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# Opioid and Nonopioid Analgesic Prescribing Patterns of Hepatologists for Medicare Beneficiaries

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INTRODUCTION: Opioids are commonly prescribed to patients with chronic liver disease, but little is known regarding medication prescribing patterns of hepatologists. Opioid use increased until national guidelines limited opioid prescriptions in early 2016. We aimed to describe rates of opioid and nonopioid analgesics to Medicare beneficiaries by hepatologists from 2013 to 2017 and identify demographic characteristics associated with higher prescribing.

**METHODS:** 

Prescription data from 2013 to 2017 by 761 hepatologists identified in the Centers for Medicare and Medicaid Services Part D Public Use File were analyzed. Annual prescription volumes were compared for providers with >10 annual prescriptions of a given drug type. Provider characteristics associated with opioid prescriptions were identified through multivariate logistic regression analyses.

**RESULTS:** 

The proportion of hepatologists prescribing >10 annual opioid prescriptions decreased from 29% to 20.6%. Median annual opioid prescriptions per hepatologist significantly decreased from 24 to 20. Tramadol remained the most prescribed analgesic. Nonopioid analgesic prescription volume did not increase significantly. Provider characteristics associated with increased opioid prescriptions included male sex, practice location in the South and Midwest (vs West), more years in practice, and a greater proportion of beneficiaries who are white or with low-income subsidy claims. Characteristics associated with fewer prescriptions included non-university-based practice, having a greater proportion of female beneficiaries, and later prescription year.

**DISCUSSION:** 

Hepatologists are prescribing less opioids. However, the prevalence of tramadol use and the lack of increase in nonopioid analgesic use highlights the need for advancing the science and training of pain management in chronic liver disease and targeted implementation of nonopioid treatment programs.

**KEYWORDS:** opioid analgesics; analgesics; cirrhosis; hepatology; pain management

SUPPLEMENTARY MATERIAL accompanies this paper at http://links.lww.com/CTG/B181.

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#### INTRODUCTION

Morbidity and mortality related to prescription opioid use are increasing in the United States (US) (1-4), and patients with chronic liver disease are uniquely vulnerable to such opioidrelated harms (1,5). Among ambulatory gastrointestinal visits, chronic liver disease is one of the leading gastrointestinal conditions associated with opioid prescriptions (6). Nearly 1 in 5 patients with cirrhosis receive an opioid prescription during ambulatory encounters despite only one-third of such encounters being associated with a pain diagnosis (7). Along with increased risk of overdose, opioid use is also associated with increased risk of hepatic encephalopathy (5,8–10), sedation, gut dysbiosis (11), prolonged hospital stays (12), increased hospitalizations (11,13), and higher post-transplant mortality (14) in this population. Although opioid prescriptions for patients with cirrhosis typically originate from primary care providers compared with specialists (7), hepatologists, who are likely aware of opioid-related harms among patients with chronic liver disease, are paradoxically more likely than general gastroenterologists to be high opioid prescribers (15). This may be due to hepatologists managing a larger proportion of patients with advanced chronic illnesses and symptom severity than general gastroenterologists (6,15). A study

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of Medicare data showed persistent growth in opioid prescriptions from 2007 to 2012 (16), and prescriptions were 3 times as high in 2015 as 1999 (17) with one-third of Medicare beneficiaries receiving an opioid prescription in 2016 (18). In response, national agencies such as the Centers for Disease Control launched widespread efforts to limit opioid prescriptions in March 2016 (19–21) and recommended nonopioid pharmacologic therapy as a preferred treatment for chronic pain (22). However, patients with chronic liver disease may remain at higher risk based on our previous findings (7,15). Understanding trends and provider factors associated with high opioid prescription use among hepatologists is critical toward highlighting clinical care gaps and framing opportunities for quality improvement surrounding pain management in patients with chronic liver disease.

