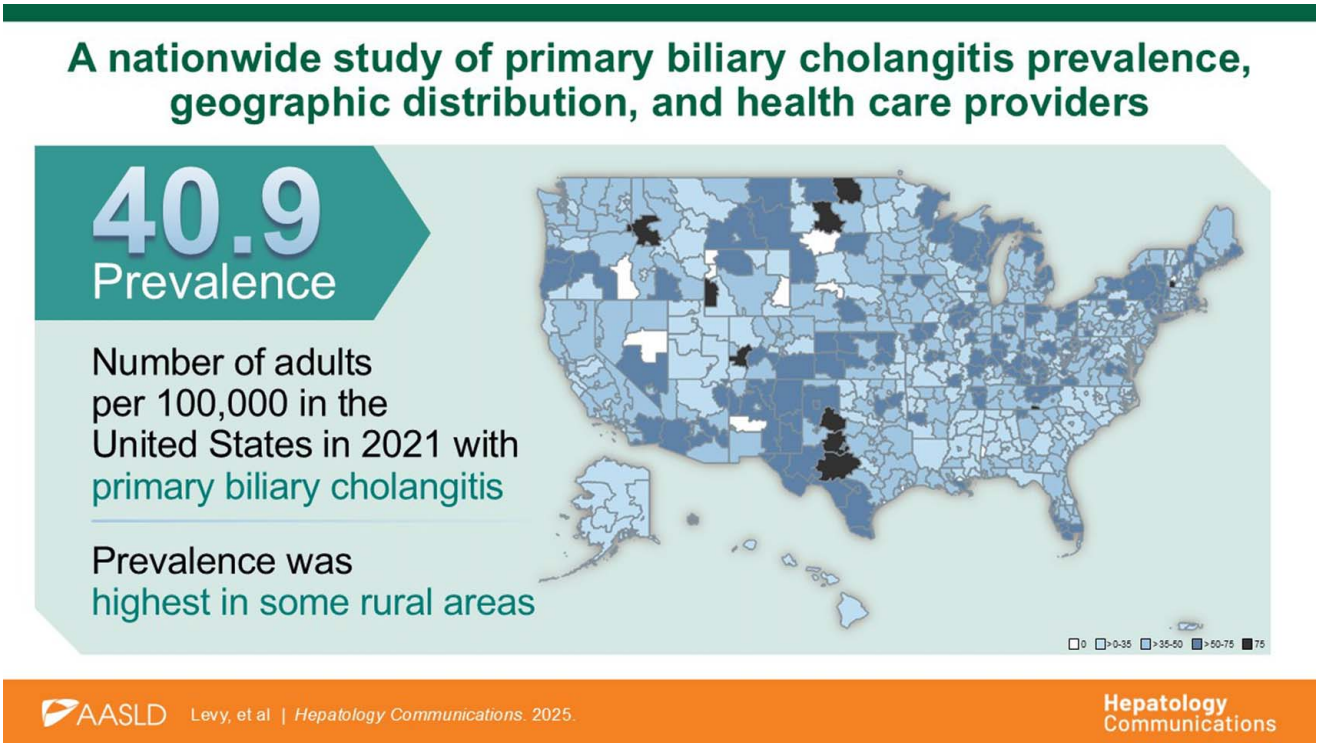
# A nationwide study of primary biliary cholangitis prevalence, geographic distribution, and health care providers

## VISUAL ABSTRACT



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# A nationwide study of primary biliary cholangitis prevalence, geographic distribution, and health care providers

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## Abstract

**Background:** Prevalence estimates of primary biliary cholangitis (PBC) in the United States have evolved with the introduction of newer real-world data capture approaches. Little is known about the geographic distribution of PBC in the United States and the health care provider (HCP) landscape for patients with PBC. This real-world study aimed to estimate the prevalence of PBC in the United States, assess regional variability in its prevalence, and describe HCPs for patients with PBC.

**Methods:** Patients with PBC were identified using Komodo's Healthcare Map, a large national administrative claims database. PBC prevalence per 100,000 adults was adjusted by age and gender at the 3-digit ZIP Code tabulation area level. Patients' PBC-related medical or pharmacy claims were used to determine HCP specialties and affiliations (academic vs. nonacademic); the latest claim and all claims were examined.

**Results:** The adjusted 2021 PBC prevalence was 40.9 per 100,000 adults. The highest absolute number of patients with PBC in the United States was in heavily populated urban areas, but prevalence adjusted for population size was highest in some rural areas. Among all claims, most (83.2%) patients received care from a specialist (gastroenterologist/hepatologist) at one time. However, only approximately half (53.5%) of patients with PBC, irrespective of therapy use, were most recently treated for PBC by a specialist.

**Conclusions:** This is the most comprehensive and contemporary estimation of PBC prevalence in the United States to date. The pockets of high prevalence of PBC located in some rural areas highlight the need to better

**Abbreviations**: APP, advanced practice provider; FOLD, Fibrotic Liver Disease Consortium; GI, gastroenterology; HCP, health care provider; ICD, International Classification of Diseases; NPI, National Provider Identifier; OCA, obeticholic acid; PBC, primary biliary cholangitis; UDCA, ursodeoxycholic acid; ZCTA3, 3-digit ZIP Code tabulation area.

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evaluate PBC risk factors and potential barriers in access to specialist care once patients are diagnosed. Greater awareness of PBC and its management are needed.

