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Association of Mental Health Conditions and Treatments With Long-term Opioid Analgesic Receipt Among Adolescents

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Key Points

Question

To what extent are adolescents with preexisting mental health conditions more likely than adolescents without those conditions to receive long-term opioid therapy?

Findings

In a cohort of more than 1 million commercially insured adolescents receiving opioids nationwide, 3.0 per 1000 recipients transitioned to long-term opioid therapy within 3 years. Adolescents with a range of prior mental health conditions and treatments had substantially higher rates of transitioning from initial opioid receipt to long-term opioid therapy.

Meaning

Long-term opioid therapy rates were low among commercially insured adolescent opioid recipients overall but were substantially higher among those with preexisting mental health conditions and treatments.

Abstract

Importance

Adults with mental health conditions are more likely than those without to receive long-term opioid therapy. Less is known about opioid therapy among adolescents, especially those with mental health conditions.

Objective

To examine associations between preexisting mental health conditions and treatments and initiation of any

opioid and long-term opioid therapy among adolescents.

Design, Setting, and Participants

A cohort of 1 224 520 incident opioid recipients without cancer diagnoses aged 14 to 18 years at first receipt was extracted from nationwide commercial health care claims data from January 1, 2003, to December 31, 2014. Analysis was conducted from August 19, 2016, to November 16, 2017. Associations between preexisting mental health conditions and treatments and any opioid receipt were examined by comparing recipients with nonrecipients matched on sex, calendar year and years of age of first enrollment, and months of enrollment (prior to the index month for recipients, ever for nonrecipients). Associations between preexisting mental health conditions and treatments and subsequent long-term opioid therapy were examined among recipients with at least 6 months' follow-up using Cox proportional hazards regressions adjusted for demographics.

Exposures

Mental health condition diagnoses and treatments recorded in inpatient, outpatient, and filled-prescription claims prior to opioid receipt.

Main Outcomes and Measures

Opioid receipt, defined as any opioid analgesic prescription claim, and long-term opioid therapy, defined as more than 90 days' supply within a 6-month window having no gaps in supply of more than 32 days.

Results

Of the 1 224 520 new opioid recipients included, the median age at first receipt was 17 years (interquartile range, 16-18 years), and 51.1% were female. Median follow-up after first receipt was 625 days (interquartile range, 255-1268 days). Adolescents with anxiety, mood, neurodevelopmental, sleep, and nonopioid substance use disorders and most mental health treatments were significantly more likely to receive any opioid (odds ratios from 1.13 [95% CI, 1.10-1.16] for nonopioid substance use disorders to 1.69 [95% CI, 1.58-1.81] for nonbenzodiazepine hypnotics). Among the 1 000 453 opioid recipients (81.7%) who had at least 6 months' follow-up, the cumulative incidence of long-term opioid therapy was 3.0 (95% CI, 2.8-3.1) per 1000 recipients within 3 years after first opioid receipt. All preexisting mental health conditions and treatments were strongly associated with higher rates of long-term opioid therapy (adjusted hazard ratios from 1.73 [95% CI 1.54-1.95] for attention-deficit/hyperactivity disorder to 8.90 [95% CI, 5.85-13.54] for opioid use disorder).

Conclusions and Relevance

Commercially insured adolescents with many types of preexisting mental health conditions and treatments were modestly more likely to receive any opioid and were substantially more likely to subsequently transition to long-term opioid therapy relative to those without, although overall rates of long-term opioid therapy were low.

Introduction

Opioid analgesics are the controlled medications most commonly prescribed to adolescents.[1] An estimated 2.9% of US children and adolescents received prescription opioids in 2012.[2] Adolescents treated with opioids are at risk of negative consequences. For example, hospitalizations associated with prescription opioid poisoning were 10.2 per 100 000 adolescents in 2012.[3]

Against the background of 33 091 total opioid overdose deaths in 2015[4] and increasing attention to opioid

therapy for adults with chronic pain,[5,6] identifying appropriate prescription practices and concomitant treatment needs for adolescents receiving opioids is essential. Yet little is known about long-term opioid therapy (LTOT) patterns or safety among adolescents.[7] Among adults, there is clear evidence that those patients at greatest risk of adverse opioid-related outcomes—notably including those with preexisting substance use disorder (SUD) and other mental health conditions[8,9,10]—are actually most likely to receive prescribed opioids in greater quantities.[11,12] Limited evidence supports similar prescription patterns among adolescents.[2,13,14,15,16]

