Association of Opioids Prescribed to Family Members and Opioid Overdose Among Adolescents and Young Adults

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Abstract

Importance.—Family members are cited as a common source of prescription opioids used for nonmedical reasons. Yet, the overdose risk associated with exposure to opioids prescribed to family members among adolescents and young adults (youth) is not well-established.

Objective.—To assess the association between opioids prescribed to family members and pharmaceutical opioid overdose among youth.

Design, Setting, and Cohort.—A retrospective cohort study of family units with youth ages 11 to 26 enrolled in a Kaiser Permanente Colorado health plan in 2006, followed through June 2018. Time to first overdose was modeled using Cox regression.

Exposures.—Opioid prescriptions and dosage dispensed to family members and youth in the past month.

Outcome.—Fatal and non-fatal pharmaceutical opioid overdoses identified in vital records and emergency department and inpatient settings, respectively.

Results.—The study population consisted of 72 040 adolescents and young adults (mean age across follow-up: 19.3 years; 50.9% female) nested in 45 145 family units. Youth were more

commonly exposed to prescription opioids dispensed to a family member than through their own prescription. Across follow-up, 36.5% of youth filled at least one opioid prescription, and 65.9% of youth had one or more family members with a prescription. Exposure to family members with opioid prescriptions in the past month was associated with increased pharmaceutical opioid overdose risk (adjusted hazard ratio [aHR], 2.17; 95% CI, 1.24–3.79), independent of opioids prescribed to youth (aHR, 6.62; 95% CI, 3.39–12.91). Concurrent exposure to opioid prescriptions from youth and family members was associated with significantly increased overdose risk (aHR, 12.99; 95% CI, 5.08–33.25). High dosage of total morphine milligram equivalents (MME) prescribed to family members in the past month was associated with youth overdose (0 MME [reference], >0-<200 MME [aHR, 1.39; 95% CI, 0.51–3.81], 200-<600 MME [aHR, 1.49; 95% CI, 0.59–3.77], and   600 MME [aHR, 2.93; 95% CI, 1.55–5.56]).

Conclusion and Relevance.—Among youth linked to family members, exposure to family members prescribed opioids was associated with increased pharmaceutical opioid overdose, independent of opioids prescribed to youth. Further interventions targeting youth and families are needed, including counseling patients about risks of opioids to youth in their families.

Introduction

Opioid exposures and overdoses among adolescents and young adults (termed youth) represent a significant public health problem.[1–3] Despite state and national efforts to reduce opioid prescribing[4–6], the volume of opioids prescribed to youth and adults remains substantial.[7–9] In 2017, more than 191 million opioid prescriptions were dispensed in the United States, more than three times the number prescribed in 1999.[9] While overdose risks associated with a number of opioid prescribing patterns at the individual-level, such as high-dose, have been established[10–13], less is known about opioid exposures from family members.

Growing evidence suggests that the family is an important factor in the spread and consumption of prescription opioids by providing access to opioids and facilitating the sharing of information and practices related to their use.[14–18] Thus, opioids prescribed to youth and their family members represent two distinct but potentially linked sources of exposure that together put youth at risk of overdose. Prevention efforts may need to target both youth and their families in order to adequately address overdose risk. Yet, the relative associations of opioids prescribed to youth and their family members and overdose have not been well-established. We conducted a retrospective cohort study that linked youth and their family members in a health plan and tested the association of opioid prescribing to the family and pharmaceutical opioid overdose among youth. Our objectives were to assess overdose risk associated with past-month opioid prescriptions to youth and to their family members, opioid dosages, and timing of exposures.