**Keywords:** epidemiology, liver disease, PBC, regional variability, specialist

## INTRODUCTION

Primary biliary cholangitis (PBC) is a rare chronic, autoimmune, cholestatic liver disease characterized by the destruction of intrahepatic bile ducts that predominantly affects women.[1,2] PBC commonly presents with nonspecific symptoms such as fatigue and pruritus, and without treatment, the disease slowly progresses to cirrhosis approximately 10–20 years after diagnosis.[3,4] However, the clinical presentation and natural course of PBC are highly variable among patients.[4] PBC progression confers economic burden to payers and patients, including risk of hospitalizations, progression to cirrhosis and its complications, and liver transplantation.[5] Ursodeoxycholic acid (UDCA), the first-line treatment for PBC, has been approved by the US Food and Drug Administration since 1997.[6] For patients with inadequate response or intolerance to UDCA, the US Food and Drug Administration conditionally approved obeticholic acid (OCA) in 2016[7] and, more recently, seladelpar and elafibranor in 2024 as second-line therapies.[8,9] Off-label use of fibrates may also be considered in patients with inadequate response to UDCA.[2,3]

While significant progress has been made in understanding the natural history and overall management of PBC, better knowledge of epidemiology and geographic variation in the United States is needed to improve access to care.[10] To date, the global prevalence of PBC has largely been extrapolated from regional databases with relatively small patient cohorts.[11–19] The prevalence estimates of PBC vary substantially, ranging from 1.91 to 40.2 per 100,000 persons, with discrepancies likely due to differing study methods assessing unique populations and geographic areas.[20–22] Additionally, it has been shown that global PBC prevalence has increased over time, perhaps contributing further to the wide range of reported prevalence estimates.[23]

One of the largest and most recent epidemiologic studies of PBC in the United States identified a 12-year period (2003–2014) prevalence of 29.3 per 100,000 persons.[10] This overall prevalence varied by geographic region and patient demographics, such as age, gender, and race. Using the same clinical database (the Fibrotic Liver Disease [FOLD] Consortium) of 11 health systems spanning 4 US Census Bureau–defined regions, the prevalence of PBC was found to have increased annually from 2006 (21.7 per 100,000 persons) to 2014 (39.2 per 100,000 persons).[24] This reported prevalence of 39.2 per 100,000 persons in 2014 is the most comprehensive assessment to date of PBC prevalence in the United States.

Since 2014, PBC disease nomenclature has changed,[25] and the management and available therapeutic options for PBC have evolved.[2,3] Furthermore, in 2015, the International Classification of Diseases, Ninth Revision (ICD-9) transitioned to ICD-10, resulting in a more specific diagnosis code for PBC.[26] A contemporary description of PBC prevalence in the United States using a robust national database is needed to better reflect improved disease awareness, as well as improved coding and capture in medical claims data. Additionally, no study has performed a granular analysis of the geographic distribution of PBC in the United States, which is particularly important given the evolution of understanding about the sociodemographic and potential environmental risk factors for PBC.[27]

The objectives of this study were to estimate the overall prevalence of PBC in the United States and assess the regional variability by 3-digit ZIP Code tabulation area (ZCTA3) using a large national administrative claims database, as well as to describe the health care providers (HCPs) and their prescribing practices for patients with PBC.

## METHODS

Komodo's Healthcare Map (Komodo Health), which includes administrative claims data on approximately 330 million patients and 15 million new clinical encounters daily, was used for this study.[28] Patients were included in the prevalence numerator if they had either $\geq 1$ inpatient or $\geq 2$ outpatient claims at least a day apart with a diagnosis code for PBC (ICD-9 code [571.6] or ICD-10 code [K74.3])[29] between January 1, 2014, and December 31, 2021, and they were 18 years of age or above at the time of initial claim with a PBC diagnosis code. The prevalence denominator comprised individuals 18 years of age or above in 2021. Patients were excluded from the study if they died on or before January 1, 2021, per the Komodo Health

mortality table, had missing information on their 3-digit ZIP Code and/or gender in 2021 Komodo Health enrollment periods, or there was suspicion of patient duplication in Komodo Health.

The 3-digit ZIP Codes were mapped to ZCTA3s, with certain ZCTA3s combined into groups to allow for 1-to-1 mapping. ZCTAs, as defined by the US Census Bureau, are "generalized areal representations of the geographic extent and distribution of the point-based ZIP Codes built using 2020 Census tabulation blocks."[30] ZCTAs, rather than ZIP Codes, were used for this analysis because the Census Bureau produces population data at the ZCTA3 level.

PBC prevalence per 100,000 adult population was adjusted by age and gender at the ZCTA3 level, which was derived from the 2021 American Community Survey.[31] Adjustment via direct standardization accounted for differences in coverage and representativeness of Komodo Health, as well as the age and gender distribution of patients in Komodo Health by ZCTA3. In the age, gender, and ZCTA3 groups where the Komodo Health population was larger than the Census population, the Census population was used as the denominator.

The absolute number of PBC cases, as well as the unadjusted, age-adjusted, and gender-adjusted PBC prevalence per 100,000 adults, were estimated. Descriptive analyses were used to assess the demographic characteristics of individuals with PBC. Choropleth maps of the United States were generated to display the geographic distribution of patients with PBC by ZCTA3, and 4 Census Bureau–defined regions (Northeast [Connecticut, Maine, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, Vermont], Midwest [Illinois, Indiana, Iowa, Kansas, Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, South Dakota, Wisconsin], West [Alaska, Arizona, California, Colorado, Hawaii, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington, Wyoming], and South [Alabama, Arkansas, Delaware, District of Columbia, Florida, Georgia, Kentucky, Louisiana, Maryland, Mississippi, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia, West Virginia]) were used to further characterize regional prevalence.[32]

In an exploratory analysis, HCPs were identified using patients' latest medical claim with a primary diagnosis of PBC or pharmacy claims for UDCA, OCA, or fenofibrate with a nonmissing National Provider Identifier (NPI) number. Additionally, all PBC-related claims occurring during the study period (2014–2021) were assessed in a separate analysis. Komodo Health's provider summary table supplied the HCP's primary health care organization and HCP primary type/specialty. HCPs were categorized as specialists (gastroenterologists and hepatologists), general medicine physicians (comprising general practice, family practice, internal medicine, and geriatric medicine), advanced practice providers (APPs; including specialist APPs as specialty designation was not available for this category), or other. Komodo Health's Health Care Organization master table was then used to determine if the HCP's primary health care organization was an academic institution/center. If a claim date had multiple claims with multiple primary NPI numbers or prescriber NPI numbers (for pharmacy claims) with different specialties and/or primary affiliations, then data from all primary HCPs/prescribing HCPs (ie, all claims) were included in the analyses summarizing HCP specialties and academic affiliation.