The aim of this study was to (i) describe the types and rates of opioid and nonopioid analgesics prescribed to Medicare beneficiaries by hepatologists between 2013 and 2017 and (ii) identify demographic characteristics of hepatologists and their patient panels associated with opioid prescriptions. We hypothesized that the rate of high opioid prescribing would decrease over time in response to the opioid epidemic and shift toward a multimodal pain management approach. Among drug types, we hypothesized that oxycodone and hydromorphone would be most likely to be prescribed, given more favorable pharmacokinetics in chronic liver disease (5,23–25).

#### **METHODS**

#### Data source

We conducted a retrospective cross-sectional study using publicly available Medicare Part D Public Use File (PUF) data from 2013 to 2017 provided by the Centers for Medicare and Medicaid Services (CMS) (26). This database includes information on drugs prescribed by US healthcare providers to the approximately 70% of Medicare beneficiaries enrolled in the Medicare Part D Prescription Drug program (27), which includes US adults older than 65 years and individuals with disabilities eligible for Medicare. Each observation in the data set contains prescription data from an individual provider for each drug or drug class prescribed by that provider each year. For each drug or drug class prescribed, the total number of prescriptions, number of unique beneficiaries who received prescriptions, day supply, and total associated drug costs are reported. Opioid prescription data were reported as aggregate class data as well as individual opioid types (i.e., oxycodone and tramadol).

Prescriber and beneficiary demographics are incorporated from the National Plan and Provider Enumeration System using National Provider Identifiers (NPIs). Descriptive features of each prescriber, such as gender and primary practice address associated with NPI, and their Part D patient cohort, including panel size, gender, race, and proportion of patients with low-income subsidy claims, are reported. Consistent with methodology used in our previous study (28), NPI numbers were used to link the Part D PUF data to the Medicare Physician Compare National Downloadable File in 2019, which contains information on prescribers' year of medical school graduation, gender, and practice address. University affiliation status was designated based on review of online physician career profiles.

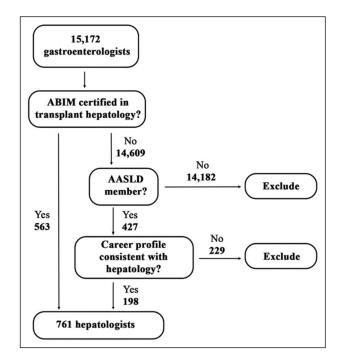
#### Cohort identification

We first included all gastroenterologists with at least one opioid prescription to Medicare beneficiaries in the Part D PUF database from 2013 to 2017, which is based on self-reported specialty. The data set included 15,172 self-identified gastroenterologists. Providers were identified as a hepatologist if they (i) were board-certified in transplant hepatology per the American Board of Internal Medicine or (ii) were active members of the American Association for the Study of Liver Diseases and have evidence of primary clinical interests, leadership, or research in hepatology based on review of online career profiles (Figure 1). A research assistant (P.I.) performed profile reviews and any concerns with classification were resolved in consultation with a board-certified transplant hepatologist (A.P.).

#### Variables of interest

Study outcomes included (i) prescription and prescriber volume trends of opioid analgesics by hepatologists with >10 annual opioid prescriptions, (ii) prescription volume trends of nonopioid analgesics by hepatologists with >10 annual nonopioid analgesic prescriptions, and (iii) demographic characteristics and geographic distribution associated with opioid prescriptions among all hepatologists.

Data were decomposed into opioid types, tricyclic antidepressants (TCAs), serotonin-norepinephrine reuptake inhibitors (SNRIs), gabapentinoids, and muscle relaxants. Individual drug types included in the analyses were derived from the corresponding drug list (29) provided on the CMS website and are described in Supplementary Digital Content (see Supplementary Table 1, http://links.lww.com/CTG/B181). Codeine in combination with promethazine was not included given its primary indication for cough. Analgesics that are available over the counter, such as nonsteroidal anti-inflammatory drugs, acetaminophen, lidocaine patches, and topical capsaicin, were not



**Figure 1.** Flow chart. About 761 hepatologists were identified as having either (i) board certification in transplant hepatology by the American Board of Internal Medicine (ABIM) or (ii) membership in the American Association for the Study of Liver Diseases (AASLD) and online career profile consistent with a practice in hepatology.

