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World J Gastrointest Surg 2024 April 27; 16(4): 1130-1148

ISSN 1948-9366 (online) DOI: 10.4240/wjgs.v16.i4.1130

ORIGINAL ARTICLE

# **Observational Study**

# Burden of gallstone disease in the United States population: Prepandemic rates and trends

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Specialty type: Gastroenterology and hepatology

# Provenance and peer review:

Invited article; Externally peer reviewed.

Peer-review model: Single blind

# Peer-review report's scientific quality classification

Grade A (Excellent): 0 Grade B (Very good): B Grade C (Good): C, C Grade D (Fair): D Grade E (Poor): 0

P-Reviewer: Ker CG, Taiwan; Qiao T, China; Reshetnyak VI, Russia; Yang LY, China

Received: November 14, 2023 Peer-review started: November 14,

First decision: January 5, 2024 Revised: January 23, 2024 Accepted: March 20, 2024 Article in press: March 20, 2024 Published online: April 27, 2024



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# Abstract

# **BACKGROUND**

Gallstone disease is one of the most common digestive disorders in the United States and leads to significant morbidity, mortality, and health care utilization.

# **AIM**

To expand on earlier findings and investigate prepandemic rates and trends in the gallstone disease burden in the United States using national survey and claims databases.

# **METHODS**

The National Ambulatory Medical Care Survey, National Inpatient Sample, Nationwide Emergency Department Sample, Nationwide Ambulatory Surgery Sample, Vital Statistics of the United States, Optum Clinformatics® Data Mart, and Centers for Medicare and Medicaid Services Medicare 5% Sample and Medicaid files were used to estimate claims-based prevalence, medical care including cholecystectomy, and mortality with a primary or other gallstone diagnosis. Rates were age-adjusted (for national databases) and shown per 100000 population.

# RESULTS

Gallstone disease prevalence (claims-based, 2019) was 0.70% among commercial insurance enrollees, 1.03% among Medicaid beneficiaries, and 2.09% among Medicare beneficiaries and rose over the previous decade. Recently, in the United States population, gallstone disease contributed to approximately 2.2 million ambulatory care visits, 1.2 million emergency department visits, 625000 hospital discharges, and 2000 deaths annually. Women had higher medical care rates with a gallstone disease diagnosis, but mortality rates were higher among men. Hispanics had higher ambulatory care visit and hospital discharge rates compared with

Whites, but not mortality rates. Blacks had lower ambulatory care visit and mortality rates, but similar hospital discharge rates compared with whites. During the study period, ambulatory care and emergency department visit rates with a gallstone disease diagnosis rose, while hospital discharge and mortality rates declined. Among commercial insurance enrollees, rates were higher compared with national data for ambulatory care visits and hospitalizations, but lower for emergency department visits. Cholecystectomies performed in the United States included 605000 ambulatory laparoscopic, 280000 inpatient laparoscopic, and 49000 inpatient open procedures annually. Among commercial insurance enrollees, rates were higher compared with national data for laparoscopic procedures.

#### **CONCLUSION**

The gallstone disease burden in the United States is substantial and increasing, particularly among women, Hispanics, and older adults with laparoscopic cholecystectomy as the mainstay treatment. Current practice patterns should be monitored for better health care access.

Key Words: Gallstone disease; Burden; Cholecystectomy; Mortality; Health care use; Cholelithiasis; Gallstones; Epidemiology

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Core Tip: We used national survey and claims databases to investigate prepandemic rates and trends in the United States gallstone disease burden. Gallstone disease prevalence (claims-based, 2019) ranged from 0.70% to 2.09% and rose over a decade. Gallstone disease contributed to approximately 2.2 million ambulatory care visits, 1.2 million emergency department visits, 625000 hospital discharges, and 2000 deaths annually. Medical care was higher among women, Hispanics, and older adults and lower among Blacks. Ambulatory care and emergency department visit rates with gallstone disease rose while hospital discharge and mortality rates declined. Cholecystectomies performed included 605000 ambulatory laparoscopic, 280000 inpatient laparoscopic, and 49000 inpatient open procedures annually.