Finally, in a separate exploratory analysis, the number of patients who filled prescriptions for UDCA and/or second-line therapy (ie, OCA or fenofibrate) before 2022 was assessed. In this analysis, patients were required to have $\geq$30 days of pharmacy enrollment at any point on or after their initial PBC diagnosis date up until December 31, 2021. The specialty/type of prescribers was also examined, where available. As patients may have been prescribed UDCA and/or second-line therapy by different HCPs over time (eg, a gastroenterologist, an APP, and a general medicine physician), prescriptions from all HCPs were included in the analysis.

Only deidentified patient data from Komodo Health were used in this study and may be considered exempt. The study was not submitted to an Institutional Review Board for review.

# RESULTS

## Study population

A total of 41,426 of the 106.8 million adults in Komodo Health met all study selection criteria. Most of the patients were female (83.0%), with a mean (SD) age in 2021 of 61.9 (13.2) years (Table 1). Of the 31,806 (76.8% of total) patients with race/ethnicity information available, 67.6% were White, 16.9% were Hispanic/Latino, 7.6% were Black/African American, 3.5% were Asian or Pacific Islander, and 4.3% were classified as "other." Commercial and Medicare were the most common types of insurance coverage (45.8% and 31.6% of patients, respectively).

## Prevalence

The adjusted prevalence of adult patients with PBC in 2021 was 40.9 per 100,000 persons, for an estimated total of 105,506 adults with PBC in the United States (including Puerto Rico) in 2021 (Table 2). This national prevalence of PBC in the adult population in 2021 was then reported by region, with prevalence per 100,000 adults in the Northeast, Midwest, West, and South of 43.8 (19,881 estimated total cases), 43.0 (23,038 estimated total cases), 39.6 (23,839 estimated total cases), and 39.5 (37,989 estimated total cases),

**TABLE 1** Demographics of patients with primary biliary cholangitis in 2021 (N = 41,426)

| Characteristic | n (%) |
|---|---|
| Gender, n (%) | |
| Female | 34,381 (83.0%) |
| Male | 7045 (17.0%) |
| Age in 2021, y, mean (SD) | 61.9 (13.2%) |
| Race/ethnicity, n (%)[a] | 31,806 (100%) |
| White | 21,505 (67.6%) |
| Hispanic/Latino | 5391 (16.9%) |
| Black/African American | 2411 (7.6%) |
| Asian or Pacific Islander | 1117 (3.5%) |
| Other race | 1382 (4.3%) |
| Insurance coverage, n (%)[b] | |
| Medicare | 13,100 (31.6%) |
| Medicaid | 5110 (12.3%) |
| Commercial | 18,990 (45.8%) |
| Other[c] | 3666 (8.8%) |

[a]Race/ethnicity was missing in 23.2% (n = 9620) of the total sample.
[b]Patients were categorized as having 1 type of insurance, with a hierarchy of Medicare > Medicaid > commercial > other. Insurance coverage was missing in 1.4% (n = 560) of the total sample.
[c]Includes self-insured, exchange (marketplace), or any other insurance besides Medicare, Medicaid, and commercial.

respectively. A sensitivity analysis, including only patients with a PBC diagnosis based on the ICD-10 diagnosis code, resulted in an adjusted prevalence of 38.3 per 100,000 adult population with similar regional prevalence and estimated total patient counts (Table 2). Whereas the highest estimated absolute number of patients with PBC occurred in dense urban areas (Supplemental Figure S1, http://links.lww.com/HC9/B937), the prevalence per 100,000 adult population was highest in some rural areas located in Texas, North Dakota, Colorado, Wyoming, Idaho, Washington, Vermont, and North Carolina (Figure 1).

**TABLE 2** 2021 adjusted primary biliary cholangitis prevalence in adults and estimated total patient count by region in the United States[a]

| Original analysis (ICD-9 and ICD-10 codes) | | |
|---|---|---|
| Region | Adjusted prevalence per 100,000 | Estimated total patient count |
| Overall | 40.9 | 105,506 |
| Northeast | 43.8 | 19,881 |
| Midwest | 43.0 | 23,038 |
| West | 39.6 | 23,839 |
| South | 39.5 | 37,989 |
| Sensitivity analysis (ICD-10 code only) | | |
| Overall | 38.3 | 98,844 |
| Northeast | 40.9 | 18,538 |
| Midwest | 40.6 | 21,716 |
| West | 36.7 | 22,076 |
| South | 37.2 | 35,785 |

[a]Including Puerto Rico.
Abbreviation: ICD, International Classification of Diseases.