Given the rarity of LTOT among youths, however, few studies have had sufficient sample sizes to examine associations between LTOT and specific mental health conditions during adolescence in particular.[17] Our previous report used nationwide commercial health care insurance claims to demonstrate increased rates of LTOT among patients, including adolescents and young adults, with mental health conditions and treatments.[18] The present study used the same data source to focus exclusively on adolescents aged 14 to 18 years initiating opioid receipt. Specifically, we examined initial opioid receipt and the subsequent transition to LTOT with the goal of evaluating associations across a wide range of preexisting mental health conditions and their treatments. The large scale of the study permitted consideration of rare yet serious conditions (eg, youth-onset opioid use disorder [OUD] and self-injurious behavior) and potentially harmful combined therapies (eg, benzodiazepines[6,19]).

Methods

Data Source

This study used data from the 2003-2014 Truven Health MarketScan Commercial Claims and Encounters (MarketScan) databases of commercial health care insurance claims. Approximately half of the US population had commercial insurance in 2014, and MarketScan data include claims for inpatient and outpatient services and filled prescriptions obtained from employers and health plans.[20] There were approximately 154 million unique enrollee observations from 2003 to 2014, including employees, their spouses and dependents, COBRA (Consolidated Omnibus Budget Reconciliation Act) continuers, and early retirees. This study was determined to be exempt by the Indiana University and University of Chicago institutional review boards, and the need for patient informed consent was waived because no personal identifiers were involved.

Opioid Recipient Sample

We identified a cohort of adolescents who filled an initial opioid prescription. Of the 2 308 252 MarketScan enrollees aged 14 to 18 years initiating opioid receipt, 1 283 773 (55.6%) were enrolled for at least 12 consecutive calendar months prior to the month of the index (first) opioid prescription fill and were therefore considered new recipients. Months with any covered days were counted as enrolled, including only those years in which enrollees had prescription coverage. We subsequently excluded patients who had received a cancer diagnosis in the year before or 1.5 years after the index prescription (n = 55 692) or those without valid enrollment at the time the index prescription was filled (n = 3561), resulting in a sample of 1 224 520 patients (53.0% of all adolescent initiators). We followed up enrollees from their index prescription until their first disenrollment or December 31, 2014 (whichever occurred first), to examine subsequent LTOT. To compare opioid recipients with nonrecipients, we also identified a sample of control patients who filled no opioid prescriptions, matched 1:1 to recipient cases.

Opioid Prescription

We identified prescription claims for any opioid analgesic.[21] Nontransdermal buprenorphine hydrochloride

was excluded because it was assumed to have been used for OUD treatment.[22] By contrast, prescription claims for methadone hydrochloride were included because they are unlikely to represent methadone treatment of OUD, which is likely to be recorded in other service claims.[23] All opioid prescriptions (and all patients with index prescriptions) with dates outside the included years, days' supply that were nonpositive or more than 180 days, or quantities (eg, pills and milliliters of solution) that were nonpositive or more than 1000 were excluded to guard against invalid records.[24]

We defined LTOT as receipt of more than 90 days' supply of opioids within a 6-month window having no gaps in supply greater than 32 days.[18,25,26] We considered the first fill date for a window meeting these criteria the onset of LTOT. We determined, using fill dates and days' supply, whether each day during follow-up was covered by a prescription for any opioid, with 2 exceptions. First, we assumed that any overlapping prescriptions for the same drug (eg, short-acting hydrocodone products) were taken sequentially. Second, we assumed that buprenorphine transdermal patches were worn for 7 days, fentanyl transdermal patches for 3 days, and that they were used sequentially.[21] We rounded the number of patches up to the nearest integer when necessary to calculate integer days' supply.