Methods

Study Design and Cohort

We conducted a retrospective cohort study of family units enrolled in a Kaiser Permanente Colorado (KPCO) health care plan. KPCO is an integrated healthcare plan and delivery

system that serves approximately 640,000 members. The cohort consisted of index youth and their family members. Index youth were all individuals ages 11 to 26 currently or newly enrolled in 2006 who obtained their insurance coverage as a dependent of a primary health plan member. Individuals up to age 26 are typically eligible for insurance coverage as a dependent. We did not require youth healthcare utilization as a criterion for inclusion because our focus was on opioid exposure in the family. Index youth were linked to at least one other family member using the primary subscriber's unique plan identifier. We excluded 124 youths who enrolled as a dependent member but did not match to any family members. Youth were followed through age 26, first observed pharmaceutical opioid overdose, disenrollment from KPCO, death, or the end of the observation period on June 30, 2018, whichever occurred first. Youth with gaps in insurance coverage reentered the cohort upon re-enrollment, and time disenrolled was excluded from the analysis. The KPCO Institutional Review Board approved the study, with a waiver of informed consent. The study followed the Strengthening the Reporting of Cohort Studies in Epidemiology (STROBE) reporting guideline.

Exposure

During each index youth's follow-up, we identified opioid prescriptions dispensed in the past month to youth and separately to members of their family unit between study entry and June 30, 2018 using National Drug Codes (NDC) in outpatient pharmacy dispensings and billing claims. For dosage, we summed the total morphine milligram equivalents (MME) of all prescription opioids dispensed in the past month to all family members and separately to index youth themselves. Total MME in the past month was subsequently divided into approximate terciles separately for family members (>0-<200 MME, 200-<600 MME, 600 MME) and index youth (>0-<120 MME, 120-<225 MME, 225 MME). Exposures were constructed as time-varying measures and updated each month of the index youth's follow-up.

Covariates

We adjusted models for clinical factors shown to be associated with overdose in prior studies, including: drug use disorder, alcohol use disorder, and tobacco use; major depressive, anxiety, and mood disorders; and pain.[19–22] A history of each was treated as a time-varying measure and was updated monthly during follow-up as youth acquired the clinical diagnosis. Models also included time-varying measures of ever having one or more comorbidities in the Quan-Deyo Modified Charlson Comorbidities Index (CCI)[23,24] during follow-up and separate indictors of common psychotropic medications (benzodiazepines, stimulants, and anti-depressants) dispensed to youth and family members in the past month. The CCI measure was dichotomized due to little variation in the number of comorbidities among index youth. Models were also adjusted for demographic factors, including gender, race (white, non-white, missing race), ethnicity (Hispanic and non-Hispanic), and age at each month of follow-up (11–15, 16–20, 21–26). Youth with missing data on race (44.1%) were grouped in a separate category. Finally, models included subscriber unit size and tract-level median family income based on the 2006–2010 American Community Survey 5-Year estimates.

Outcome

We identified non-fatal and fatal pharmaceutical opioid overdoses in emergency department and inpatient settings among index youth using the *International Classification of Diseases, Ninth (ICD-9) and Tenth (ICD-10) Revision* codes from medical billing claims and state vital records. For non-fatal pharmaceutical opioid overdoses, we used *ICD-9* codes 965.0, 965.00, 965.02, 965.09, E850.1, and E850.2 and *ICD-10* codes T40.0X1-T40.0X4, T40.2X1-T40.2X4, T40.3X1-T40.3X4, and T40.4X1-T40.4X4. For fatal pharmaceutical opioid overdoses, we used *ICD-10* codes that indicate drug poisoning as the underlying cause of death (X40-X44, X60-X64, X85, Y10-Y14) and pharmaceutical opioids involvement as a contributing cause (T40.2-T40.3). The study analyzed the first incident pharmaceutical opioid overdose during follow-up.

Statistical Analyses

To assess the association between exposure to prescription opioids and time to first pharmaceutical opioid overdose among index youth, we fitted Cox proportional-hazards models to calculate adjusted hazard ratios (aHRs) and 95% confidence intervals (CI). We used the counting process method to model opioid prescriptions as a time-varying four-level exposure: no opioid prescription, prescriptions to only youth, prescriptions to only family members, or prescriptions to both youth and family members in the past month. This allowed us to assess the association of prescribed opioids in the family in the past month and pharmaceutical opioid overdose among index youth, independent of and concurrent with opioids prescriptions to index youth themselves. We also tested a dose-response association by examining total MME dispensed to all family members and youth themselves in the past month in a separate model. Robust standard errors were calculated by clustering at the family unit level to adjust for correlation of survival times among index youth in the same family. The proportional hazards assumption for time-constant covariates was assessed using tests of Schoenfeld residuals.