## Health care providers

This study also quantified the type/specialty of HCPs that manage patients with PBC and their primary affiliation (academic vs. nonacademic), where available. Among the 36,700 patients with clinician primary specialty information available, approximately half (53.5%) of patients with PBC, irrespective of therapy use, were treated by a gastroenterologist or hepatologist as reported in their most recent medical or pharmacy claim for PBC (Table 3). Among patients treated by a specialist per their latest claim, 42.5% were treated by an HCP with an academic affiliation. The remainder of patients were treated by an APP (inclusive of specialist physician assistants or nurse practitioners; 19.3%), a general medicine physician (18.1%), or a physician of another specialty (11.7%). Among patients treated by an APP or general medicine physician as reported in their most recent claim, 46.0% and 23.1%, respectively, were treated by an HCP with an academic affiliation.

In the analysis of all PBC-related medical and pharmacy claims occurring during the study period (n = 36,837 with clinician primary specialty information available), 83.2% of patients were treated by a specialist; 51.1% of these patients were treated by a specialist with an academic affiliation (Table 3). The remainder of patients were treated by a general medicine physician (43.9%), an APP (43.3%), or a physician of another specialty (45.5%). A minority (29.1%) of patients were treated by a general medicine physician with an academic affiliation, whereas approximately half (51.1%) of patients were treated by an APP with an academic affiliation.

Among the 37,929 patients with at least a month of pharmacy coverage at any time during the study period on or after their first PBC diagnosis per Komodo Health, 28,869 (76.1%) patients had a claim for UDCA between their first PBC diagnosis and 2021 (Table 4). Most (73.6%) patients prescribed UDCA had $\geq 1$ prescription from a specialist (gastroenterologist or hepatologist), whereas 36.9% and 27.4% of patients had $\geq 1$ prescription from an APP or general medicine physician, respectively. For PBC therapy overall, 73.8% of patients had $\geq 1$ prescription from a specialist, and 37.7% had $\geq 1$ prescription from an APP (inclusive of specialist APPs).

## DISCUSSION

This analysis provides the most comprehensive, population-based estimate of PBC prevalence in the United States to date. Komodo Health allows for a

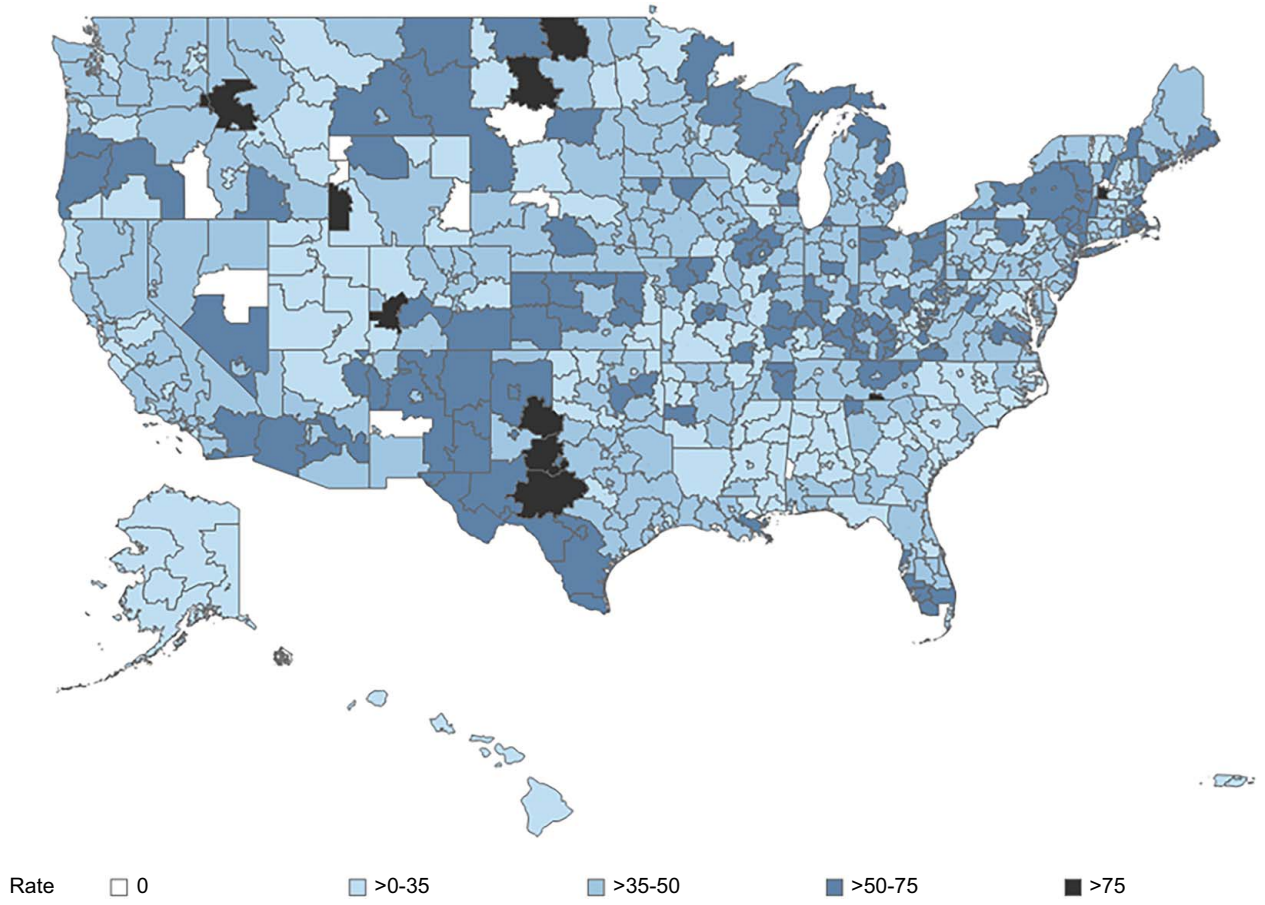


**FIGURE 1** 2021 prevalence of primary biliary cholangitis per 100,000 adult population by 3-digit ZIP Code tabulation area. Rate is defined as number of patients per 100,000 adult population.

contemporary, robust, and inclusive estimation of the national prevalence of PBC in the United States.