Citation: Unalp-Arida A, Ruhl CE. Burden of gallstone disease in the United States population: Prepandemic rates and trends. World J Gastrointest Surg 2024; 16(4): 1130-1148

URL: https://www.wjgnet.com/1948-9366/full/v16/i4/1130.htm

**DOI:** https://dx.doi.org/10.4240/wjgs.v16.i4.1130

# INTRODUCTION

Gallstones (cholelithiasis) are concretions, usually composed of cholesterol or bilirubin, which develop in the gallbladder. Gallstones may form if bile contains excess cholesterol or bilirubin or insufficient bile salts. Most gallstones in the United States and western countries are cholesterol gallstones. Risk factors include older age, female sex, Native American and Hispanic ethnicity, overweight or obesity, diabetes, smoking, higher parity among women, rapid weight loss, and genetic factors. Non-Hispanic black race-ethnicity, greater alcohol consumption, increased serum cholesterol, and greater physical activity are associated with lower risk[1]. Though the majority remain asymptomatic, gallstones can block bile ducts causing acute right upper quadrant pain and if untreated, can lead to complications, including choledocholithiasis, cholangitis, and cholecystitis. Symptomatic gallstones are usually treated by cholecystectomy. Over the long-term, gallstone disease may negatively impact survival. In the United States population over a 20-year period, persons with gallstone disease had increased mortality overall and from cardiovascular disease and cancer[2]. This relationship was found for both ultrasound-diagnosed gallstones and cholecystectomy. Among over a million persons with an electronic health record gallstone disease diagnosis, mortality was 15.1% compared with 9.7% for the whole electronic health record sample [3].

Gallstones are common and lead to significant morbidity, mortality, and health care utilization in the United States and worldwide. More than 20 million people in the United States have ultrasound-detected gallbladder disease[1]. The prevalence of symptomatic gallstone disease has doubled in the United States population over the past three decades[4]. There were an estimated 1.8 million ambulatory care visits with an all-listed gallstone diagnosis in 2004 and rates were relatively stable over time[5]. There were 622000 overnight hospitalizations with an all-listed gallstone diagnosis in 2004. Hospitalization rates declined by 40% from 1991 due to the shift to outpatient laparoscopic cholecystectomy[5]. There were 2155 deaths with gallstones as underlying or other cause in 2004 and mortality rates fell between 1979 and 2004 by 70% [5,6]. Based on data from the National Survey of Ambulatory Surgery conducted by the National Center for Health Statistics of the Centers for Disease Control and Prevention, gallstone disease resulted in 503000 laparoscopic cholecystectomies in 2006[7]. Gallstone disease health care use and mortality varied among demographic groups. Urgent action is needed to address healthcare disparities across population groups[8].

A more recent report on the burden of gastrointestinal, liver, and pancreatic disease in the United States found that cholelithiasis was the physician diagnosis for 863000 office visits and 327000 emergency department visits in the United States in 2016[9]. Cholelithiasis and cholecystitis was the 10th most common among all-listed digestive disease diagnoses from emergency department visits in 2018 with 1.5 million visits and the 5th most common among all-listed digestive disease diagnoses in United States hospitals in 2018 with 741000 admissions[9].

Current estimates of the gallstone disease burden in the United States are useful to all multidisciplinary clinicians, researchers, public health professionals, and policy makers for better planning. We used national survey and claims databases to expand on earlier findings and estimate current trends in the gallstone disease burden in the United States.

# MATERIALS AND METHODS

#### Data sources

The National Ambulatory Medical Care Survey (NAMCS), Healthcare Cost and Utilization Project (HCUP) National Inpatient Sample (NIS), HCUP Nationwide Emergency Department Sample (NEDS), HCUP Nationwide Ambulatory Surgery Sample (NASS), Vital Statistics of the United States, Optum Clinformatics® Data Mart (CDM), and the Centers for Medicare and Medicaid Services (CMS) Medicare 5% Sample and Medicaid databases were used to estimate claims-based prevalence, medical care including cholecystectomy, mortality, and years of potential life lost prior to age 75 years with a primary or other gallstone diagnosis.

# National databases

The NAMCS is conducted in the United States by the National Center for Health Statistics of the Centers for Disease Control and Prevention (CDC)[10]. It is an annual nationally representative sample survey of office-based outpatient visits to non-federal health care providers. It is a multistage stratified probability sample of geographically defined areas, physician practices within these areas, and patient visits within physician practices.

The HCUP NIS, NEDS, and NASS are maintained by the Agency for Healthcare Research and Quality. The NIS consists of a nationally representative sample of discharges from all participating non-federal hospitals collected annually [11]. It contains data from more than 7 million hospital stays each year (unweighted) and estimates more than 35 million hospitalizations nationally (weighted). Data collected include up to 15 diagnoses and 7 surgical procedures.