Table 1. Provider and patient panel characteristics of hepatologists with at least one opioid prescription to Medicare beneficiaries from 2013 to 2017 (n = 761)

| Provider characteristics   | Count  | %                   |
|----------------------------|--------|---------------------|
| Male                       | 567    | 74.5                |
| Region                     |        |                     |
| Midwest                    | 203    | 26.7                |
| Northeast                  | 169    | 22.2                |
| South                      | 249    | 32.7                |
| West                       | 140    | 18.4                |
| Practice setting           |        |                     |
| Not university-affiliated  |        |                     |
| University-affiliated      |        |                     |
|                            | Median | Interquartile range |
| Patient panel size (count) | 131    | 69–221              |

included given that they were unlikely to capture true rates of recommended use by providers and use among patients.

53.7%

71.4%

46.1%

% Panel with female patients

% Panel with white patients

% Panel with low income and resources

Detailed prescription data were reported as aggregate class data for opioids only if an individual provider prescribed either 0 or >10 opioid prescriptions in a year. Detailed prescription data by providers who prescribed between 1 and 10 opioid prescriptions in a year were intentionally suppressed by CMS and labeled as missing data because of privacy (27). Prescription data for individual opioid (i.e., oxycodone) and nonopioid (i.e., gabapentin) analgesics were reported for prescribers with >10 prescriptions of the individual drug in each year. Nonopioid analgesic classes (i.e., TCAs and SNRIs) were created by combining prescription data for individual drugs in the class. For example, to calculate the number of prescriptions for SNRIs for the year 2017, prescription counts for desvenlafaxine, duloxetine, venlafaxine, and milnacipran by providers with >10 prescriptions for each individual drug in 2017 were calculated and combined. Analysis of trends of opioid and

nonopioid analgesic prescription counts were, therefore, limited to providers with >10 prescriptions in each year. This is consistent with the methodology used in our previous study (28).

Descriptive features of prescribers and their Part D patient cohorts were used to determine demographic characteristics associated with opioid prescribing behavior. Providers with missing opioid class data, meaning that they had 1–10 annual prescriptions, were given an average of "5" as recommended by the CMS (27) and used in other studies (30). Similar to our previous study (28), this methodology was also used to calculate state-level geographic distribution of average opioid prescriptions. Two or fewer hepatologist prescribers in Alaska, Montana, West Virginia, and Wyoming led us to exclude those states in state-level geographic distribution.

#### Statistical analysis

All analyses were performed using R 4.2.2. Multivariate regression analyses were used to identify provider characteristics associated with greater opioid prescriptions using total claim counts including refills. Specifically, a negative binomial model was fit because of the skew (right tail) characteristic of prescription/count data using the R library MASS (31). A geographic distribution map was created using data from 2017 to reflect providers' most recent practice location.

This study was exempt from review by the institutional review board at the University of California, Los Angeles.

#### **RESULTS**

46.8%-60.4%

56.4%-82.1%

32.1%-58.8%

We identified 761 hepatologists with at least one opioid prescription to Medicare beneficiaries over the study period (Figure 1) with provider characteristics described in Table 1. All hepatologists prescribed >10 opioids in at least one of the years between 2013 and 2017. The most prescribed opioids over the study period, by number of prescriptions, were tramadol (52%), followed by hydrocodone (17.2%) and oxycodone (13.2%).