The demographics of the PBC population, predominantly composed of White women approximately 60 years of age, are in line with prior studies in the United States.[10,15] Notably, 17% of patients in this study were male, a relatively high percentage compared with other US-based studies,[15,33] but similar to that from the FOLD

**TABLE 3** Provider primary specialties managing patients with primary biliary cholangitis

| | Latest PBC-related medical or pharmacy claim (n = 36,700)[a] | | All PBC-related medical and pharmacy claims (n = 36,837)[b] | |
|---|---|---|---|---|
| Primary specialty | n (%)[c] | Academic primary affiliation, n (%)[d] | n (%)[e] | Academic primary affiliation, n (%)[f] |
| GI/hepatology | 19,638 (53.5%) | 8138 (42.5%) | 30,649 (83.2%) | 15,276 (51.1%) |
| General medicine[g] | 6625 (18.1%) | 1383 (23.1%) | 16,169 (43.9%) | 4301 (29.1%) |
| APP | 7100 (19.3%) | 3050 (46.0%) | 15,934 (43.3%) | 7440 (51.1%) |
| Other | 4289 (11.7%) | 1916 (48.9%) | 16,744 (45.5%) | 8804 (56.8%) |

*Note:* Among encounters with a nonmissing primary specialty.

[a]The latest PBC-related medical or pharmacy claim occurred in 2021.

[b]The additional all-claims analysis included all PBC-related medical and pharmacy claims that occurred from 2014 to 2021.

[c]Percentages do not add up to 100% because patients could have multiple primary NPI numbers for providers with different specialties and/or affiliations on their last claim date. Only the primary specialty of the provider was considered.

[d]Analysis only included providers who were able to be classified as either academic or nonacademic in affiliation. The total n's for this subpopulation were 19,137; 5982; 6626; and 3919 for GI/hepatology, general medicine, APP, and other, respectively.

[e]Percentages do not add up to 100% owing to considerable overlap as HCP primary specialty categories were not mutually exclusive. For each claim, only the primary specialty of the provider was considered.

[f]Analysis only included providers who were able to be classified as either academic or nonacademic in affiliation. The total n's for this subpopulation were 29,873, 14,768, 14,556, and 15,500 for GI/hepatology, general medicine, APP, and other, respectively.

[g]Includes general practice, family practice, internal medicine, and geriatric medicine.

Abbreviations: APP, advanced practice provider; GI, gastroenterology; NPI, National Provider Identifier; PBC, primary biliary cholangitis.

**TABLE 4** Ursodeoxycholic acid and/or second-line therapy prescriptions during the study period (2014–2021) by provider specialty

| Patients with PBC (N = 37,929) | | |
|---|---|---|
| **Patients ever prescribed therapy by recorded specialty, n (%)** | **UDCA** | **Any PBC therapy (UDCA and/or second-line therapy[a])** |
| Total | 28,869 (76.1%) | 29,196 (77.0%) |
| GI/hepatology | 21,245 (73.6%) | 21,558 (73.8%) |
| APP | 10,666 (36.9%) | 11,014 (37.7%) |
| General medicine[b] | 7899 (27.4%) | 8210 (28.1%) |
| Other | 2965 (10.3%) | 3110 (10.7%) |

*Note:* Percentages among different provider types do not add up to 100% as patients may have been prescribed UDCA and/or second-line therapy by different providers over time; prescriptions from all providers were included in the analysis. The denominators for the percentage calculations among different provider types are the number of patients prescribed UDCA (28,869) or patients prescribed UDCA and/or second-line therapy (29,196).

[a]Includes OCA or fenofibrate.

[b]Includes general practice, family practice, internal medicine, and geriatric medicine.

Abbreviations: APP, advanced practice provider; GI, gastroenterology; OCA, obeticholic acid; PBC, primary biliary cholangitis; UDCA, ursodeoxycholic acid.

database (18%).[10] Additionally, nearly 17% of the study population with information available on race/ethnicity were Hispanic/Latino, and 8% were Black/African American. These are also comparable percentages with those from the FOLD database[10] but higher than those seen in other US-based studies.[15,33] Finding diverse and inclusive study cohorts, such as this one, is an important means of working toward health equity among patients with PBC. Black patients are significantly less likely to receive treatment with first-line UDCA than White patients[10] and have increased odds of mortality among PBC-related hospitalizations.[34] Compared with White patients, Hispanic patients have a higher PBC hospitalization rate[34] and lower rates of response to UDCA,[35] and both Black and Hispanic patients are more likely to have advanced PBC.[33] Developing a better understanding of PBC epidemiology in the United States, especially among the non-White population, is a critical step in providing more equitable care.

The adjusted 2021 adult prevalence of 40.9 per 100,000 persons in this study is similar to the highest previous estimate of PBC prevalence (40.2 per 100,000 persons) from Olmsted County, Minnesota.[15] Compared with the small community analysis from Olmsted County performed over 25 years ago,[15] the present study provides an updated and population-adjusted estimation of overall PBC prevalence in the United States. These data also support the observed increase in PBC prevalence in the United States from 2006 (21.7 per 100,000 persons) to 2014 (39.2 per 100,000 persons).[24] This increase in prevalence may be attributed to increased disease awareness, better disease reporting, more precise diagnosis codes, timely patient identification, improved patient survival associated with PBC treatment, and access to larger databases capturing the population with PBC.[23,24]

These data are the first to highlight the geographic diversity of PBC prevalence in the United States. As PBC has been associated with certain infections, cigarette smoking, pollutants, groundwater contamination, Superfund toxic waste sites, and coal mining,[27,36–38] the regional spikes in prevalence observed in this study may be behaviorally and/or environmentally related. A link between the genome and the environment in the form of epigenetic changes may also contribute to differences in disease presentation, progression, and treatment response, all of which are highly variable among patients.[39] The observed localized concentrations of higher PBC prevalence in some rural areas suggest the need to further explore potential environmental, behavioral, and/or genetic risk factors.