Prior Mental Health

We identified mental health conditions from inpatient or outpatient claims before the month of the first opioid prescription receipt. Diagnoses were recorded in service claims using *International Classification of Diseases, Ninth Revision* (*ICD-9*) codes for attention-deficit/hyperactivity disorder (ADHD), anxiety disorders, bipolar or other (nondepressive) mood disorders, depressive disorders, nonopioid SUDs, OUD, schizophrenia spectrum disorders, sleep disorders, and suicide attempt or other self-injury.

We identified prior psychoactive medications using claims for filled prescriptions of the following drug classes: ADHD medications, antipsychotics, benzodiazepines, mood stabilizers, nonbenzodiazepine hypnotics, OUD medications (ie, naltrexone products; buprenorphine with or without naloxone hydrochloride, excluding the buprenorphine transdermal patch Butrans and the injectable buprenorphine hydrochloride Buprenex), serotonin-norepinephrine reuptake inhibitors (SNRIs), and selective serotonin reuptake inhibitors (SSRIs). To distinguish medications used in pain from medications used for psychiatric treatment, we excluded duloxetine hydrochloride from the SNRIs and all antiepileptic drugs except lamotrigine from the mood stabilizers. We also identified claims for psychotherapy, regardless of diagnosis (*Current Procedural Terminology, 4th Edition*, codes 90804, 90816, 90806, 90818, 90808, 90821, 90845, 90846, 90847, 90849, 90853, 90832, 90834, and 90837). We required adolescents to be at least 13 years old at claims for prior mental health diagnoses and treatments to avoid including claims of questionable validity (eg, early childhood SUD). Diagnosis codes and generic medication names are provided in eTables 1 and 2 in the Supplement.

Statistical Analysis

Any Opioid Receipt We first used a matched case-control approach to examine whether prior mental health conditions were associated with initial receipt of any opioid. Given the variability in enrollment and demographics, we matched opioid recipients 1:1 to nonrecipient controls on exact values of sex, calendar year and years of age of first enrollment, and months of enrollment (prior to the index month for recipients, ever for nonrecipients).[27] For this enrollment length to correspond with eligibility for mental health conditions and treatments, we only counted enrollment when enrollees were at least 13 years old.

Of the opioid recipients, 5.8% could not be matched to nonrecipients. Randomly selecting 40% of the recipients yielded greater success (0.02% unmatched); thus, we used this subset for the matched-pair analysis (n = 489 704 pairs). Selected recipients were similar to the full cohort on index age and year, sex, months of prior enrollment, and opioid drugs received. We compared the odds of any opioid receipt

between matched recipients and nonrecipients by using separate conditional logistic regressions for each predictor.

Long-term Opioid Therapy In our primary analyses, we used a cohort design to examine whether prior mental health predicted the transition from initial opioid receipt to long-term therapy (ie, among opioid recipients only). Because follow-up could be right censored, we used Kaplan-Meier estimates and separate Cox proportional hazards regressions for each predictor, with time since index opioid prescription fill as the time scale.[28] We also examined the number of different types of mental health conditions (0, 1, or 2+) to index comorbidity.[29] Because our LTOT definition required 6-month windows, we set censoring dates to 6 months prior to the end of observed follow-up (ie, the last date at which an adolescent could begin a 6-month window). Thus, adolescents could begin LTOT at any time from index opioid fill until censoring. This rule additionally required 6 months or more of follow-up, excluding 224 067 adolescents from these analyses (n = 1 000 453). The Cox regressions were adjusted for sex, index age, and index year.

We conducted 5 sensitivity analyses. First, we restricted the sample to patients with painful condition diagnoses in the 90-day period that ended with the index date to examine associations among adolescents more likely to be receiving opioid therapy for those conditions (eTable 1 in the Supplement).[17,30] Second, we included a linear time-by-predictor interaction to evaluate and account for potential violations of the proportional hazards assumption. Third, we used a stricter definition of LTOT that required opioid supply on every day within a 6-month window to examine the sensitivity of the associations to the outcome criterion. Fourth, we counted only past year mental health claims so that all recipients had equivalent time for predictors. Fifth, we restricted the sample to patients with 2010 index dates, which decreased the likelihood of bias from (1) changes in data collection (MarketScan records include additional diagnosis fields from 2009 onward) or (2) inadvertently counting individuals as multiple enrollees in multiple years (ie, if an adolescent switched MarketScan-covered insurers). We analyzed data using SAS, version 9.4 (SAS Institute Inc). We report 95% CIs, which correspond to 2-sided tests of statistical significance at $P < .05$.