#### **Opioid prescription trends**

The proportion of hepatologists with >10 annual opioid prescriptions appeared stable from 29% in 2013 to 29.4% in 2014 before declining to 20.6% by 2017 (Table 2). The total number of opioid prescriptions peaked in 2014 at 306,402 before decreasing to 215,099 in 2017, with a significant decrease in median prescription volume per hepatologist (Table 2).

Table 2. Total number, mean, and SD of opioid prescriptions and total number of beneficiaries prescribed opioids by hepatologists

|   |             | 2013     |        | 2014 20  |        | 2015     | 2015   |           | 2016 |        | 2017     |  |
|---|-------------|----------|--------|----------|--------|----------|--------|-----------|------|--------|----------|--|
|   |             | N        | %      | N        | %      | N        | %      | N         | %    | N      | %        |  |
| Total hepatologists (N = 761)                                 |             | 221      | 29.0   | 224      | 29.4   | 210      | 27.6   | 178       | 23.4 | 157    | 20.6     |  |
| Total count of opioid prescriptions                           |             | 276,677  |        | 306,402  |        | 300,263  |        | 248,224   |      | 215,09 | 9        |  |
| Total count of patients prescribed w                          | ith opioids | 39,750   |        | 43,931   |        | 44,334   |        | 38,524    |      | 34,513 | 3        |  |
|   | Median      | IQ (+/-) | Median | IQ (+/-) | Median | ı IQ(+/- | ·) Med | dian IQ ( | +/-) | Median | IQ (+/-) |  |
| Opioid prescriptions <sup>a</sup>                             | 24          | 26       | 25     | 24.5     | 22.5   | 21       | 2      | 1 :       | 18   | 20     | 17       |  |
| Patients prescribed with opioids                              | 16          | 9        | 17     | 9.5      | 17     | 8        | 15     | 5.5       | 8    | 16     | 6        |  |
| Opioid prescription duration (d) <sup>b</sup>                 | 20.9        | 8.8      | 20     | 10.9     | 18.3   | 10.8     | 19     | 9.1 1     | 0.4  | 19.8   | 12.4     |  |
| <sup>a</sup> <i>P</i> <0.001.<br><sup>b</sup> <i>P</i> <0.02. |             |          |        |          |        |          |        |           |      |        |          |  |

Tramadol prescriptions peaked in 2014 with 14,220 total prescriptions by 20.2% of hepatologists (Table 3). Although prescription volume subsequently declined, this decrease was not statistically significant and tramadol remained the most prescribed analgesic in 2017. Although hydrocodone and oxycodone prescriptions decreased, the trends were not statistically significant (Table 3). Other opioid types, including hydromorphone, fentanyl, and morphine, had stable low prescription volumes with <500 total prescriptions in any year (Table 3). In a subgroup analysis of geographic distribution of opioid prescriptions, we found that tramadol prescriptions were the highest in the South and remained relatively stable (see Supplementary Figure 1, http://links.lww.com/CTG/B181).

# Demographic characteristics associated with high opioid prescribing

Male sex (vs female sex) of providers, practice location in the South or Midwest (compared with the West), greater years in practice, and having a greater proportion of beneficiaries who are white or with low-income subsidy claims were associated with greater total opioid prescription count (Table 4). Prescription year, practice in a nonuniversity setting, and having an increased proportion of female beneficiaries in a provider's panel were inversely associated with greater total opioid prescription count (Table 4).

#### Geographic distribution

A distribution map (Figure 2) presents descriptive data from 2017 for providers in states with at least 3 providers. Although there was variation in prescription volume among states, the Southeastern United States had a higher concentration of states with higher average opioid prescriptions per provider.