We conducted secondary analysis to examine the timing of exposure from most recent to more distant, defined as one or more opioid prescriptions dispensed to family members, youth themselves, or both in the past three, six, or twelve months. To assess the influence of drug use disorder on our estimates, we also conducted a sensitivity analysis that excluded youth with a drug use disorder prior to their first opioid prescription.

All statistical analyses were performed using Stata version 15.1. Statistical significance was based on two-sided tests with a threshold of $p<0.05$.

Results

The study consisted of 72 040 index adolescents and young adults aged 11 to 26 (mean [standard deviation (SD)] age across follow-up, 19.3 years [3.7]; 36 646 [50.9%] females [Table 1]) nested in 45 145 family units (mean [SD] number of family members, 4 [1.4]). The mean (SD) length of follow-up for index youth was 4.9 (3.8) person-years. During the entire follow-up, 4 347 (6.0%) individual youth had a drug use disorder, 9 498 (13.2%) had a major depressive disorder, 9 365 (13.0%) had an anxiety disorder, and 31 357 (43.5%) had

one or more acute or chronic pain diagnoses. The chief pain diagnoses were headaches/ migraines, low back pain, and knee pain. Comorbidities were more common among youth exposed to opioid prescriptions (their own or from family members) compared to the full cohort.

Opioid Prescriptions

There were 647 767 total opioid prescriptions dispensed to index youth (103 489 [16.0%]) prescriptions) or members of their family (544 278 [84.0%] prescriptions) during follow-up. The most common opioids among index youth were hydrocodone (46.0% of opioid prescriptions), short-acting oxycodone (32.7%), and tramadol (6.9%). Similarly, among family members, the leading opioids were hydrocodone (39.2%), short-acting oxycodone (33.0%), and tramadol (10.6%). During follow-up, 36.5% of index youth filled at least one opioid prescription, 65.9% had a family member with at least one prescription, and 5.9% filled their own prescription and had a family member with a prescription in the same month. Among youth with at least one family member who had an opioid prescription, the median total MME (interquartile range [IQR]) in the family over the past month was 300 (150–896), and among youth who had at least one prescription themselves the median total MME (IQR) in the past month was 150 (100–300).

Pharmaceutical Opioid Overdose Incidence Rate

Among index youth there were 103 incident prescription opioid overdose events during follow-up (incidence rate, 29.0 per 100 000 person-years), of which 14 were fatal (Table 2). Compared to no exposure to an opioid prescription in the past month, prescriptions to one or more family members (unadjusted incidence rate ratio, 2.7; 95% CI, 1.5–4.8) and to index youth themselves (unadjusted incidence rate ratio, 14.8; 95% CI, 7.8–26.2) were associated with higher rates of overdose. While concurrent exposure to opioid prescriptions to both family members and youth themselves in the past month was rare (0.2% of total person-years), it was associated with markedly higher rates of overdose compared to no exposure (unadjusted incidence rate ratio, 40.7; 95% CI, 15.8–88.8).

Opioid Prescriptions and Risk of Pharmaceutical Opioid Overdose Among Youth

In adjusted Cox proportional-hazards models (Table 3, Model 2), compared no exposure to opioid prescriptions, prescriptions to one or more family members in the past month was independently associated with a two-fold increase in the risk of overdose among index youth (aHR, 2.17; 95% CI, 1.24–3.79). Prescriptions to index youth themselves in the past month was associated with more than a seven-fold increase in the risk of overdose (aHR, 6.62; 95% CI, 3.39–12.91). Concurrent prescriptions to both family members and youth in the past month was associated with a fifteen-fold increase in overdose risk (aHR, 12.99; 95% CI, 5.08–33.25).

An analysis of dose response indicated that only the highest total dosage of opioids prescribed to family members in the past month was associated with risk of overdose (Table 2, Model 3): 0 MME (reference), >0-<200 MME (aHR, 1.39; 95% CI, 0.51–3.81), 200-<600 MME (aHR, 1.49; 95% CI, 0.59–3.77), and 600 MME (aHR, 2.93; 95% CI, 1.55–5.56). In the same model, the total dosage of opioids prescribed to youth themselves similarly showed

an apparent dose-response association: 0 MME (reference), >0-<120 MME (aHR 2.67; 95% CI, 0.63–11.28), 120-<225 MME (aHR 5.22; 95% CI, 1.87–14.60), and 225 MME (aHR 8.77; 95% CI, 4.05–18.99).

