Starting Young: Trends in Opioid Therapy Among US Adolescents and Young Adults With Inflammatory Bowel Disease in the Truven MarketScan Database Between 2007 and 2015

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Background: Opioids are commonly prescribed for relief in inflammatory bowel disease (IBD). Emerging evidence suggests that adolescents and young adults are a vulnerable population at particular risk of becoming chronic opioid users and experiencing adverse effects.

Objectives: This study evaluates trends in the prevalence and persistence of chronic opioid therapy in adolescents and young adults with IBD in the United States.

Method: A longitudinal retrospective cohort analysis was conducted with the Truven MarketScan Database from 2007 to 2015. Study subjects were 15–29 years old with ≥2 IBD diagnoses (Crohn's: 555/K50; ulcerative colitis: 556/K51). Opioid therapy was identified with prescription claims within the Truven therapeutic class 60: opioid agonists. Persistence of opioid use was evaluated by survival analysis for patients who remained in the database for at least 3 years following index chronic opioid therapy use.

Results: In a cohort containing 93,668 patients, 18.2% received chronic opioid therapy. The annual prevalence of chronic opioid therapy increased from 9.3% in 2007 to 10.8% in 2015 ($P < 0.01$), peaking at 12.2% in 2011. Opioid prescriptions per patient per year were stable (approximately 5). Post hoc Poisson regression analyses demonstrated that the number of opioid pills dispensed per year increased with age and was higher among males. Among the 2503 patients receiving chronic opioid therapy and followed longitudinally, 30.5% were maintained on chronic opioid therapy for 2 years, and 5.3% for all 4 years.

Conclusion: Sustained chronic opioid use in adolescents and young adults with IBD is increasingly common, underscoring the need for screening and intervention for this vulnerable population.

Key Words: opioids, chronic opioid therapy, adolescents and young adults, Crohn's disease, ulcerative colitis

INTRODUCTION

Opioid use among individuals with inflammatory bowel disease (IBD) has become a topic of increasing interest in light of the current opioid epidemic in the United States. Over the past 2 decades, the sale of prescription opioids quadrupled, and by 2015, 2 million people were dependent on prescription opioid medications.[1] Between 1997 and 2015, more than 183,000 people died from overdoses related to prescription opioids in the United States, with rates increasing 4-fold.[2,3] Unintentional overdose on opioids has risen to become the leading cause of death for young adults aged 25–44 years.[4] As death rates rise among young people taking opioids, it is important to understand the trends in opioid use among adolescents and young adults prescribed opioids for medical management.

In IBD management, opioids are commonly prescribed for temporary pain relief around the time of surgery and during acute disease exacerbations. Emerging evidence shows that a subset of individuals with IBD—approximately 6% of youth and 3%–13% of adults—receive chronic opioid therapy for uncontrolled disease activity and persistent pain.[5,6] Opioids are an important and effective method of addressing acute and procedural pain, but evidence of efficacy for chronic pain is limited.[7] Chronic opioid therapy can have the unexpected result of narcotic bowel syndrome[8] with a negative cycle of increased pain, opioid use, and dependence. Chronic opioid therapy among IBD patients has also been associated with psychiatric

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comorbidities and lower quality of life.[5, 6, 9] Additionally, opiate use is a risk factor for serious infections, even after adjusting for severity of disease and use of immunosuppressive agents.[10]

A recent population-based study in Canada highlighted that IBD is an independent risk factor for chronic opioid therapy, particularly among children and young adults.[11] Heavy opioid use in this sample also strongly predicted non-malignancy-related mortality. A cross-sectional study utilizing a US population–based registry showed that chronic opioid therapy was more common among pediatric IBD populations compared with the general pediatric population, particularly among those aged 15–18 years.[5] This research highlights the increased risk and negative outcomes associated with chronic opioid therapy in IBD populations and the need to better understand opioid use among adolescents and young adults in the United States, where opioid use is higher than in Canada.

Adolescents and young adults with IBD are a particularly vulnerable population given their complex disease phenotype, self-management challenges around development of autonomy, and transition from pediatric to adult care.[12–14] These factors may increase adolescents' and young adults' risk for uncontrolled disease activity and associated pain, and treatment with opioids. Prescription opioid use among adolescents and young adults is predictive of future opioid use and misuse,[15, 16] regardless of the indication. Taken together, this research highlights the increased risk and negative outcomes associated with chronic opioid therapy among adolescents and young adults with IBD and the critical need to better understand opioid use among adolescents and young adults in the United States. This study is the first to evaluate trends in the prevalence and persistence of chronic opioid therapy longitudinally among adolescents and young adults with IBD in the United States in a large nationally representative insurance claims database.