#### Nonopioid analgesic trends

By total count of nonopioid analgesics, gabapentinoids were the most prescribed nonopioid analgesic (63.3%). Gabapentinoid

| Year                 | 2013   | 2014   | 2015   | 2016   | 2017   |
|----------------------|--------|--------|--------|--------|--------|
| n                    | 579    | 603    | 641    | 659    | 675    |
| Codeine              |        |        |        |        |        |
| Prescription (count) | 260    | 275    | 479    | 421    | 397    |
| Prescriber (count)   | 3      | 2      | 5      | 3      | 3      |
| % Hepatologists      | 0.50%  | 0.30%  | 0.80%  | 0.50%  | 0.40%  |
| Fentanyl             |        |        |        |        |        |
| Prescription (count) | 60     | 0      | 110    | 175    | 245    |
| Prescriber (count)   | 1      | 0      | 1      | 2      | 2      |
| % Hepatologists      | 0.20%  | 0.00%  | 0.20%  | 0.30%  | 0.30%  |
| Hydrocodone          |        |        |        |        |        |
| Prescription (count) | 7,763  | 6,298  | 2,635  | 2038   | 1774   |
| Prescriber (count)   | 55     | 49     | 29     | 23     | 20     |
| % Hepatologists      | 9.50%  | 8.50%  | 5.00%  | 4.00%  | 3.50%  |
| Hydromorphone        |        |        |        |        |        |
| Prescription (count) | 84     | 415    | 395    | 320    | 0      |
| Prescriber (count)   | 2      | 6      | 6      | 5      | 1      |
| % Hepatologists      | 0.30%  | 1.00%  | 0.90%  | 0.80%  | 0.10%  |
| Morphine             |        |        |        |        |        |
| Prescription (count) | 55     | 65     | 235    | 125    | 48     |
| Prescriber (count)   | 1      | 1      | 4      | 2      | 0      |
| % Hepatologists      | 0.20%  | 0.20%  | 0.60%  | 0.30%  | 0.00%  |
| Oxycodone            |        |        |        |        |        |
| Prescription (count) | 2,985  | 4,005  | 3,595  | 2,612  | 2,481  |
| Prescriber (count)   | 32     | 41     | 35     | 22     | 26     |
| % Hepatologists      | 5.50%  | 6.80%  | 5.50%  | 3.30%  | 3.90%  |
| Tramadol             |        |        |        |        |        |
| Prescription (count) | 13,069 | 14,220 | 13,828 | 11,141 | 9,636  |
| Prescriber (count)   | 117    | 123    | 115    | 95     | 86     |
| % Hepatologists      | 20.20% | 20.40% | 17.90% | 14.40% | 12.70% |

Table 4. Regression model of provider characteristics associated with greater opioid prescriptions among hepatologists

| Variable                            | β             | Confid<br>inte | P             |         |
|-------------------------------------|---------------|----------------|---------------|---------|
|                                     |               | 2.5%           | 97.5%         |         |
| Provider sex (male) <sup>a</sup>    | 0.23          | 0.11           | 0.35          | < 0.001 |
| Provider years of practice          | 0.02          | 0.01           | 0.02          | < 0.001 |
| Year                                | -0.14         | -0.17          | -0.10         | < 0.001 |
| Midwest (vs West)                   | 0.32          | 0.18           | 0.42          | < 0.001 |
| Northeast (vs West)                 | 0.00          | -0.16          | 0.15          | 0.95    |
| South (vs West)                     | 0.50          | 0.36           | 0.63          | < 0.001 |
| Nonacademic (vs academic)           | -0.20         | -0.31          | -0.09         | < 0.001 |
| % Panel with female patients        | <b>-</b> 1.89 | <b>-</b> 2.50  | <b>-</b> 1.26 | < 0.001 |
| % Panel with white patients         | 0.26          | 0.07           | 0.44          | 0.004   |
| % Panel with low income             | 1.31          | 0.91           | 1.71          | < 0.001 |
| <sup>a</sup> Males prescribed more. |               |                |               |         |

prescription volume increased from 2013 to 2017 and was the second most prescribed analysesic in 2017, although this trend was not statistically significant (Figure 3). Tricyclic antidepressants and muscle relaxant prescription volume had milder insignificant increases but were more frequently prescribed than oxycodone and hydrocodone in 2017. SNRI prescriptions remained stable.