The HCUP NEDS consists of a nationally representative sample of hospital-owned emergency department visits from non-federal hospitals collected annually regardless of whether they result in admission[12]. It contains data from over 30 million emergency department visits each year (unweighted) and estimates approximately 145 million emergency department visits (weighted).

The HCUP NASS consists of a nationally representative sample of major ambulatory surgery encounters performed in hospital-owned facilities[13]. It contains approximately 7.8 million ambulatory surgery encounters each year and approximately 10.8 million ambulatory surgery procedures (unweighted) and estimates approximately 10.3 million ambulatory surgery encounters and 13.5 million ambulatory surgery procedures (weighted). Major ambulatory surgeries are defined as selected major therapeutic procedures that require the use of an operating room, penetrate or break the skin, and involve regional anesthesia, general anesthesia, or sedation to control pain.

The Vital Statistics of the United States: Multiple Cause-of-Death Data are managed by CDC and include all deaths occurring within the United States collected annually [14]. An underlying cause and up to 20 contributing causes of death were derived from death certificates.

# Claims databases

Optum's CDM is comprised of administrative health care claims for members of large commercial health plans [15]. Administrative claims submitted by providers and pharmacies are verified, adjudicated, and de-identified before inclusion in CDM. The population includes individuals in all 50 states. The database includes approximately 17 to 19 million annual covered individuals for over 68 million unique members from January 2007 through December 2020. Most commercial insurance enrollees are employed persons who receive health insurance through their employer.

CMS created the Medicare 5% sample to be representative of the entire population of Medicare beneficiaries and it is housed in the CMS Chronic Conditions Data Warehouse [16]. Data are linked by a unique, unidentifiable beneficiary key.

The CMS Medicaid files include the entire population of Medicaid beneficiaries and are housed in the CMS Chronic Conditions Data Warehouse [6]. Data are linked by a unique, unidentifiable beneficiary key. Medicaid eligibility is based on income below a certain level that varies among states, so Medicaid beneficiaries represent a low-income population.

# Gallstone disease and cholecystectomy definitions

Gallstone disease morbidity was identified by an International Classification of Diseases (ICD), Ninth Revision, Clinical Modification (ICD-9-CM) code of 574 or an ICD, Tenth Revision, Clinical Modification (ICD-10-CM) code of K80, and gallstone disease mortality by an ICD, Tenth Revision (ICD-10) code of K80. The first-listed diagnosis was considered the primary diagnosis and all remaining diagnoses were considered secondary and included under 'all-listed'. For national event-level data sources, diagnoses were counted only once under the all-listed category, irrespective of the number of actual diagnoses listed on a medical record or death certificate. In other words, if there was more than one gallstone disease diagnosis listed on a medical record or death certificate, only one diagnosis was counted for the 'all-listed' category.

Laparoscopic cholecystectomy was identified by a Current Procedural Terminology (CPT®) code of 47562, 47563 or 47564, an ICD-9 Procedure Coding System (PCS) code of 51.23 or 51.24, or an ICD-10-PCS code of 0FT44 or 0FB44. Open cholecystectomy was identified by a CPT® code of 47600, 47605, 47610, 47612 or 47620, an ICD-9-PCS code of 51.21 or 51.22, or an ICD-10-PCS code of 0FB40, 0FB43, or 0FT40.

# Statistical analysis

Because of potential short-term effects of the coronavirus disease 2019 (COVID-19) pandemic on gallstone disease healthcare utilization and mortality, statistics highlighted in the text are for 2019, while figures present trends through

#### National databases

Estimates for the total population and by age, sex, race, and Hispanic origin were calculated for each year of national data. Event counts are shown as number in thousands. For calculating United States population rates, annual population data were derived from the national population estimates program of the United States Census Bureau and the CDC. For all rate calculations, population estimates used as the denominator were mid-year population counts by age, sex, race, and Hispanic origin. Rates were age-adjusted by direct standardization using the year 2000 population estimates and are shown per 100000 population[17]. NAMCS, NIS, NEDS, and NASS data were weighted to generate national estimates. Ambulatory care visit (NAMCS) data points were 3-year averages to provide more stable estimates. Ambulatory care numbers and rates represent visits, not persons with a visit. Hospital numbers and rates represent discharges, not persons with an inpatient stay.