Results

Of the 1 224 520 new adolescent opioid recipients, 51.1% were female. The median age at first receipt was 17 years (interquartile range, 16-18 years). The median follow-up after first receipt was 625 days (interquartile range, 255-1268 days).

During follow-up, adolescents filled 2 349 173 opioid prescriptions. Hydrocodone accounted for 61.6% of opioids received (among 72.6% of recipients). Other common opioid products included oxycodone (21.9% of recipients), codeine (18.8%), tramadol (7.3%), and propoxyphene (5.6%). Some adolescents received multiple opioid drugs. Methadone (0.1% of prescriptions) was relatively uncommon.

Mental Health and Any Opioid Receipt

In comparisons of opioid recipients and matched nonrecipients, adolescents with most prior mental health conditions and treatments were more likely than adolescents without such conditions or treatments to receive any opioid (Table 1). Associations were generally weak in magnitude, with relative increases in the odds of opioid receipt ranging from 13% for nonopioid SUDs (odds ratio [OR], 1.13; 95% CI, 1.10-1.16) to 69% for nonbenzodiazepine hypnotics (OR, 1.69; 95% CI, 1.58-1.81). Associations for suicide attempt or other self-injury, schizophrenia spectrum disorders, OUD, and OUD medications were weaker and not statistically significant. The Figure displays associations between prior mental health and receipt of any opioid and LTOT.

Mental Health and LTOT

Of the 1 000 453 opioid recipients (81.7%) with at least 6 months of follow-up, 51.1% were female, and the median age was 17 years (interquartile range, 16-18 years). Among these adolescents, the estimated cumulative incidence of LTOT after first opioid receipt was 1.1 (95% CI, 1.1-1.2) per 1000 recipients within 1 year, 3.0 (95% CI, 2.8-3.1) per 1000 recipients within 3 years, 8.2 (95% CI, 7.8-8.6) per 1000 recipients within 6 years, and 16.1 (95% CI, 14.2-18.0) per 1000 recipients within 10 years. The prevalence of mental health conditions and treatments in this sample is shown in eTable 3 in the Supplement.

All mental health conditions and treatments were associated with higher rates of transitioning from a first opioid prescription to long-term therapy. Table 2 provides the estimated incidence of LTOT among those with and without mental health conditions and treatments. Adjusted relative increases in the rate of LTOT ranged from a factor of 1.73 for ADHD (hazard ratio [HR], 1.73; 95% CI, 1.54-1.95) to approximately 4-fold for benzodiazepines (HR, 3.88; 95% CI, 3.39-4.45) and nonopioid SUDs (HR, 4.02; 95% CI, 3.48-4.65) to 6-fold for nonbenzodiazepine hypnotics (HR, 6.15; 95% CI, 5.01-7.55) and to nearly 9-fold for OUD (HR, 8.90; 95% CI, 5.85-13.54). In addition, relative to no condition, the number of condition types was also associated with higher LTOT rates (1 condition: HR, 2.21; 95% CI, 2.01-2.43; 2 or more conditions: HR, 4.01; 95% CI, 3.62-4.46).

Given the strong associations for OUD, we explored other mental health factors and opioid receipt among those with preexisting OUD. These adolescents were more likely than adolescents without OUD to have other mental health conditions and treatments (eTable 4 in the Supplement). For example, 76.1% of adolescents with OUD had other SUDs, 61.0% had depressive disorders, and 52.6% had received an SSRI. During follow-up, those with preexisting OUD received opioid drugs similar to those received by adolescents without OUD, although the former were more likely to receive certain opioids (eg, oxycodone and tramadol; eTable 5 in the Supplement). Of those with preexisting OUD, 15.5% filled a prescription for OUD medication treatment during follow-up.