METHODS

Study Design

We performed a longitudinal retrospective cohort analysis of Crohn's disease (CD) and ulcerative colitis (UC) patients in the Truven MarketScan Commercial Claims and Encounters Database from 2007 to 2015. The Truven MarketScan Database consists of de-identified outpatient, inpatient, and pharmaceutical claims of approximately 40–50 million privately insured patients each year. These claims originate from more than 150 large employer-sponsored health insurance plans with patient coverage in all 50 states. The database includes patient characteristics (eg, age, sex, geographic region), financial variables (eg, inpatient, outpatient, and pharmaceutical costs), and pharmacy-level data (eg, National Drug Code, days' supply, strength, administration method). All financial variables are scaled to February 2017 dollars using the Consumer Price Index (CPI).

Patient Identification

Patient inclusion criteria included (1) age 15–29 years[17–19]; (2) 2 or more distinct IBD diagnoses (defined under the International Classification of Diseases, Ninth Revision [ICD-9] as 555.xx for CD and 556.xx for UC, and the ICD-10 codes K50.xx and K51.xx, respectively; this stringent method of IBD classification has been examined and used previously in administrative data[20–23]); and (3) enrollment in a health plan that submitted at least 1 pharmaceutical claim. To classify a patient as CD or UC, the total number of distinct CD and UC diagnoses were summed, and if 80% or more of these diagnoses were 555.xx/K50.xx or 556.xx/K51.xx, the patient was classified as CD or UC, respectively. If neither was satisfied, the patient was classified as having interderminate colitis (IC) (see Figure 1 for a flow diagram of study population selection).

Chronic Opioid Therapy Classification

Chronic opioid therapy was determined using dispensed prescription drug claims. Opioid medications included in the Truven database included those categorized as therapeutic class 60: analgesics/antipyretics, opiate agonists (see Supplementary Table 1 for the full list of the medications included in this category). When examining the overall prevalence of chronic opioid therapy in our sample, a patient was classified as meeting criteria for chronic opioid therapy if s/he had ≥3 separate opioid drug claims on distinct dates within a 2-year rolling window (based on criteria established in a previous study utilizing the Truven database[5]). Only individuals with continuous enrollment in an insurance plan were included in this sample. Multiple opioid drugs dispensed on the same day were counted as a single opioid prescription. For this portion of the study, opioid drug claims within 30 days of a major abdominal operation were excluded.

When examining the prevalence of chronic opioid therapy per year from 2007 to 2015, criteria for chronic opioid therapy were modified to allow for assessment of longitudinal trends. In these analyses, a patient met criteria for chronic opioid therapy if s/he had at least 2 separate opioid drug claims on distinct dates within 1 year.

To account for fluctuations in total Truven enrollment, chronic opioid therapy was represented using a standardized index score (total number of opioid drug claims per year from members who met criteria for chronic opioid therapy in that specific year divided by the total number of members who met criteria for chronic opioid therapy in that year).

To evaluate persistence of opioid use, Kaplan-Meier survival analysis was conducted for those patients who met the modified chronic opioid therapy criteria (≥2 separate opioid prescriptions in 1 year) and remained in the database for at least 3 years following index chronic opioid therapy use. Patients who first met chronic opioid therapy criteria within 30 days after surgery were included in this analysis to study the

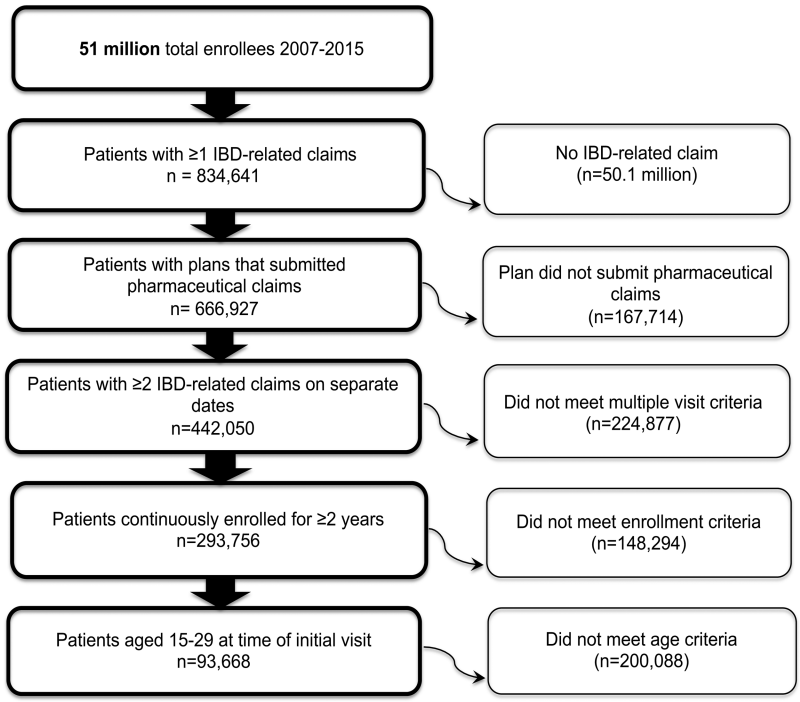

FIGURE 1. Study population selection. This flow diagram outlines the study population selection in the Truven MarketScan Database. It demonstrates step by step how the chronic opioid therapy sample was created.