#### Claims databases

Enrollees/beneficiaries were considered gallstone disease patients if they had one or more claims with an ICD-9-CM or ICD-10-CM diagnostic code indicative of gallstone disease in any diagnostic code field. The claims-based prevalence was calculated as the percentage of privately insured enrollees/beneficiaries who qualified as gallstone disease patients in a given year. Estimates were reported overall and stratified by age, gender, race/ethnicity, and region.

Optum® CDM member eligibility files containing birth year, demographics, and eligibility period were linked to inpatient confinement (acute care hospital or skilled nursing facility stay), medical (health care professional services), medical diagnosis, and pharmacy claims files. Privately insured enrollees were included if they: (1) Had a single consistent birth year recorded in CDM; (2) Resided in the United States; and (3) Were continuously enrolled for at least one full calendar year. Inpatient hospitalizations were defined as having an inpatient hospital place of service. Ambulatory visits were evaluation and management visits with an office, outpatient hospital, or ambulatory surgical center place of service.

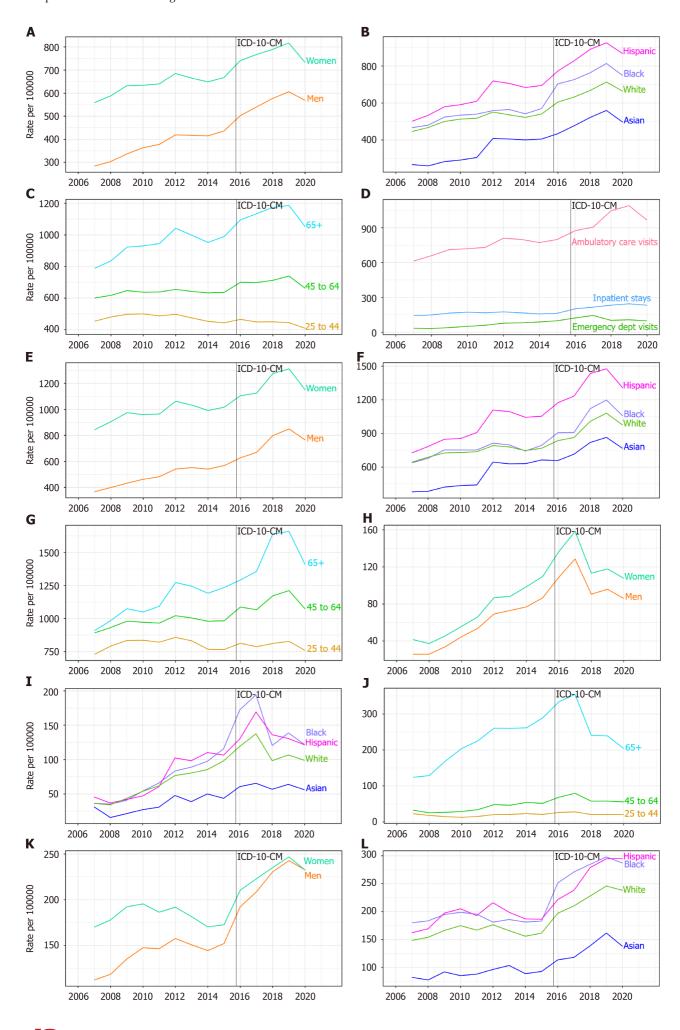
The CMS Medicare 5% sample study population/denominator consisted of beneficiaries who were 65 years or older as of January 1st of the year, resided in the 50 United States states or Washington DC, and were enrolled in fee-for-service Part A or Part B Medicare benefits or in the Medicare Advantage program (Part C/Health Maintenance Organization benefits) at any time during the year. The denominator file which contains demographic and enrollment data was linked by the beneficiary unique identifier to institutional (hospital inpatient stays, hospital outpatient services, skilled nursing facilities, home health agencies and hospice care organizations) or non-institutional (also called Part B; health care professionals, supplies, and services) medical claims files. Estimates from the 5% sample are multiplied by 20 to represent national estimates.

The CMS Medicaid study population/denominator consisted of beneficiaries who were 19 to 64 years as of January 1st of the year, resided in the 50 United States states or Washington DC, and were enrolled in Medicaid benefits at any time during the year. The denominator file which contains demographic and enrollment data was linked by the beneficiary unique identifier to institutional or non-institutional medical claims files. Medicaid eligibility is based on income below a certain level that varies among states, so Medicaid beneficiaries represent a low-income population.