Sensitivity Analysis

Sensitivity analyses supported the overall LTOT conclusions (eTables 6 and 7 in the Supplement). First, among the 229 913 opioid recipients (23.0%) with past 90-day painful condition diagnoses, the cumulative incidence of LTOT was 6.6 (95% CI, 6.1-7.0) per 1000 within 3 years. Most mental health associations persisted among these recipients. The HRs for LTOT ranged from 1.59 (ADHD medications 95% CI, 1.35-1.86) to 6.33 (nonbenzodiazepine hypnotics 95% CI, 4.84-8.26). Only the OUD medication association was not statistically significant (HR, 2.23; 95% CI, 0.31-15.83).

Second, few tests of the proportional hazards assumption indicated changes in associations over time, and none altered the overall interpretations. Associations were stronger earlier in follow-up for anxiety disorders, benzodiazepines, sleep disorders, nonbenzodiazepine hypnotics, and, especially, OUD. Extrapolating from the HR at the start of follow-up (13.93) and the interaction term, the OUD HR would decrease to 5.25 by year 3.

Third and fourth, the results did not substantively differ for the stricter LTOT definition or past-year mental health predictors, respectively. Fifth, associations were of comparable magnitudes for the 2010 index cohort. As expected given the decreased statistical power, CIs were larger, although only the suicide attempt or other self-injury, ADHD medication, and OUD medication associations were nonsignificant.

Discussion

In this nationwide study of commercially insured adolescents, LTOT was relatively uncommon. The estimated incidence of LTOT receipt was 3.0 per 1000 adolescents within 3 years of filling an initial opioid prescription. Although adolescents with a wide range of preexisting mental health conditions and treatments were modestly more likely than adolescents without those conditions or treatments to receive an

initial opioid, the former had substantially higher rates of subsequent transitioning to LTOT. Associations were strongest for OUD, OUD medications, nonbenzodiazepine hypnotics, and other SUDs. The associations were stronger sooner after first opioid receipt for OUD, as well as for anxiety and sleep disorders and their treatments, suggesting that adolescents with these conditions and treatments were more likely to quickly transition into LTOT.

These findings extend prior health care record studies of opioid receipt among young people. One smaller study of adolescents and young adults with chronic pain found similar associations but lacked statistical power to examine LTOT among those with SUDs.[17] Our prior study of MarketScan recipients across ages included analyses of mental health and LTOT among adolescents and young adults but did not focus primarily on adolescents.[18] The present results described among adolescents, in particular, nationwide patterns of opioid initiation and LTOT across diverse preexisting mental health conditions and treatments. Indeed, the magnitudes of those associations appeared equivalent or stronger than have been found for older patients,[18] despite the relative rarity of LTOT among adolescents.

These results raise questions about how adolescents with mental health conditions—and OUD especially—develop greater likelihoods of LTOT given no greater opioid effectiveness in these populations.[31] Adolescents with OUD appeared to differ primarily in the amount of opioids (ie, LTOT) rather than in which opioid drugs they received. Hypotheses have been suggested at multiple levels of analysis.[17,32] For example, researchers have proposed neurobiological vulnerabilities, including reward deficits.[33,34] At the symptom level, chronic pain and mental health conditions are often comorbid, and mental health severity may lead to intensification of pain.[34,35] Indeed, we found extensive mental health comorbidity among adolescents with OUD. Moreover, decisions to write and to fill prescriptions likely result from complex interactions among patients, guardians, and health care professionals. These decisions could reflect patient distress and perceived need for care, stigma-related or other impediments to appropriate interventions, and communication barriers among health care professionals.[11,31,36] Similarities between the present results and findings for adults suggest commonalities in these processes across development.[8,17,18]

Opioid prescription remains common overall,[37] and there is increasing recognition of overdose risk and related health consequences.[4,5] Hospitalizations for self-inflicted opioid poisoning among adolescents have increased,[3] and receipt of prescribed opioids among youths is associated with later misuse.[38] It is, therefore, noteworthy that preexisting OUD and other SUDs, mood disorders, self-injurious behavior, and multiple comorbid types of conditions were all substantially positively associated with receipt of LTOT in the present analyses. There is a clear need for mental health assessment among adolescents being considered for opioid therapy.[32,35] Such an assessment may help inform decision making regarding pain treatment as well as illuminate the possible value of concomitant mental health interventions. In addition, because of the associated overdose risk,[19,39] benzodiazepine-opioid combined therapy has been strongly discouraged.[6] Associations found here between prior benzodiazepine receipt and opioid therapy highlight the need to consider the potential risks of polypharmacy. We caution, however, that these data cannot determine whether benzodiazepines and opioids were taken concurrently, whether they were prescribed by the same health care professionals, or whether patient safeguards were put into place.