long-term effects of their initial opiate exposure. Survival was defined as ≥2 separate opioid prescriptions per year. Failure was defined as <2 opioid prescriptions per year.

Variable Classification

Covariates of interest were classified using patient data during the study period. Demographic information included age, sex, geographic regions, and type of insurance plan. IBD medications included any pharmaceutical prescription or respective Healthcare Common Procedure Coding System/J-code for biologics (infliximab, adalimumab, certolizumab, golimumab, natalizumab, vedolizumab, ustekinumab) and any pharmaceutical prescription for corticosteroids (prednisone, prednisolone, methylprednisolone, hydrocortisone, budesonide), 5-aminosalicylic acid (5-ASA; mesalamine, sulfasalazine), or immunomodulator (6-mercaptopurine, methotrexate, azathioprine). Health care utilization included the number of IBD-related hospitalizations, IBD-related surgeries, emergency department (ED) visits, outpatient visits, and polypharmacy. Health care costs included high-cost patients (defined as annual health care costs >$50,000),[24] total costs per year, and mean hospitalization cost. Comorbidities commonly associated with chronic opioid therapy were defined a priori based on clinical judgment and past research with population-based databases[5] and the Truven database using ICD-9 and ICD-10 codes. These comorbidities included abdominal pain, joint pain, chronic back pain, migraines, chronic pain unspecified, osteoarthritis, rheumatoid arthritis, depression, anxiety, tobacco, substance abuse, and alcohol abuse (see Supplementary Table 2 for the full list of ICD-9/10 codes).

Statistical Analysis

Descriptive statistical analyses and Kaplan-Meier survival analyses were performed to assess the prevalence and persistence of chronic opioid therapy in this sample. Chi-square and 2-tailed Student *t* tests were used to compare the characteristics of individuals who received chronic opioid therapy with those who did not. Post hoc analyses included 2 Poisson regressions adjusting for age and sex to calculate the number of opioid pills dispensed per year, with age stratified as 15–19 years, 20–24 years, and 25–29 years. The first regression compared those who met the criteria for chronic opioid therapy with those who did not. The second regression compared those who had at least 1 opioid drug claim at any point between 2007 and 2015 with those who did not have an opioid drug claim. A multivariable logistic regression was used to estimate the outcome of chronic opioid therapy, adjusting for age bins (15–19 years, 20–24 years, 25–29 years), sex, geographical region, disease type, pain conditions, anxiety, depression, and substance abuse. The medication possession ratio (MPR) was also calculated for individuals meeting criteria for chronic opioid therapy and those who did not. MPR is the ratio of the days' supply of opioids dispensed divided by the number of days individuals were observed in the database. Statistical significance was assessed at

the level of $\alpha = 0.05$. All analyses were performed using Stata/SE 14.2 (College Station, TX, USA).

RESULTS

Descriptive Statistics

Our sample contained 93,668 IBD patients aged 15–29 years. Of those, 17,084 (18.2%) received chronic opioid therapy at some point during the study period. Demographics of those who received chronic opioid therapy and those who did not are included in Table 1. Female sex and Crohn's disease were significantly associated with chronic opioid therapy. Patients receiving chronic opioid therapy had greater use of biologic (36.8% vs 26.2%) and corticosteroid (75.2% vs 46.1%) medications.

Patients receiving chronic opioid therapy had significantly more comorbidities than those not meeting chronic opioid therapy criteria. Specifically, these patients had higher rates of comorbid pain, arthritis, anxiety, depression, and substance diagnoses compared with nonchronic opioid therapy patients (all $P < 0.01$).

Trends in Chronic Opioid Therapy

The prevalence of chronic opioid therapy increased from 9.3% in 2007 to a peak of 12.2% in 2011, then declined slightly to 10.8% in 2015 ($P < 0.01$) (Fig. 2). The number of opioid prescriptions per patient per year remained relatively stable between 2007 and 2015 (5.0–5.2; $P > 0.05$). The mean number of pills per prescription was 65.