In secondary analysis (Table 4), one or more opioid prescriptions in the past three months to family members (aHR, 1.85; 95% CI, 1.11–3.11), youth themselves (aHR, 5.86; 95% CI, 3.33–10.30), or both (aHR, 6.56; 95% CI, 2.87–14.99) were associated with lower risks compared to prescriptions in the past month. The overdose risk diminished for youth prescriptions in the past six months (aHR, 4.65; 95% CI, 2.69–8.04) and past twelve months (aHR, 3.93; 95% CI, 2.23–6.92), while it was variable for prescriptions to family members or both groups in the past six months (family members [aHR, 1.93; 95% CI, 1.19–3.13]; both [aHR, 3.68; 95% CI, 1.71–7.89]) and past twelve months (family members [aHR, 1.74; 95% CI, 1.02–2.98]; both [aHR, 4.46; 95% CI, 2.36–8.43]). While the risk of overdose persisted with exposure in the past 12 months, the month following an opioid prescription was associated with the most pronounced risk.

In sensitivity analysis (eTable 1 in the Supplement), excluding youth with a diagnosed drug use disorder prior to their first opioid prescription (n=2 518) did not alter the study conclusion that opioid prescriptions were associated with youth overdose.

Discussion

Exposure to family members with opioid prescriptions in the past month was associated with increased risk of pharmaceutical opioid overdose, independent of youth being prescribed opioids. In addition, concurrent opioid prescriptions among youth and family members in the past month, time immediately following prescriptions, and high dose were all associated with elevated risks. Findings suggest that exposure to prescribed opioids in the family pose serious risk of pharmaceutical opioid overdose to youth.

Several potential mechanisms could explain the association between prescribed opioids from family members and overdose among youth. First, and most directly, opioid prescriptions to family members may provide ready access to opioids. Unsecured and leftover medications may be misused, and medications may also be shared among family members.[18] Second, family exposure may reflect parents and siblings who model behaviors, attitudes, and norms regarding medical and nonmedical use of opioids.[14] This can influence youth preferences and contribute to initiation of opioid use, misuse, and opioid-related complications. Third, family exposure may also be a marker for problems related to parents' opioid use – such as aberrant pain medication seeking behaviors, intermittent over-sedation, and the development of opioid use disorders (OUD) – that may impair parenting ability, diminish the quality of parent-child relationships, and induce stress and instability in the home.[25] Poor parental discipline skills, neglect, and mistreatment have been shown to be associated with risk of adolescent substance use problems.[26] Finally, there may be shared risk factors that link patterns of opioid use youth and their family members, including genetic predisposition, common health conditions, social stressors (e.g., housing instability, financial insecurity, and marital dissolution), and local availability of opioids.[16,27–30]

Our study contributes to an early but growing literature on the risks of opioid exposures in the family and opioid initiation[16], long-term opioid use[15], and overdose[31]. We tested and quantified the risk associated with prescribed opioids in the family, while adjusting for opioids prescribed to youth. Since youth may be widely exposed to family members with prescription opioids, the associated overdose risk for youth, even if modest relative to the risk associated with youth's own prescriptions, may be significant at the population-level. Findings also highlight the need for greater attention to the magnified overdose risk associated with concurrent opioids use among youth and their family members. Greater combined opioid dosage from concurrent exposure may contribute to such risk.