# RESULTS

# Claims-based prevalence

Among 13.7 million commercial insurance enrollees, 96000 had a gallstone disease diagnosis resulting in a claims-based prevalence of 0.70% (2019). Claims-based prevalence was higher among 39.6 million Medicaid beneficiaries, of whom 408000 had a gallstone disease diagnosis for a claims-based prevalence of 1.03% (2019). Claims-based prevalence was highest among Medicare beneficiaries. Among 54.4 million Medicare beneficiaries, 1.1 million had a gallstone disease diagnosis resulting in a claims-based prevalence of 2.09% (2019). Prevalence increased with age among all three groups. Prevalence was higher among women compared with men among commercial insurance enrollees and Medicaid beneficiaries but was higher among male Medicare beneficiaries in recent years. Among commercial insurance enrollees, prevalence was highest among Hispanics, followed by Blacks, then Whites, and was lowest among Asians. Among Medicaid beneficiaries, prevalence was highest among American Indians/Alaska natives and lowest among Asians. It was intermediate among Hispanics, Whites, Hawaiians/Pacific Islanders, and Blacks in that order. Among Medicare beneficiaries, prevalence was higher among Whites compared with Blacks. Prevalence rose by over 60% (0.43 to 0.70 from 2007 to 2019) among commercial insurance enrollees and by almost a third (1.59 to 2.09 from 2006 to 2019) among Medicare beneficiaries. This increasing trend was seen among each sex and race-ethnicity group but was primarily limited to persons 65 years and older (Tables 1-3, Figures 1A-C, 2A and B).



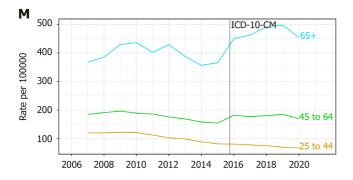
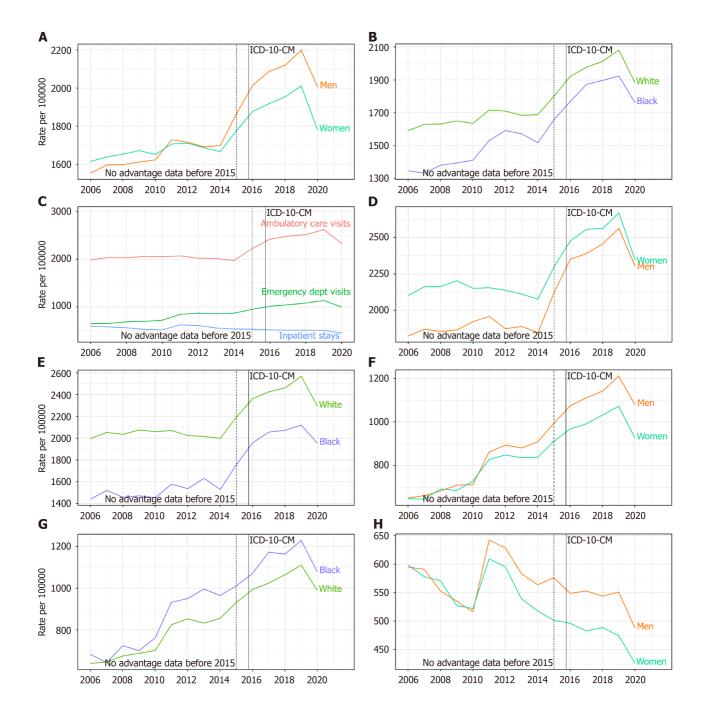


Figure 1 Rates with all-listed gallstone disease diagnoses among persons with commercial insurance in the United States, 2007-2020. A: Claims-based prevalence by sex; B: Claims-based prevalence by race-ethnicity; C: Claims-based prevalence by age; D: Total visits; E: Ambulatory care visits by sex; F: Ambulatory care visits by race-ethnicity; G: Ambulatory care visits by age; H: Emergency department visits by sex; I: Emergency department visits by raceethnicity; J: Emergency department visits by age; K: Inpatient stays by sex; L: Inpatient stays by race-ethnicity; M: Inpatient stays by age. Source: Optum Clinformatics® Data Mart. ICD: International Classification of Diseases.