Persistence of Chronic Opioid Therapy

To evaluate chronic opioid use longitudinally, 2503 patients were identified who met chronic opioid therapy criteria in an index year and were enrolled in the data set for at least 3 subsequent years (years 2–4). Of these patients, 132 met criteria for chronic opioid therapy in all 4 years. Patients receiving chronic opioid therapy for 4 years were significantly more likely to take biologic and corticosteroid medications and to have higher rates of comorbid pain and psychiatric and substance diagnoses compared with patients who met criteria for chronic opioid therapy for 1–3 years ($P < 0.01$) (Table 2).

Kaplan-Meier survival analysis was used to evaluate the persistence of opioid therapy (Fig. 3). Results showed that 30.5% continued to receive chronic opioid therapy in year 2, 10.7% in year 3, and 5.3% in year 4. Of note, 54.65% of patients who met criteria for chronic opioid therapy in the index year never met criteria for chronic opioid therapy again during their enrollment in the database.

Health Care Utilization and Costs

There were significant differences between health care utilization and costs among patients who met criteria for chronic opioid therapy for 4 years, patients who met criteria for chronic opioid therapy for 1–3 years, and those who did not meet criteria for chronic opioid therapy ($P < 0.001$) (Table 3). Patients receiving chronic opioid therapy for 4 years went to the ED more (96.2% vs 88.1% in 1–3-year group vs 48.5% in the no chronic opioid therapy group) and were hospitalized more often (25% hospitalized ≥5 times per year vs 10.6% in the 1–3-year group vs 5.4% in the no chronic opioid therapy group). Patients who met chronic opioid therapy criteria for 4 years were also more frequently classified as high-cost patients, with annual health care costs exceeding $50,000 (28.8% vs 13.9% in the 1–3-year group vs 9.2% in the no chronic opioid therapy group). Those receiving chronic opioid therapy for 4 years had higher mean annual total costs of care (mean per-member, per-year cost of $44,766 vs $28,139 in 1–3-year group vs $20,473 in the no chronic opioid therapy group).

Post Hoc Analyses

Poisson regressions adjusting for age and sex were conducted post hoc to provide additional information about the number of opioid pills dispensed per year for individuals receiving chronic opioid therapy and those who received at least 1 opioid. Results demonstrated that among patients in our sample who met criteria for chronic opioid therapy, the number of opioid pills dispensed per year increased with age and was higher among males. Males 25–29 years old received approximately 309 pills per year. A similar trend was seen when looking at all 15–29-year-old patients in the database who received at least 1 opioid prescription. The number of pills per year increased with age; however, in this group, females had a slighter higher count than males. Of note, the opioid pill count was higher in every age and sex subgroup for individuals who met the criteria for chronic opioid therapy (Supplementary Fig. 1).

These results were further supported by the MPR analyses, which were calculated to provide additional information about the amount of opioid dispensed to individuals who met criteria for chronic opioid therapy. Results demonstrated that the median MPR was larger among adolescents and young adults receiving chronic opioid therapy compared with those who did not meet criteria for chronic opioid therapy. Individuals receiving chronic opioid therapy had an opioid MPR of 0.03, compared with 0.0007 among those who did not meet criteria for chronic opioid therapy. Of note, the top quartile of individuals in the chronic opioid therapy population had a higher opioid MPR of 0.1.

Lastly, multivariable logistic regression was conducted post hoc to provide information about predictors of chronic opioid therapy in this sample. Results showed that if a patient was diagnosed with depression, substance abuse, or a pain condition, the odds of receiving chronic opioid therapy was approximately 2–3 times higher (Table 4).