Limitations

Like other health care records research, this study was constrained by several limitations. First, MarketScan data capture only conditions that were diagnosed and recorded in included claims, likely underestimating the prevalence of SUDs and other mental health conditions.[40,41] Second, only claimed prescription fills are recorded. Unfilled prescriptions and medications obtained via other means are not available.[42] For example, although prior OUD diagnosis might indicate use of illicitly obtained opioids, it could also reflect use of prescribed opioids not recorded in claims (eg, purchased out of pocket), which could help explain

the association between OUD and LTOT.[18] Conversely, we could not confirm that adolescents consumed the drugs obtained through their filled prescriptions. However, varying our predictor and outcome indices produced converging results. Third, these data could not elucidate the severity of adolescents' pain or mental health conditions. Finally, this study was limited to commercially insured adolescents, although a prior study found similar associations between mental health conditions and any opioid receipt among adolescents enrolled in commercial insurance and Medicaid.[14]

Conclusions

In this study of nationwide commercial health care claims, relatively few adolescents who received an initial opioid subsequently transitioned to LTOT. Adolescents with preexisting mental health conditions and treatments, however, were substantially more likely than adolescents without such conditions and treatments to transition from opioid initiation to LTOT. Given the limited support for the efficacy of opioid therapy for chronic pain among youths,[7] research is needed to understand potential adverse effects of LTOT among adolescents as well as the role that preexisting mental health conditions may play in harmful outcomes.

Notes

Supplement.

eTable 1. *International Classification of Diseases, Ninth Revision* (*ICD-9*) Codes

eTable 2. Generic Drug Names

eTable 3. Prior Mental Health Prevalence for Long-term Follow-up Sample

eTable 4. Prior Mental Health Conditions and Treatments Among Adolescents With and Without Prior Opioid Use Disorder

eTable 5. Opioid Analgesic and Opioid Use Disorder Medication Receipt in Follow-up Among Adolescents With and Without Prior Opioid Use Disorder

eTable 6. Pain Condition Cohort and Test of Proportional Hazards

eTable 7. Additional Sensitivity Analyses

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Figures and Tables

Table 1.

Prior Mental Health Conditions and Treatments and Any Opioid Receipt[a]

Prior Mental Health Factor	No. (%)		Odds Ratio (95% CI)
	Nonrecipients (n = 489 704)	Recipients (n = 489 704)	
Anxiety			
Anxiety disorder	20 649 (4.2)	26 005 (5.3)	1.28 (1.25-1.30)
Benzodiazepine	6880 (1.4)	11 079 (2.3)	1.63 (1.58-1.68)
Mood			
Bipolar or other mood disorder	10 184 (2.1)	11 857 (2.4)	1.17 (1.14-1.20)
Depressive disorder	28 680 (5.9)	36 299 (7.4)	1.29 (1.27-1.31)
Suicide attempt or self-injury	1213 (0.2)	1263 (0.3)	1.04 (0.96-1.13)
Mood stabilizer	3336 (0.7)	4324 (0.9)	1.30 (1.24-1.36)
SNRI	1573 (0.3)	2453 (0.5)	1.56 (1.47-1.67)
SSRI	23 944 (4.9)	33 777 (6.9)	1.45 (1.42-1.47)
Neurodevelopment			
ADHD	31 437 (6.4)	38 863 (7.9)	1.26 (1.24-1.28)
ADHD medication	34 213 (7.0)	44 929 (9.2)	1.35 (1.33-1.37)
Psychosis			
Schizophrenia spectrum disorder	2259 (0.5)	2259 (0.5)	1.00 (0.94-1.06)
Antipsychotic	8663 (1.8)	10 196 (2.1)	1.18 (1.15-1.22)
Sleep			
Sleep disorder	6444 (1.3)	8645 (1.8)	1.35 (1.31-1.39)
Nonbenzodiazepine hypnotic	1375 (0.3)	2318 (0.5)	1.69 (1.58-1.81)
Substance use			
Nonopioid SUD	9037 (1.8)	10 189 (2.1)	1.13 (1.10-1.16)
OUD	612 (0.1)	564 (0.1)	0.92 (0.82-1.03)
OUD medication	206 (0.04)	203 (0.04)	0.99 (0.81-1.20)
Psychotherapy			
For any diagnosis	40 820 (8.3)	55 390 (11.3)	1.41 (1.39-1.43)