These data, in an overall population diagnosed with PBC with patients in varying stages of the disease, also show that the vast majority (83.2%) of patients, irrespective of therapy use, received care from a specialist (gastroenterologist or hepatologist) at some point during the study period. However, only about half (53.5%) of patients were seen by a specialist at their most recent visit with a PBC-related claim, suggesting that there may still be barriers to specialist care for some patients in the United States. It is also possible that these patients were seen by specialist APPs practicing in a gastroenterology/hepatology setting. Most patients were prescribed PBC therapies by a gastroenterologist, hepatologist, or APP. These data highlight the need for continuous access to specialist care once patients are diagnosed with PBC so that specialists who are familiar with PBC can provide PBC-specific care. Access to specialists is important for patients with PBC, particularly as the therapeutic landscape for PBC continues to evolve. Additional studies are required to assess potential differences in PBC care by region, population setting (eg, urban vs. rural), and care setting (eg, larger academic centers vs. community care).

Approximately 75% of patients in this analysis filled a UDCA prescription, which is in line with rates from prior PBC studies.[10,24,40] Further, $<10\%$ of patients filled a prescription for second-line therapy, leaving a meaningful proportion of patients who were not being treated with available first-line or second-line therapies during the study period. Although claims databases do not describe why patients may not have filled their prescriptions, the substantial proportion of patients not on therapy emphasizes a need for greater awareness of PBC and its management. Additional analyses may help to better elucidate these gaps in treatment among an overall patient population with PBC in varying stages of the disease.

There are several limitations to this study. As claims data are collected for billing purposes, undercoding and overcoding are possible. Since Komodo Health includes individuals with health insurance and a health encounter, this study's prevalence estimates may be conservative; uninsured and undiagnosed individuals may not be included in this data set, and not all patients enrolled in health insurance may be part of Komodo Health. Additionally, patients with either an ICD-9 code of 571.6 (nonspecific for PBC) or an ICD-10 code of K74.3 (specific for PBC) were eligible to be included in the study. While the ICD-9 code for PBC is not as specific as the ICD-10 code, a sensitivity analysis performed with only patients diagnosed with PBC based on the PBC-specific ICD-10 code showed similar results to the original study analysis, demonstrating that overestimation of prevalence due to the use of the ICD-9 code for PBC was unlikely.

Komodo Health may have limitations inherent to secondary databases, including missing information, variables, and subgroups of interest.[41] For example, 14.1% of patients had a last claim date without a nonmissing HCP, in which case their most recent claim with a nonmissing NPI number was chosen for the last claim analysis. As this claim only reflects a specific point in time of a patient's treatment journey, it is possible that this claim did not capture the HCP primarily responsible for the patients' PBC management. All PBC-related claims occurring during the study period were also examined to provide a broader overview of PBC providers during a multiyear period. The all-claims analysis, reflecting different lengths of available data during which the HCP category could be captured, yielded overlapping (ie, not mutually exclusive) HCP categories. The all-claims analysis indicates that while there is a record of gastroenterology/hepatology care in the majority (83.2%) of patients with PBC at one time, all patients may not have had equal or recent access to specialist care throughout their journey. As both methods (last claim and all claims) of assessing HCPs had limitations, a study assessing the patient journey is needed to better understand the different HCPs involved in patients' care.

A limitation of NPI-based classification of HCPs' primary specialties is the selection of a single primary taxonomy code, even if HCPs practice in multiple specialties. It is possible that HCPs' practice information and/or primary taxonomy was not accurate or up to date. Additionally, while details about HCP practices and work settings are not readily available in a claims database, this analysis did include the designation for academic setting from Komodo Health, where available, to provide insight into where patients with PBC are obtaining care. However, the representation of academic vs. private practices in Komodo Health has not been assessed; hence, this cannot be ruled out as a potential source of bias. A meaningful proportion of patients in this analysis was not prescribed PBC therapy, which may be owing to clinicians practicing in isolation or in nonacademic settings with more restricted access to medical meetings, up-to-date management information, and specialist support for multidisciplinary care. Further analysis would be required to determine differences in patient care, if any, between academic and nonacademic HCPs for patients with PBC, but this is beyond the scope of the study. Given the lack of completeness of HCP data, the HCP analysis in this study was considered exploratory.

Data on how PBC was diagnosed in study patients (ie, biochemical evidence of cholestasis, antimitochondrial antibody assay, histopathology) are also not captured in Komodo Health. Lastly, pharmacy claims for fenofibrate, which is more traditionally used for lipid disorders, were used in the determination of HCP specialty and affiliation. However, fenofibrate comprised only 1.7% of pharmacy claims in this analysis.

In summary, this study provides the most comprehensive population-based estimate to date of the prevalence of PBC in the United States using a large national claims database. The prevalence estimates of PBC and regional variability, especially in some rural areas, highlight the need to further examine potential risk factors for PBC. Additionally, most patients with PBC, irrespective of therapy use, were treated by a specialist (gastroenterologist or hepatologist) at some point during the study period, but only approximately half received specialist care in their most recent claim. Greater access to specialist care once patients are diagnosed to support awareness of PBC and its management is needed.