TABLE 1: Overall Sample Characteristics

	No Chronic Opioid Therapy (n = 76,584)	Chronic Opioid Therapy (n = 17,084)	*P*
Sex, No. (%)			
Female	38,548 (50.3)	10,134 (59.3)	<0.001
Age			
Mean (median), y	23.0 (23)	23.6 (24)	<0.001
15–19 y, No. (%)	18,512 (24.2)	3267 (19.1)	<0.001
20–24 y, No. (%)	26,505 (34.6)	5710 (33.4)	
25–29 y, No. (%)	31,567 (41.2)	8107 (47.5)	
Geographic region, No. (%)			
Northeast	18,148 (23.7)	2833 (16.6)	<0.001
North Central	18,910 (24.7)	4087 (23.9)	
South	27,151 (35.5)	7076 (41.4)	
West	10,805 (14.1)	2800 (16.4)	
Other	1570 (2.1)	288 (1.7)	
Insurance,[a] No. (%)			
EPO/PPO	49,299 (69.3)	10,934 (68.1)	<0.001
HMO/Cap POS[b]	9915 (13.9)	2437 (15.2)	
HDHP/CDHP	5915 (8.3)	1123 (8.3)	
POS	5040 (7.1)	1331 (7.0)	
COMP	954 (1.3)	234 (1.5)	
IBD type, No. (%)			
Crohn's disease	38,860 (50.7)	10,039 (58.8)	<0.001
Ulcerative colitis	31,884 (41.6)	5546 (32.5)	
Indeterminate colitis	5840 (7.6)	1499 (8.8)	
IBD medications, No. (%)			
Biologics	20,069 (26.2)	6292 (36.8)	<0.001
Corticosteroids	35,301 (46.1)	12,838 (75.2)	<0.001
Immunomodulators	21,955 (28.7)	5789 (33.9)	<0.001
5-ASA	44,020 (57.5)	9910 (58)	0.21
Comorbidities, %			
Pain			
Abdominal pain	56	85.5	<0.001
Joint pain	21	46.4	<0.001
Chronic back pain	6.3	22.9	<0.001
Migraines	6.3	19	<0.001
Chronic pain, unspecified	1.2	14.2	<0.001
Osteoarthritis	1.5	6.2	<0.001
Rheumatoid arthritis	1.3	3.8	<0.001
Psychiatric			
Depression	22.2	55.2	<0.001
Anxiety	14.2	35.1	<0.001
Substance use			
Tobacco	5.7	22.4	<0.001
Substance abuse	1.6	8.7	<0.001
Alcohol abuse	1.9	5.6	<0.001

[a]Patients were classified under the insurance plan of their first UC or CD diagnosis.
[b]HMO/Cap POS are capitated plans. All other plans are noncapitated.

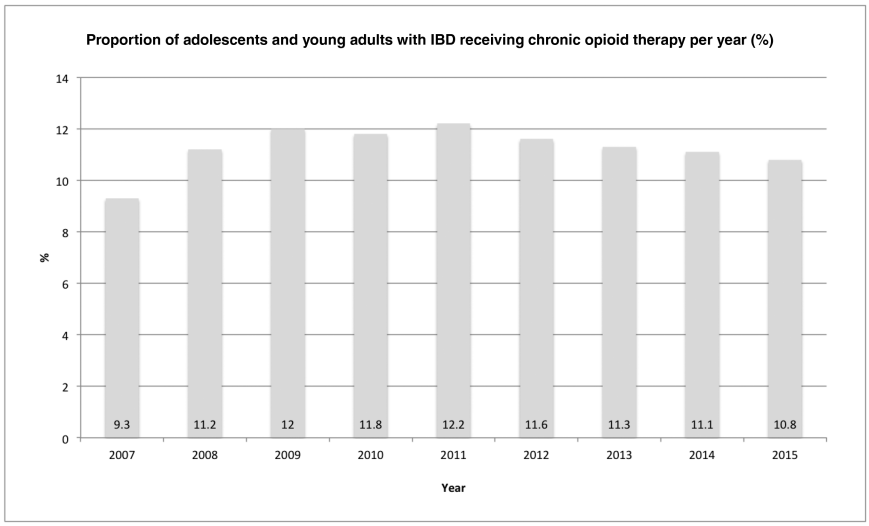

FIGURE 2. Prevalence of chronic opioid therapy. The prevalence of chronic opioid therapy among adolescents and young adults with IBD between 2007 and 2015 was calculated using the Truven MarketScan Database. The proportion of individuals meeting criteria for chronic opioid therapy increased from 9.3% in 2007 to a peak of 12.2% in 2011, then declined to 10.8% in 2015 ($P < 0.01$).

DISCUSSION

To our knowledge, this is the first nationally representative longitudinal study in the United States to examine chronic opioid therapy among adolescents and young adults with IBD. This research is of particular importance given the current opioid epidemic and the growing awareness that adolescents and young adults are a vulnerable IBD population at risk of becoming chronic opioid users[5, 11] with future opioid use and misuse in adulthood.[15, 16] The current study results highlight that a significant proportion of adolescents and young adults in the United States received chronic opioid therapy between 2007 and 2015, with 18% receiving 3 or more opioid prescriptions within a 2-year period.

When examining the prevalence of chronic opioid therapy, rates have increased over time, peaking in 2011 (12% meeting criteria for chronic opioid therapy), mirroring national trends. Despite national efforts to decrease opioid prescriptions and use, rates of chronic opioid therapy persisted and remained high through 2015. Adolescents and young adults meeting criteria for chronic opioid therapy received a surprisingly large number of opioids, approximately 5 prescriptions per patient per year, with 65 pills per prescription. Post hoc analyses demonstrated that the number of opioid pills dispensed per year increased with age and was higher among males. Of note, males aged 25–29 years received approximately 309 pills per year.

