired deformities (excluding spinal disorders), spinal cord injury, Lyme disease, Neuropathic pain
** Chronic use defined by 70+ days supply in a 90 day period, receiving 6+ dispenses in a year

Table 4. Odds of Receiving a Chronic Pain Diagnosis and Chronic Opioid Prescriptions among Individuals with Versus without Mental Illness

Supplementary Files
This is a list of supplementary files associated with this preprint. Click to download.
Tables.pdf