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## CONFLICTS OF INTEREST

Cynthia Levy: Institutional research grants from Calliditas, CymaBay, Escient, Gilead, GSK, Intercept, Ipsen, Kowa, Mirum, Target RWE, and Zydus; consulting fees from Calliditas, CymaBay, Gilead, GSK, Intercept, Ipsen, Kowa, Mirum, and Target RWE. Joanna P. MacEwan and Alina Levine: Employees of Genesis Research Group. Radhika Nair, and Leona Bessonova: Employees of Intercept. Darren Wheeler: Former

employee of Intercept. Aparna Goel: Consulting/advisory boards for Gilead, Intercept, Ipsen, and Mirum. Robert G. Gish: Grant/research support from Gilead; consultant and/or advisor for Abbott, AbbVie, Altimmune, Antios, Arrowhead, Dynavax, Eiger, Eisai, Enyo, Genentech, Genlantis, Gerson Lehrman Group, Gilead, Helios, HepaTx, HepQuant, Intercept, Janssen, Merck, Pfizer, Topography Health, and Venatorx; current activity with scientific or clinical advisory boards for AbbVie, Dynavax, Genlantis, Gilead, Helios, HepaTx, HepQuant, Intercept, Janssen, Pfizer, and Prodigy; current clinical trials alliance with Topography Health; chair of clinical advisory board for Prodigy; advisory consultant (diagnostic companies) for Fujifilm/Wako, Perspectum, Quest, and Sonic Incytes; data safety monitoring board for CymaBay, Durect, and Takeda; speakers' bureau for activities focused on hepatitis B, C, and D virus, and liver cancer, specifically epidemiology, diagnosis, and treatment. In addition, there were program presentations on vaccination for hepatitis B virus and the management of complications of cirrhosis; speaker's contract for promotional talks for AbbVie, BMS, Eisai, Genentech, Gilead, and Intercept; minor stock shareholder (liver space noted only) for CoCrystal and RiboScience; stock options with AngioCrine, Eiger, Genlantis, HepaTx, and HepQuant. Alan Bonder: Consulting for Chemomab, CymaBay, Genfit, and Guidepoint; research grants from Chemomab, CymaBay, Gilead, GSK, Intercept, and Mirium; medical monitor for Pfizer. Keri-Ann Buchanan-Peart has no conflicts to report.

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## REFERENCES

1. Younossi ZM, Bernstein D, Shiffman ML, Kwo P, Kim WR, Kowdley KV, et al. Diagnosis and management of primary biliary cholangitis. Am J Gastroenterol. 2019;114:48–63.
2. Hirschfield GM, Beuers U, Corpechot C, Invernizzi P, Jones D, Marzioni M, et al.; European Association for the Study of the Liver. EASL Clinical Practice Guidelines: The diagnosis and management of patients with primary biliary cholangitis. J Hepatol. 2017;67:145–72.
3. Lindor KD, Bowlus CL, Boyer J, Levy C, Mayo M. Primary biliary cholangitis: 2018 practice guidance from the American Association for the Study of Liver Diseases. Hepatology. 2019;69:394–419.
4. Chascsa DMH, Lindor KD. Emerging therapies for PBC. J Gastroenterol. 2020;55:261–72.
5. Gerussi A, Restelli U, Croce D, Bonfanti M, Invernizzi P, Carbone M. Cost of illness of primary biliary cholangitis—A population-based study. Dig Liver Dis. 2021;53:1167–70.
6. Axcan Pharma US, Inc. RSO 250® / URSO Forte® (ursodiol). Full Prescribing Information. Axcan Pharma US, Inc.; 2009.
7. Intercept Pharmaceuticals, Inc. OCALIVA® (obeticholic acid). Full Prescribing Information. Intercept Pharmaceuticals, Inc.; 2022.
8. Gilead Sciences, Inc. LIVDELZI® (seladelpar). Full Prescribing Information. Gilead Sciences, Inc.; 2024.
9. Ipsen Biopharmaceuticals, Inc. IQIRVO® (elafibranor). Full Prescribing Information. Ipsen Biopharmaceuticals, Inc.; 2024.
10. Lu M, Li J, Haller IV, Romanelli RJ, VanWormer JJ, Rodriguez CV, et al. Factors associated with prevalence and treatment of primary biliary cholangitis in United States health systems. Clin Gastroenterol Hepatol. 2018;16:1333–41.
11. Kim KA, Ki M, Choi HY, Kim BH, Jang ES, Jeong SH. Population-based epidemiology of primary biliary cirrhosis in South Korea. Aliment Pharmacol Ther. 2016;43:154–62.
12. Boonstra K, Kunst AE, Stadhouders PH, Tuynman HA, Poen AC, van Nieuwkerk KMJ, et al. Rising incidence and prevalence of primary biliary cirrhosis: A large population-based study. Liver Int. 2014;34:e31–8.
13. Lleo A, Jepsen P, Morenghi E, Carbone M, Moroni L, Battezzati PM, et al. Evolving trends in female to male incidence and male mortality of primary biliary cholangitis. Sci Rep. 2016;6:25906.
14. Byron D, Minuk GY. Clinical hepatology: Profile of an urban, hospital-based practice. Hepatology. 1996;24:813–5.
15. Kim WR, Lindor KD, Locke GR III, Therneau TM, Homburger HA, Batts KP, et al. Epidemiology and natural history of primary biliary cirrhosis in a US community. Gastroenterology. 2000;119:1631–6.
16. Hurlburt KJ, McMahon BJ, Deubner H, Hsu-Trawinski B, Williams JL, Kowdley KV. Prevalence of autoimmune liver disease in Alaska Natives. Am J Gastroenterol. 2002;97:2402–7.
17. Myers RP, Shaheen AAM, Fong A, Burak KW, Wan A, Swain MG, et al. Epidemiology and natural history of primary biliary cirrhosis in a Canadian health region: A population-based study. Hepatology. 2009;50:1884–92.
18. Liu H, Liu Y, Wang L, Xu D, Lin B, Zhong R, et al. Prevalence of primary biliary cirrhosis in adults referring hospital for annual health check-up in Southern China. BMC Gastroenterol. 2010;10:100.
19. French J, van der Mei I, Simpson S Jr, Ng J, Angus P, Lubel J, et al. Increasing prevalence of primary biliary cholangitis in Victoria, Australia. J Gastroenterol Hepatol. 2020;35:673–9.
20. Boonstra K, Beuers U, Ponsioen CY. Epidemiology of primary sclerosing cholangitis and primary biliary cirrhosis: a systematic review. J Hepatol. 2012;56:1181–8.
21. Watson RG, Angus PW, Dewar M, Goss B, Sewell RB, Smallwood RA. Low prevalence of primary biliary cirrhosis in Victoria, Australia. Melbourne Liver Group. Gut. 1995;36:927–30.
22. Podda M, Selmi C, Lleo A, Moroni L, Invernizzi P. The limitations and hidden gems of the epidemiology of primary biliary cirrhosis. J Autoimmun. 2013;46:81–7.
23. Colapietro F, Bertazzoni A, Lleo A. Contemporary epidemiology of primary biliary cholangitis. Clin Liver Dis. 2022;26:555–70.
24. Lu M, Zhou Y, Haller IV, Romanelli RJ, VanWormer JJ, Rodriguez CV, et al. Increasing prevalence of primary biliary cholangitis and reduced mortality with treatment. Clin Gastroenterol Hepatol. 2018;16:1342–50.
25. Beuers U, Gershwin ME, Gish RG, Invernizzi P, Jones DEJ, Lindor K, et al. Changing nomenclature for PBC: From 'cirrhosis' to 'cholangitis'. J Hepatol. 2015;63:1285–7.
26. Transition to ICD-10. Office of Workers' Compensation Programs. Accessed May 29, 2024. https://www.dol.gov/agencies/owcp/FECA/ICD10transition#:~:text=On%20October%201%2C%202015%2C%20the,is%20mandatory%20throughout%20the%20country