It is also noteworthy to highlight that in a subsample of adolescents and young adults (enrolled in the database for at least 4 years), almost one-third of patients receiving chronic opioid therapy in 1 year continued to use opioids and meet criteria for chronic opioid therapy in the following year, and 5% in each of the subsequent 3 years. These results underscore that a small subset of adolescents and young adults with IBD are at particularly high risk for continued opioid use and related negative outcomes and merit increased clinical attention. Providers caring for IBD patients should receive additional education about this high-risk population of IBD patients including the unique developmental considerations of adolescents and young adults that could be contributing to continued opioid use (eg, development of autonomy and changing roles in disease management—shifting responsibilities from parents to adolescents and young adults). It will also be important to better understand the clinical profile and potential protective factors of the 54.65% of adolescents and young adults who never met criteria for chronic opioid therapy again after the index year. This information could support targeted intervention efforts for the small subset of patients who continue to struggle with persistent opioid use. Overall, increased awareness about this distinct group of high-risk adolescents and young adults with IBD will support greater collaboration between gastroenterologists and multidisciplinary teams to better monitor and wean opioids following surgery.

The study corroborates past research demonstrating that female sex, Crohn's disease, and comorbid psychiatric and pain conditions are associated with chronic opioid therapy among children and adults with IBD.[5, 6, 25] Our findings also support and extend past research demonstrating that chronic opioid therapy is related to increased health care utilization among children with IBD.[5] In the current study, chronic opioid therapy was associated with higher health care utilization (eg, IBD surgeries, ED visits, hospitalizations) and health care costs among adolescents and young adults with IBD, especially among those with persistent chronic opioid therapy. Interestingly, 97% of individuals receiving chronic opioid therapy were on

TABLE 2: Longitudinal Chronic Opioid Therapy Sample Characteristics

	Chronic Opioid Therapy in Year 1; Enrolled ≥4 y (n = 2503)	Persistent Chronic Opioid Therapy ≥4 y (n = 132)	*P*
Sex, No. (%)			
Female	1444 (57.7)	87 (65.9)	0.062
Age			
Mean (median), y	22.9 (24)	23.9 (26)	0.009
15–19 y, No. (%)	761 (30.4)	30 (22.7)	
20–24 y, No. (%)	637 (45.5)	26 (19.7)	0.01
25–29 y, No. (%)	1105 (44.1)	76 (57.6)	
IBD type, No. (%)			0.078
Crohn's disease	1426 (57.0)	83 (62.9)	
Ulcerative colitis	851 (34.0)	33 (25)	
Indeterminate colitis	226 (9.0)	16 (12.1)	
IBD medications, No. (%)			
Biologics	1096 (43.8)	74 (56.1)	0.006
Corticosteroids	2118 (84.6)	128 (97.0)	<0.001
Immunomodulators	1107 (44.2)	79 (59.8)	<0.001
5-ASA	1748 (69.8)	93 (70.4)	0.88
Comorbidities, %			
Pain			
Abdominal pain	88.3	97.7	0.001
Joint pain	53.6	68.2	0.001
Chronic back pain	26.1	47.7	<0.001
Migraines	20.8	46.2	<0.001
Chronic pain, unspecified	9.6	40.9	<0.001
Osteoarthritis	7.2	12.1	0.035
Rheumatoid arthritis	4.3	8.3	0.03
Psychiatric			
Depression	31.4	56.1	<0.001
Anxiety	35.5	68.9	<0.001
Substance use			
Tobacco	18.9	31.8	<0.001
Substance abuse	7	20.5	<0.001
Alcohol abuse	6.1	6.8	0.742

corticosteroids and only 56% were on biologic agents. Taken together, such findings suggest that this population may have severe disease with poor disease control, adding to past research that has demonstrated that adolescents and young adults with IBD are a vulnerable IBD population (eg, complex disease phenotype, self-management challenges).[12–14] This underscores the importance of improved medical management and supporting adherence among adolescents and young adults. An important future direction would be for transition and young adult programs to target chronic opioid therapy prevention in their efforts to address the specific needs of adolescents and young adults with IBD.