Our findings suggest that clinicians prescribing opioids in adult medicine should consider counselling patients about the risks of opioids to youth in their families. Reducing opioid prescriptions to adults has been a focus of recent prevention efforts and can contribute to decreasing opioid exposure in the home. The Centers for Disease Control and Prevention (CDC) established guidelines recommending prescribing limits in the treatment of chronic pain with regard to opioid initiation, dosage, and duration to curb unnecessary exposure and excess supply.[6] Limiting access to opioids, however, should be balanced against the risks of complications induced by volatile dosing and undertreatment of pain.[32,33]

In response to concerns that prescribed opioids in the home may be misused among youth, federal agencies have supported common-sense educational campaigns to encourage safe storage and proper disposal of medications.[34,35] The evidence base to support such interventions, however, is not currently robust.[18,36] While home safety interventions may serve as an effective primary prevention for youth who have not yet initiated opioid use, such interventions may have unintended consequences. For example, a change in access to opioids in the home may push youth who are already misusing into the illicit drug market, where unknown quality and potency of heroin and fentanyl could magnify overdose risk.[37] Thus, further research on best practices and potential adverse impacts of well-intended interventions are needed.

Interventions that focus on restricting and controlling access to prescription opioids alone are just one of several efforts needed to curb the current epidemic that is increasingly centered on illicit opioids.[37,38] Undiagnosed and untreated opioid use disorder (OUD) may contribute to prescription misuse and high overdose risk. Efforts should include increased screening and treatment paired with interventions to address social and economic determinants of OUD more broadly.[29,39,40] Given the prevalence of nonmedical use of prescription opioids and rates of overdoses[9,41], harm reduction strategies are also needed, such as increased access to overdose reversal medication through standing orders and co-dispensing.

In the current epidemic, addressing early exposures to opioids, including those from opioids prescribed to family members, among youth may be important to preventing OUD and use of illicit opioids.[42] Adolescence and young adulthood are periods in the life course when drug use is usually initiated[43], and nonmedical use of opioids in this population is associated subsequent heroin use and OUD.[44–47]

Limitations and Strengths

Our study has certain limitations. We were unable to distinguish whether prescription opioids from family members, youth themselves, or elsewhere directly contributed to overdoses. The study did not capture all potential sources of prescription opioids, including prescriptions that were paid by cash or another health plan or were obtained from peers, family members not enrolled in the same health plan, or informal drug markets, which together may underestimate the extent of exposure to prescription opioids. On the other hand, we were unable to verify whether health plan subscriber members resided in the same household, implying that access to prescription opioids may be overstated. The study also did not account for shared genetic, social, and environmental risk factors that may put individuals in the same family at risk of overdose and could confound the relationship between exposure to opioids in household members and risk of overdose. Finally, since the study was conducted in a single health system in Colorado, findings should be replicated in other settings.

Our study also has several strengths. We leveraged electronic health records to link a large cohort of youth to their family members to assess exposure in the family. Use of pharmacy dispensing data allowed us to determine the degree and timing of opioid exposures with precision.

Conclusion

In a retrospective study of adolescents and young adults, exposure to prescription opioids in families was common. Opioids prescribed to family members were associated with increased risk of pharmaceutical opioid overdose, independent of opioids prescribed to youth. Further intervention efforts targeting youth and families are needed, including counseling patients about risks of opioids to youth in their families.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgement

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Key Points

Question:

Are opioids prescribed to family members associated with pharmaceutical opioid overdose among adolescents and young adults?

Findings:

In this retrospective cohort study that included 72 040 adolescents and young adults, exposure to family members with opioid prescriptions in the past month was associated with a two-fold increase in the risk of overdose, and youth's own prescriptions were associated with more than a six-fold increase. Concurrent exposure to prescriptions to family members and youth themselves was associated with a fifteen-fold increase in overdose risk.

Meaning:

Opioid prescriptions to family members as well as those to youth were associated with overdose.

Table 1.

Demographic and Clinical Characteristics of Adolescents and Young Adults (Ages 11–26) in Study Cohort, By Exposure