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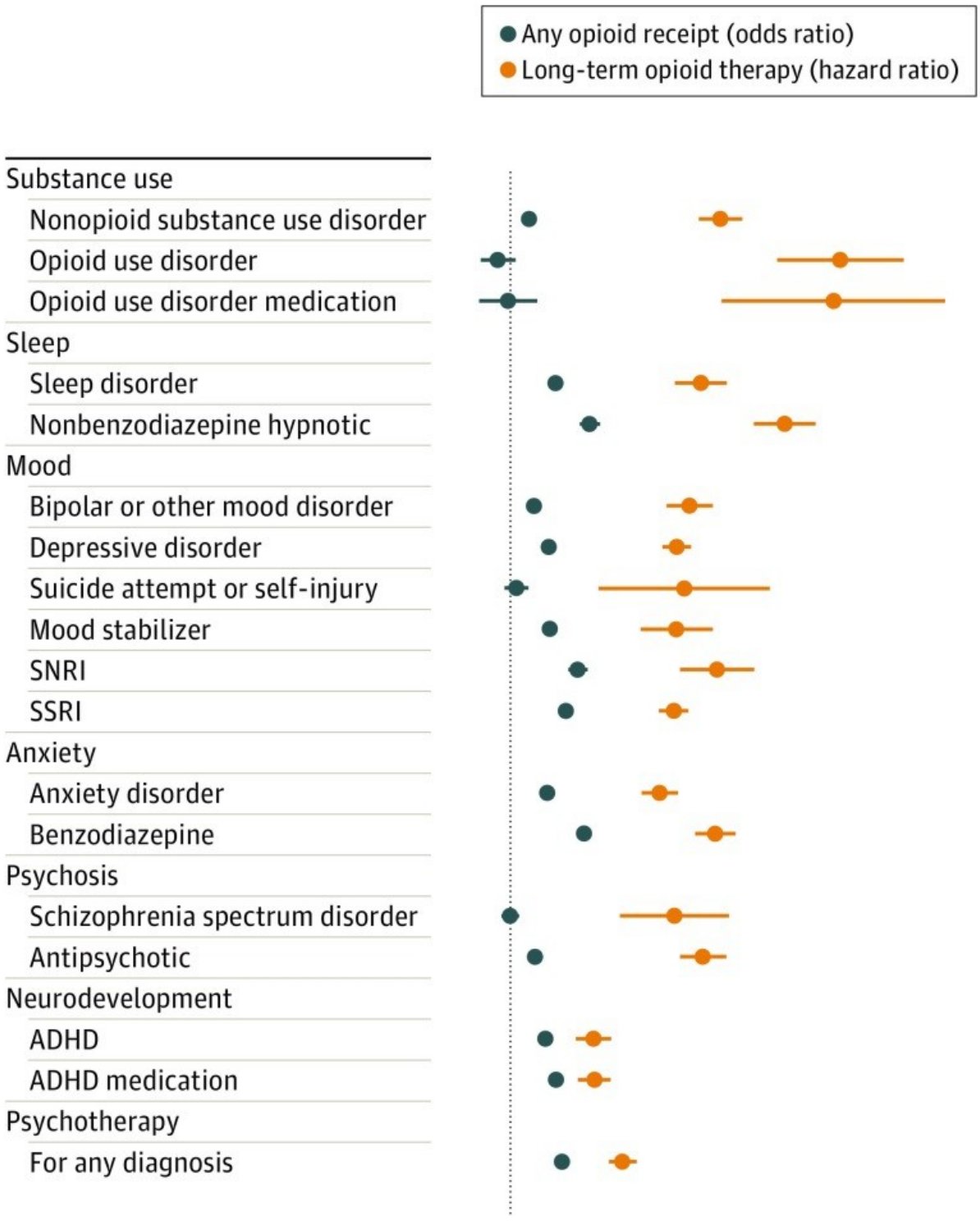
Abbreviations: ADHD, attention-deficit/hyperactivity disorder; OUD, opioid use disorder; SNRI, serotonin-norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; SUD, substance use disorder.