A range of pain conditions (eg, abdominal, joint) were associated with chronic opioid therapy in this sample. This is noteworthy as the majority of adolescents and young adults with IBD experience pain at some point in their disease course, particularly abdominal pain during disease activity. Of note, research has shown that up to 50% of adults continue to experience abdominal pain during disease remission,[26, 27] and similar trends have been documented in pediatric populations (up to 26%).[28, 29] Such factors could potentially contribute to prolonged opioid use. Additionally, among young people with chronic pain and IBD, there is a greater risk for depression and anxiety,[28] which this and other studies[5] have shown are also associated with chronic opioid therapy. Chronic pain and affective disorders among young people are also associated with worse physical and psychological outcomes in adulthood.[30] Of note, post hoc analyses have demonstrated that adolescents and young adults diagnosed with a pain condition, depression, or substance abuse were approximately 2–3 times more likely to

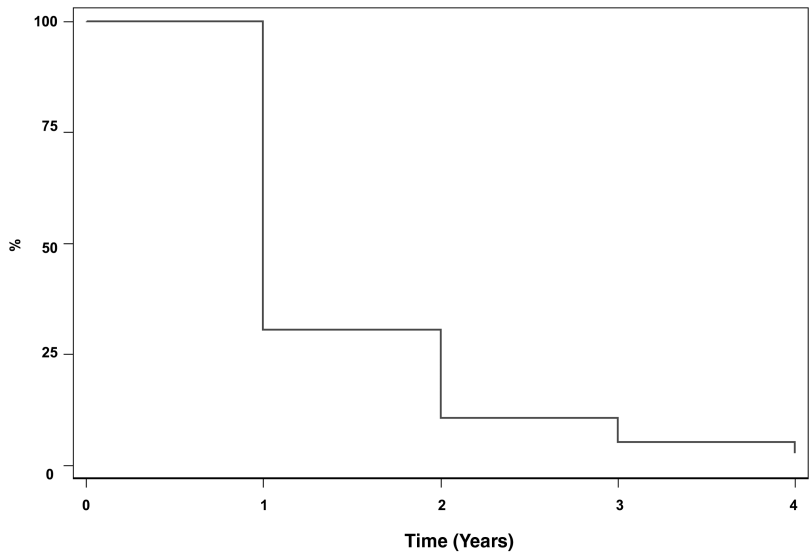

FIGURE 3. Persistence of chronic opioid therapy. Kaplan-Meier analyses were conducted to determine persistence of chronic opioid therapy for adolescents and young adults with IBD who filled ≥2 opioid prescriptions in an index year and remained in the database for ≥3 subsequent years. Analyses showed that 30.5% continued to receive chronic opioid therapy in year 2, 10.7% in year 3, and 5.3% in year 4.

receive chronic opioid therapy, underscoring that pain and psychiatric conditions may be a key predictor of chronic opioid use in this vulnerable population. Overall, there is a significant need to increase screening of adolescents and young adults in IBD clinics for chronic pain conditions and psychiatric disorders. Access to treatment for pain management and mental health challenges would support prevention efforts by targeting psychological comorbidities and reducing symptoms that may

TABLE 3: Health Care Utilization and Costs

	No Chronic Opioid Therapy; Enrollment for 2+ y (n = 76,584)	Chronic Opioid Therapy for 1–3 y; Enrollment ≥4 y (n = 2371)	Persistent Chronic Opioid Therapy ≥4 y (n = 132)	*P*
Health care utilization				
IBD hospitalizations, %				
0	74.4	36.9	15.2	<0.001
1–2	15.5	42	43.7	
3–4	4.7	10.4	16.1	
5+	5.4	10.6	25	
≥1 IBD surgeries	7.8	26.4	46.2	<0.001
Outpatient visits, mean	12.3	16.3	26.4	<0.001
≥1 ED visits	48.5	88.1	96.2	<0.001
Polypharmacy,[a] mean	3.9	4.2	5.9	<0.001
No. prescriptions, %				
0–4	65	61.7	28	
5+	35	38.3	72	<0.001
Health care costs				
High-cost patients,[b] %	9.2	13.9	28.8	<0.001
Total costs per year (SD), $	20,473 (40,105)	28,139 (30,342)	44,766 (42,823)	<0.001
Hospitalization cost (SD), $	6351 (7041)	7028 (7996)	5284 (3597)	<0.001

[a]Excluding IBD medications.
[b]High-cost patients defined as annual health care costs >$50,000.