#### **DISCUSSION**

We present findings from the first large national study investigating opioid and nonopioid analgesic prescribing behavior among US hepatologists to Medicare beneficiaries. Overall, the proportion of hepatologists providing >10 annual opioid prescriptions decreased from 29% to 20.6% from 2013 to 2017. A modest, nonsignificant increase in nonopioid, non-over-the-

counter analgesics over this timeframe was also observed, but it does not seem to fully compensate for the decline in opioid prescriptions. Tramadol was the most prescribed opioid analgesic. Those with practices in the South or Midwest and with high percentage of white, male, and low-income beneficiaries were more likely to prescribe more opioids. Our findings, taken together, can inform opioid deprescribing efforts and should further activate the gastroenterology and hepatology communities to invest efforts in education and the use of alternative pain management strategies for patients with chronic liver disease including multidisciplinary approaches, such as neuromodulators and gut-directed behavioral therapies, that are increasingly being recommended and studied for chronic abdominal pain (25,32,33).

A total of 761 hepatologists were identified as having prescribed at least one opioid prescription during the study period. Using workforce data from 2018, this represents approximately 12% of physicians who practice hepatology (34). Although a decrease in opioid prescribers among hepatologists has been observed (29%–20.6%) from 2013 to 2017, this is smaller than the decrease experienced by all gastroenterologists (26%–15%) during the same period (28). In addition, prescription rates of nonopioid analgesics, such as gabapentinoids, TCAs, SNRIs, and muscle relaxants, did not significantly increase, whereas prescription rates of nonopioid analgesics among gastroenterologists, particularly antispasmodics, did increase (28). These trends suggest that system-level initiatives and policies are needed to promote opioid deprescribing, as well as more education on alternative regimens for pain management.

The most commonly prescribed opioid among hepatologists in this study was tramadol, as compared to hydrocodone among gastroenterologists (6). Tramadol was previously considered safe for use in chronic liver disease (5,23,24,35) but is now not recommended because of the high frequency of side effects and difficulty in titration (25,36). Specific risks include high first-pass hepatic metabolism, variable pharmacokinetics, ability to lower the seizure threshold, risk of serotonin syndrome when used with other serotonergic agents, and unpredictable side effects such as

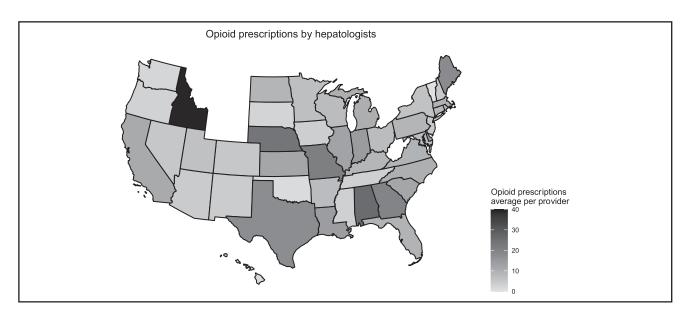


Figure 2. Opioid prescriptions by hepatologists. Geographic distribution of hepatologists. Note that all hepatologists with <10 opioid prescriptions were estimated to have 5 opioid prescriptions. Missing states (Wyoming, Alaska Montana, and West Virginia) have too few prescribers (<3) reported to include.