	Full Cohort (N=72 040)	Youth with ≥1 Own Opioid Prescriptions (N=26 284)[a]	Youth with ≥1 Family Opioid Prescriptions (N=47 461)[a]	Youth with ≥1 Own and Family Opioid Prescriptions (N=4 278)[a]
	No. (%)	No. (%)	No. (%)	No. (%)
Opioid Prescriptions Across Entire Follow-up				
Youth with at least one opioid prescription	26 284 (36.5)	-	-	-
Youth with family members who had at least one opioid prescription	47 461 (65.9)	-	-	-
Youth with at least one opioid prescription and with family members who had at least one prescription	4 278 (5.9)	-	-	-
Diagnosis History Across Entire Follow-up				
1 or More CCI Conditions	14 944 (20.7)	8 244 (31.4)	11 773 (24.8)	1 760 (41.1)
Drug Use Disorder	4 347 (6.0)	2 694 (10.2)	3 616 (7.6)	658 (15.4)
Alcohol Use Disorder	944 (1.3)	612 (2.3)	790 (1.7)	144 (3.4)
Tobacco Use	6 032 (8.4)	3 846 (14.6)	4 885 (10.3)	978 (22.9)
Major Depressive Disorder	9 498 (13.2)	5 566 (21.2)	7 688 (16.2)	1 269 (29.7)
Anxiety Disorder	9 365 (13.0)	5 639 (21.5)	7 671 (16.2)	1 308 (30.6)
Mood Disorder	2 778 (3.9)	1 586 (6.0)	2 234 (4.7)	430 (10.1)
Pain[b]	31 357 (43.5)	17 804 (67.7)	24 639 (51.9)	3 329 (77.8)
Psychotropic Medications Across Entire Follow-up				
Benzodiazepines				
Youth with at least one prescription	4 980 (6.9)	3 643 (13.9)	4 076 (8.6)	982 (23.0)
Youth with family members who had at least one prescription	18 554 (25.8)	8 912 (33.9)	16 576 (34.9)	2 423 (56.6)
Stimulants				
Youth with at least one prescription	3 851 (5.3)	2 057 (7.8)	3 172 (6.7)	438 (10.2)
Youth with family members who had at least one prescription	3 184 (4.4)	1 539 (5.9)	2 763 (5.8)	403 (9.4)
Anti-depressants				
Youth with at least one prescription	11 634 (16.1)	7 083 (26.9)	9 292 (19.6)	1 664 (38.9)
Youth with family members who had at least one prescription	29 073 (40.4)	12 903 (49.1)	24 217 (51.0)	3 106 (72.6)
Social and Demographic Factors				
Female	36 646 (50.9)	14 338 (54.6)	23 408 (49.3)	2 344 (54.8)
Race				
White	31 092 (43.2)	10 935 (56.2)	16 175 (47.3)	2 432 (56.8)

	Full Cohort (N=72 040)	Youth with ≥1 Own Opioid Prescriptions (N=26 284)[a]	Youth with ≥1 Family Opioid Prescriptions (N=47 461)[a]	Youth with ≥1 Own and Family Opioid Prescriptions (N=4 278)[a]
	No. (%)	No. (%)	No. (%)	No. (%)
Non-White	9 195 (12.8)	3 809 (14.5)	6 538 (13.8)	593 (13.9)
Missing[c]	31 753 (44.1)	7 704 (29.3)	18 473 (38.9)	1 253 (29.3)
Hispanic	8 739 (12.1)	3 836 (14.6)	6 275 (13.2)	658 (15.4)
Baseline Age				
11–15 years	31 135 (43.2)	12 875 (49.0)	23 647 (49.8)	2 189 (51.2)
16–20 years	28 018 (38.9)	10 377 (39.5)	18 765 (39.5)	1 738 (40.6)
21–26 years	12 887 (17.9)	3 032 (11.5)	5 049 (10.6)	351 (8.2)
Subscriber Unit Size (Mean)	4.4	4.4	4.6	4.7
Tract-Level Median Family Income				
<$50,000	13 026 (18.1)	4 114 (15.7)	8 152 (17.2)	715 (16.7)
$50,000 - $64,999	10 113 (14.0)	3 653 (13.9)	6 710 (14.1)	644 (15.1)
$65,000 - $79,999	15 000 (20.8)	5 518 (21.0)	9 919 (20.9)	977 (22.8)
$80,000 - $94,999	13 295 (18.5)	4 931 (18.8)	8 827 (18.6)	828 (19.4)
≥$95,000	20 606 (28.6)	8 068 (30.7)	13 853 (29.2)	1 114 (26.0)

Abbreviation: CCI = Quan-Deyo Modified Charlson Comorbidity Index

[a]Exposure is time-varying, and groups are not mutually exclusive

[b]Represents one or more chronic or acute pain diagnoses

[c]In the full cohort, 12.5% of those with missing race information are Hispanic

Table 2.