TABLE 4: Multivariable Logistic Regression

Independent Variable	Adjusted Odds Ratio for Chronic Opioid Therapy (95% CI)	Variable LRT *P*
Age, y		
15–19	Referent	<0.001
20–24	1.31 (1.25–1.38)	
25–29	1.57 (1.50–1.65)	
Sex		
Female	1.34 (1.30–1.40)	<0.001
Region		
Northeast	Referent	<0.001
North Central	1.40 (1.33–1.48)	
South	1.73 (1.64–1.81)	
West	1.76 (1.66–1.87)	
Unknown	1.17 (1.03–1.34)	
IBD		
CD	Referent	<0.001
IC	0.98 (0.92–1.04)	
UC	0.65 (0.62–0.67)	
Pain[a]	2.44 (2.33–2.57)	<0.001
Depression	1.94 (1.79–2.10)	<0.001
Anxiety	1.48 (1.37–1.60)	<0.001
Substance use	2.65 (2.12–3.32)	<0.001

Abbreviations: CI, confidence interval; LRT, likelihood ratio test.
[a]The pain variable includes common pain conditions associated with the prescription of opioids in the general population (joint pain, chronic back pain, migraines, unspecified chronic pain, osteoarthritis, and rheumatoid arthritis) (see Supplementary Table 2 for ICD-9/10 codes). Abdominal pain is excluded from this category due to our inability to differentiate IBD-related abdominal pain from other sources of abdominal pain in the sample.

contribute to prolonged opioid use. Additionally, behavioral interventions as part of multidisciplinary pain management treatment could effectively support opioid weaning.

These efforts are particularly important among adolescents and young adults with IBD as opioid use during this period predicts future use and misuse, even among individuals who have little to no history of drug use or strong disapproval of illegal drug use at baseline.[15] Furthermore, opioid use can interfere with employment (eg, through failed drug testing) during this crucial period.[31] Given the current opioid epidemic and rising deaths among young adults, it is critical that future research explore the efficacy of interventions in reducing chronic opioid therapy in adolescents and young adults with IBD.

Limitations

The Truven database solely provides information about filled opioid prescriptions. No data are available on individuals' consumption of opioids or the number of opioids prescribed and not filled. Similarly, opioid misuse (ie, use of opioids without a prescription) is not captured, likely leading to an underestimation of individuals taking chronic opioids. Second, this database is comprised of a commercially insured population. Although using an employer-based insurance database captures the largest group of individuals in the United States younger than age 65 years (2014: 47% of children, 59% of adults),[32] young people who are on Medicaid or uninsured are not represented in this study population. This sampling bias may be particularly relevant for adolescents, as more children are enrolled in Medicaid than adults.[33] Additionally, when looking at the persistence of chronic opioid therapy over time, only those who were continuously enrolled were included in the longitudinal analysis. This likely underestimates the population of individuals meeting criteria for chronic opioid therapy, as those who are unable to work due to chronic opioid therapy or IBD (eg, due to inability to pass an employer drug test, severe IBD) are excluded. Including young people only on commercial insurance likely leads to a study sample that is healthier, has a higher level of education and socioeconomic status, and/or lives in a family with more resources. Future research combining employer-based insurance and Medicaid databases would provide even more thorough coverage and further increase the accuracy of the rates of prevalence and persistence of chronic opioid therapy in the United States. Third, the definition of chronic opioid therapy used in this study has not been validated, although it has been used in published research.[5] Furthermore, the algorithm for identification

of IBD was validated in adults but has not been validated in adolescents. Although the algorithm appears to be fairly accurate, with a positive predictive value of 95%,[23] there remains some potential for misclassification of IBD, specifically CD vs UC. Validation studies comparing the various definitions of chronic opioid therapy and IBD classification from administrative data in this age group would help determine the most accurate classification criteria going forward. Fourth, the database does not provide information about where the first narcotic prescription was written (eg, ED vs outpatient gastrointestinal clinic) or the indication for prescribed medications that could have resulted in misclassification. This was addressed by applying strict criteria for chronic opioid therapy based on past research.[5] Investigators using databases who have access to these important prescription details should further explore whether such factors impact the development of chronic opioid therapy. Lastly, there were no data on specific clinical characteristics such as disease severity. Exploring clinical predictors of chronic opioid therapy over time in a more diverse IBD sample is an important area of future research.

CONCLUSIONS

This study demonstrates that in a large national sample of adolescents and young adults with IBD, a substantial proportion receive chronic opioid therapy. Rates of chronic opioid therapy have persisted over time in the United States despite national efforts to decrease opioid prescribing patterns. Inflammatory bowel disease providers should be made aware of the risk of opioid dependence among adolescents and young adults with IBD and the associated elevations in health care utilization and costs. The high prevalence of chronic opioid therapy among individuals with chronic pain, anxiety, and depression highlights the need for standardized psychosocial screening tools in IBD clinics for this vulnerable population, coupled with access to empirically supported behavioral interventions (eg, cognitive behavioral therapy). Overall, health care providers should be mindful of the potential long-term effects of starting adolescents and young adults with IBD on opioids and, when prescribed, utilize multidisciplinary pain management strategies to support timely weaning.

SUPPLEMENTARY DATA

Supplementary data are available at *Inflammatory Bowel Diseases* online.

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