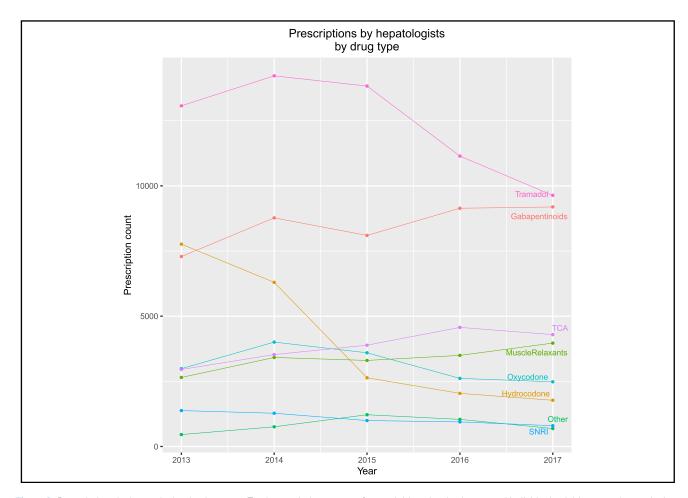


Figure 3. Prescriptions by hepatologists by drug type. Total prescription counts of nonopioid analgesic classes and individual opioids among hepatologists. "Other" includes morphine, hydromorphone, codeine, and fentanyl. SNRI, serotonin-norepinephrine reuptake inhibitor; TCA, tricyclic antidepressants.

hypoglycemia (25,35,36). An increase in tramadol prescription rates has been noted in the United States (37), as well as deaths in certain parts of the world (38). Our hypothesis that hydromorphone and oxycodone, which have better safety profiles among patients with cirrhosis (5,25,36), would be the most frequently prescribed opioids was incorrect. This may be due to the perception of hydromorphone as a more potent opioid.

Our results highlight important demographic characteristics associated with opioid prescriptions among hepatologists and their practices, which should be considered for future deprescribing efforts and investigation. First, although there was geographic variability in prescription volume among states in 2017, the Southeastern United States seemed to have a higher average opioid prescription volume. These findings are consistent with our previous analysis of all gastroenterologists (28), as well as other studies (4,37,39-43). Next, prescriptions tended to be highest among hepatologists with panels that consisted of a high volume of white, male, or low-income beneficiaries. Although studies examining the association between race, sex, and opioid prescriptions among patients with chronic liver disease reveal mixed patterns (7,10,44-46), the association between low-income and higher opioid prescriptions has been well-established in multiple cohorts involving gastroenterologists (15), elderly populations (43,47), and chronic liver disease (48). Future work that could further inform deprescribing includes surveys of clinicians and patients from high-risk areas, including the South and Midwest, that can better discern pain behaviors among patients, attitudes among clinicians regarding prescriptions, and how these relate to social determinants of health.

The lack of a sufficient rise in nonopioid analgesic prescriptions during the study's timeframe highlights potential gaps in pain management in this population. Gabapentinoid use increased from 2013 to 2017 with milder increases in tricyclic antidepressants and muscle relaxant prescriptions, although these trends were not significant. The relative increase does not compensate for the decrease in opioid prescriptions, raising concerns for potential undertreatment of pain, although providers may be using nonprescription analgesics and nonpharmacologic approaches not captured in this study. Acetaminophen is a valid and recommended treatment in this population (25,49), but utilization by providers is difficult to ascertain, given that it is typically obtained without a prescription. Future initiatives to examine pain management approaches more comprehensively among hepatologists could include surveying providers about their treatment recommendations beyond prescription medications. Important future steps include advancing the science of managing pain in chronic liver disease as well as promoting education regarding nonopioid pain regimens and nonpharmacologic approaches among hepatologists caring for this population. A recent national study found that only 57% of transplant hepatology fellows were comfortable managing pain and that <50% were comfortable managing other symptoms, such as mood and insomnia (50). Similar gaps in knowledge regarding pain management have been noted among nurses (51), but such knowledge assessments have not been captured for practicing hepatologists, which is an important area of future research. The recently published American Association for the Study of Liver Diseases practice guidance (25), as well as recent high-quality reviews (49,52), is an important resource for understanding the types of chronic pain in cirrhosis (nociceptive, neuropathic, and nociplastic pain) and the importance of using a multimodal, interdisciplinary, and personalized approach that includes nonpharmacologic interventions and addresses comorbid disorders that may contribute to pain perception, such as mood disturbances and insomnia. As the space for managing symptom science in cirrhosis emerges, the hepatology community must consider investing in ways that clinical practice models can address gaps in pain management approaches in this population.