Incidence Rates of Fatal and Non-Fatal Prescription Opioid Overdose Among Adolescents and Young Adults

Opioid Prescriptions in the Past Month	Person-Years (PY)	Overdoses, No.	Rate (95% CI), Per 100 000 PY	Unadjusted Incidence Rate Ratio (IRR) (95% CI)
No Prescription	320 519	65	20.3 (15.9–25.9)	[Reference]
Prescriptions to Only Family Members	28 912	16	55.3 (33.9–90.3)	2.7 (1.5–4.8)
Prescriptions to Only Youth	5 001	15	299.9 (180.8–497.5)	14.8 (7.8–26.2)
Prescriptions to Both Youth and Family Members	848	7	825.5 (393.7–1 732.3)	40.7 (15.8–88.8)
Overall	355 280	103	29.0 (23.9–35.2)	

Table 3.

Unadjusted and Adjusted Association of Opioid Prescriptions and Pharmaceutical Opioid Overdose Among Adolescents and Young Adults

	Model 1 Adjusted aHR (95% CI)[a,b]	Model 2 Adjusted aHR (95% CI)[a,c]
Opioid Prescription in the Past Month		
No Prescription	[Reference]	
Prescriptions to Family Members	2.17 (1.24 – 3.79)	
Prescriptions to Youth	6.62 (3.39 – 12.91)	
Prescriptions to Youth and Family Members	12.99 (5.08 – 33.25)	
Total MME to Family Members in the Past Month		
None		[Reference]
>0–<200 MME		1.39 (0.51 – 3.81)
200–<600 MME		1.49 (0.59 – 3.77)
600 MME		2.93 (1.55 – 5.56)
Total MME to Youth in the Past Month		
None		[Reference]
>0–<120 MME		2.67 (0.63 – 11.28)
120–<225 MME		5.22 (1.87 – 14.60)
225 MME		8.77 (4.05 – 18.99)

Abbreviations: HR = hazard ratio; aHR = adjusted hazard ratio; CI = confidence interval; MME = morphine milligram equivalents

[a] Covariates in adjusted models include one or more conditions in the Quan-Deyo Modified Charlson Comorbidity Index, drug use disorder, alcohol use disorder, tobacco use, major depressive disorder, anxiety disorder, mood disorder, pain diagnosis, benzodiazepines, stimulants, anti-depressants, gender, race, ethnicity, age, subscriber unit size, and tract-level median family income

[b] Model 1 specifies exposure to opioid prescriptions in the past month as a four-level time-varying measure

[c] Model 2 includes total opioid dosage (MME) in the past month for family members and youth as time-varying measures grouped into categories of approximately equal size

Table 4.

Association of Opioid Prescriptions and Pharmaceutical Opioid Overdose During Past 3-Month, 6-Month, and 12-Month Exposures

	Past 3 Months	Past 6 Months	Past 12 Months
	aHR (95% CI)[a]	aHR (95% CI)[a]	aHR (95% CI)[a]
Opioid Prescriptions			
No Prescription	[Reference]	[Reference]	[Reference]
Prescriptions to Family Members	1.85 (1.11 – 3.11)	1.93 (1.19 – 3.13)	1.74 (1.02 – 2.98)
Prescriptions to Youth	5.86 (3.33 – 10.30)	4.65 (2.69 – 8.04)	3.93 (2.23 – 6.92)
Prescriptions to Youth and Family Members	6.56 (2.87 – 14.99)	3.68 (1.71 – 7.89)	4.46 (2.36 – 8.43)

Abbreviations: aHR = adjusted hazard ratio; CI = confidence interval

[a] Covariates in adjusted models include one or more conditions in the Quan-Deyo Modified Charlson Comorbidity Index, drug use disorder, alcohol use disorder, tobacco use, major depressive disorder, anxiety disorder, mood disorder, pain diagnosis, benzodiazepines, stimulants, and anti-depressants, gender, race, ethnicity, age, subscriber unit size, and tract-level median family income