27. Zhang H, Carbone M, Lleo A, Invernizzi P. Geoepidemiology, genetic and environmental risk factors for PBC. Dig Dis. 2015;33 (suppl 2):94–101.
28. Komodo Health. Komodo Healthcare Map. Accessed May 21, 2024. https://www.komodohealth.com/healthcare-map
29. Myers RP, Shaheen AAM, Fong A, Wan AF, Swain MG, Hilsden RJ, et al. Validation of coding algorithms for the identification of patients with primary biliary cirrhosis using administrative data. Can J Gastroenterol. 2010;24:175–82.
30. ZIP Code Tabulation Areas (ZCTAs). United States Census Bureau. Updated August 10, 2023. Accessed September 19, 2023. https://www.census.gov/programs-surveys/geography/guidance/geo-areas/zctas.html
31. American Community Survey data. United States Census Bureau. Updated August 16, 2023. Accessed May 10, 2024. https://www.census.gov/programs-surveys/acs/data.html.
32. Census regions and divisions of the United States. United States Census Bureau. Accessed September 5, 2024. https://www2.census.gov/geo/pdfs/maps-data/maps/reference/us_regdiv.pdf
33. Peters MG, Di Bisceglie AM, Kowdley KV, Flye NL, Luketic VA, Munoz SJ, et al. Differences between Caucasian, African American, and Hispanic patients with primary biliary cirrhosis in the United States. Hepatology. 2007;46:769–75.
34. Adejumo AC, Akhtar DH, Dennis BB, Cholankeril G, Alayo Q, Ogundipe OA, et al. Gender and racial differences in hospitalizations for primary biliary cholangitis in the USA. Dig Dis Sci. 2021;66:1461–76.
35. Levy C, Naik J, Giordano C, Mandalia A, O'Brien C, Bhamidimarri KR, et al. Hispanics with primary biliary cirrhosis are more likely to have features of autoimmune hepatitis and reduced response to ursodeoxycholic acid than non-Hispanics. Clin Gastroenterol Hepatol. 2014;12:1398–405.
36. Dronamraju D, Odin J, Bach N. Primary biliary cirrhosis: Environmental risk factors. Dis Markers. 2010;29:323–8.
37. Ala A, Stanca CM, Bu-Ghanim M, Ahmado I, Branch AD, Schiano TD, et al. Increased prevalence of primary biliary cirrhosis near Superfund toxic waste sites. Hepatology. 2006;43:525–31.
38. Dyson JK, Blain A, Foster Shirley MD, Hudson M, Rushton S, Jeffreys Jones DE. Geo-epidemiology and environmental covariate mapping of primary biliary cholangitis and primary sclerosing cholangitis. JHEP Rep. 2021;3:100202.
39. Cheung A, LaRusso N, Gores G, Lazaridis K. Epigenetics in the primary biliary cholangitis and primary sclerosing cholangitis. Semin Liver Dis. 2017;37:159–74.
40. Gordon SC, Wu KHH, Lindor K, Bowlus CL, Rodriguez CV, Anderson H, et al. Ursodeoxycholic acid treatment preferentially improves overall survival among African Americans with primary biliary cholangitis. Am J Gastroenterol. 2020;115:262–70.
41. Cheng HG, Phillips MR. Secondary analysis of existing data: Opportunities and implementation. Shanghai Arch Psychiatry. 2014;26:371–5.

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