Our study is not without limitations. The data included prescriptions only to patients who use Medicare Part D, which is selected for patients aged 65 years and older. The Medicare Part D database did not include detailed prescription information for drugs with ≤10 annual prescriptions by a provider, which resulted in missing data and using estimated averages for prescribers with lower prescription counts. We did not have access to diagnoses or indications associated with a given prescription or if analgesics were prescribed for acute pain, chronic pain, in the post-transplant setting, or for end-of-life care, which limits interpretation. Overthe-counter analgesics and nonpharmacologic interventions may have been recommended by hepatologists and not captured by this study. Although our intention was to investigate opioid prescribing behavior among hepatologists, this study does not consider analgesic prescriptions by other specialties, such as palliative or primary care providers, who may be taking a significant role in pain management for patients with chronic liver disease as suggested by our previous study (7). Despite these limitations, our study has notable strengths. It is the first large national study investigating analgesic prescribing behavior among US hepatologists. Although the study population was limited to analgesic prescriptions by hepatologists to Medicare beneficiaries, our findings seem to be generalizable, given that provider characteristics in our study were consistent with a national workforce study of US hepatologists, who were more likely to be male, university-affiliated, and geographically located in the Southeastern United States (34). In addition, baseline patient panel characteristics were consistent with national epidemiologic studies of chronic liver disease, which further supports the generalizability of our findings. For instance, 71.4% of our study's providers' panels were white patients, which is consistent with the 75.1% of Medicare Part D enrollees who were described as being white in a 2019 study (53), as well as the 65.4% of patients with chronic liver disease described as being white in the National Health and Nutrition Examination data from 2013 to 2016 (54). Similarly, another study using National Health and Nutrition Examination data suggested that the prevalence of cirrhosis is higher in those living below the poverty level (55), which may explain why nearly half of providers' patients in our study filed low-income subsidy claims.

Opioid prescription volume by US hepatologists to Medicare beneficiaries decreased from 2013 to 2017. The concomitant mild to moderate increase in nonopioid analysics suggests that hepatologists are responding to the opioid epidemic, but this may not be sufficient. More research is needed to better understand beliefs

among hepatologists regarding opioid prescribing and pain behaviors among patients with chronic liver disease across different races, ethnicities, sexes, and practice settings who are high risk of opioid prescriptions (i.e., lower-income patients and practice setting in the South or Midwest). Advancing the science of pain management and implementation of multidisciplinary nonopioid treatment programs are critically needed to close these gaps.

#### **CONFLICTS OF INTEREST**

Guarantor of the article: Arpan Patel, MD, PhD.

Specific author contributions: P.I.: conceptualization,
methodology, investigation, writing—original draft, and
writing—review and editing. N.P.: methodology, data curation, formal analysis, writing—original draft, writing—review and editing,
and software. W.L.: conceptualization, methodology, and
writing—review and editing. A.L.: conceptualization, methodology,
and writing—review and editing. L.C.: conceptualization, methodology, and writing—review and editing. A.P.: conceptualization,
methodology, investigation, writing—original draft, writing—review
and editing, and supervision.

Financial support: None to report.

Potential competing interests: None to report.

# **Study Highlights**

### WHAT IS KNOWN

There is a high prevalence of pain and prescription opioid use among patients with chronic liver disease.

#### WHAT IS NEW HERE

- Hepatologists are responding to the opioid epidemic by decreasing opioid prescription volume.
- Limited increase in nonopioid analgesic prescriptions suggests a lack of consensus, education, and training in nonopioid analgesic use and undertreatment of pain.
- Research and targeted dissemination of guidelines in pain management in chronic liver disease are needed.

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