[a]Randomly selected 40% of recipients matched 1:1 to nonrecipients on sex, months of enrollment, and age and year of first enrollment.

Figure.



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Associations Between Prior Mental Health Conditions and Treatments and Subsequent Opioid Therapy

Any opioid receipt odds ratios are from conditional logistic regressions comparing opioid recipients (n = 489 704) with nonrecipients matched 1:1 on sex, months of enrollment, and age and year of first enrollment. Long-term opioid therapy hazard ratios are from Cox proportional hazards regressions analyzing the transition from first opioid receipt to long-term opioid therapy, adjusting for sex and age and year of first opioid receipt (n = 1 000 453). Error bars indicate 95% CIs; ADHD, attention-deficit/hyperactivity disorder; SNRI, serotonin-norepinephrine reuptake inhibitor; and SSRI, selective

serotonin reuptake inhibitor.

Table 2.

Prior Mental Health Conditions and Treatments and Long-term Opioid Therapy Among 1 000 453 Adolescents

Prior Mental Health Factor	Long-term Opioids per 1000 Recipients Within 3 y[a]		Hazard Ratio (95% CI)	
	No Predictor	With Predictor	Unadjusted[b]	Adjusted[c]
Anxiety				
Anxiety disorder	2.8	8.0	2.72 (2.42-3.06)	2.69 (2.39-3.03)
Benzodiazepine	2.8	12.2	4.07 (3.56-4.66)	3.88 (3.39-4.45)
Mood				
Bipolar or other mood disorder	2.8	10.1	3.33 (2.86-3.87)	3.28 (2.81-3.82)
Depressive disorder	2.6	9.0	3.15 (2.86-3.46)	3.01 (2.73-3.31)
Suicide attempt or self-injury	3.0	6.0	3.05 (1.73-5.38)	3.16 (1.79-5.58)
Mood stabilizer	2.9	10.3	3.12 (2.46-3.96)	3.01 (2.37-3.82)
SNRI	2.9	14.8	4.58 (3.59-5.85)	3.93 (3.08-5.02)
SSRI	2.6	9.1	3.11 (2.82-3.43)	2.95 (2.67-3.25)
Neurodevelopment				
ADHD	2.9	4.5	1.64 (1.46-1.84)	1.73 (1.54-1.95)
ADHD medication	2.8	4.7	1.67 (1.50-1.85)	1.74 (1.56-1.94)
Psychosis				
Schizophrenia spectrum disorder	3.0	6.7	3.02 (2.11-4.32)	2.96 (2.07-4.24)
Antipsychotic	2.8	11.3	3.59 (3.08-4.18)	3.58 (3.08-4.17)
Sleep				
Sleep disorder	2.9	10.8	3.58 (3.01-4.24)	3.53 (2.97-4.19)
Nonbenzodiazepine hypnotic	2.9	24.2	6.93 (5.65-8.50)	6.15 (5.01-7.55)
Substance use				
Nonopioid SUD	2.8	12.7	4.33 (3.75-5.00)	4.02 (3.48-4.65)
OUD	3.0	27.5	9.74 (6.41-14.82)	8.90 (5.85-13.54)
OUD medication	3.0	22.4	9.83 (4.69-20.63)	8.50 (4.05-17.84)
Psychotherapy				

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Abbreviations: ADHD, attention-deficit/hyperactivity disorder; OUD, opioid use disorder; SNRI, serotonin-norepinephrine reuptake inhibitor; SSRI, selective serotonin reuptake inhibitor; SUD, substance use disorder.

[a]Three-year cumulative incidence per 1000 opioid recipients.
[b]Unadjusted Cox proportional hazards regression analysis.
[c]Adjusted for sex, index age, and index year.