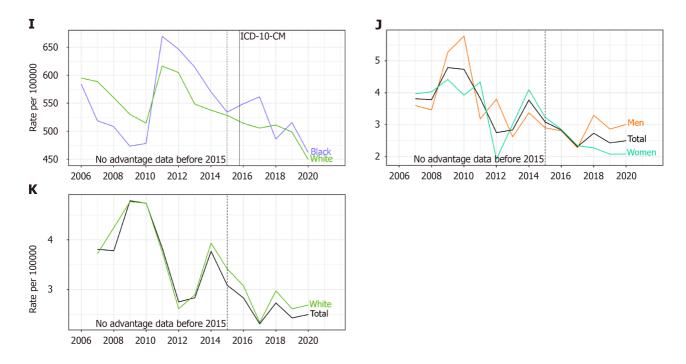


Figure 2 Rates with all-listed gallstone disease diagnoses among age-eligible fee-for-service and Advantage Medicare beneficiaries in the United States, 2006-2020. A: Claims-based prevalence by sex; B: Claims-based prevalence by race; C: Total visits; D: Ambulatory care visits by sex; E: Ambulatory care visits by race; F: Emergency department visits by sex; G: Emergency department visits by race; H: Inpatient stays by sex; I: Inpatient stays by race; J: Mortality by sex; K: Mortality by race. Source: Medicare 5% file. ICD: International Classification of Diseases.

#### Health care utilization - national data

Gallstones contributed to 2.2 million ambulatory care visits (3-year average for 2014 to 2016), 1.2 million emergency department visits (2019), and 625000 hospital discharges (2019). Ambulatory care visit, emergency department visit, and hospital discharge rates were all higher among women compared with men. Ambulatory care visit rates and hospital discharge rates were highest among Hispanics. Ambulatory care visit rates were higher among Whites compared with Blacks, but hospital discharge rates were similar. Ambulatory care visit rates increased with age. Emergency department visit rates were highest among older adults and similar among middle aged and younger adults. Hospital discharge rates increased with age, especially among persons 65+ years. Hospital discharge rates underestimate the actual burden because most hospitalizations with gallstones were for cholecystectomy and a high proportion of cholecystectomies were performed laparoscopically without an overnight stay, and therefore, were not included in hospitalization statistics (Table 4, Figure 3A-I).

From 2005 to 2016, the ambulatory care visit rate (all-listed per 100000) increased by almost 50% overall (434 to 642) and among sex, racial-ethnic, and age groups. From 2006 to 2019, the emergency department visit rate (all-listed per 100000) increased by more than a third (248 to 339). A rise was seen in both women and men and among all age groups. In contrast, the hospital discharge rate (all-listed per 100000) decreased by 17% (203 to 168) from 2006 to 2019. A decline was seen among each sex, race, and ethnic group, but primarily among older adults (Table 4, Figure 3A-I).

# Health care utilization - commercial insurance data

Among commercial insurance enrollees, rates (all-listed per 100000) were higher compared with national data for ambulatory care visits (799 vs 642 in 2015) and hospitalizations (230 vs 168 in 2019), but lower for emergency department visits (167 vs 339 in 2019). Ambulatory care visit and hospital discharge rates were higher among Hispanics compared with Whites. In contrast to national data, Blacks had higher medical care rates compared with Whites among the commercially insured. Medical care rates were lowest for Asians. Medical care rates increased among commercial insurance enrollees, primarily due to increases among persons 65 years and over (Table 1, Figure 1D-M).

# Health care utilization - Medicare data

Among Medicare beneficiaries, rates (all-listed per 100000) were higher compared with national data for ambulatory care visits (2221 vs 642 in 2015), emergency department visits (1134 vs 339 in 2019) and hospitalizations (509 vs 168 in 2019). Ambulatory care visit rates were higher among women, but in contrast to national data that included persons of all ages, emergency department visit and hospitalization rates were higher among male compared with female Medicare beneficiaries. Ambulatory care visit rates were higher among Whites compared with Blacks, but in contrast to national data, hospitalization rates were generally higher among Black compared with White Medicare beneficiaries. Emergency department visit rates were also higher among Blacks compared with Whites (Table 2, Figure 2C-I).

Table 1 Number and age-adjusted rates of claims-based prevalence, ambulatory care visits, emergency department visits, and inpatient stays with gallstone disease (all-listed diagnosis) by age, sex, race-ethnicity, and region among persons with commercial insurance in the United States, 2019

Demographic	Number of	Number of enrollees with	Claims-based	Ambulato visits	ry care	Emergend departme	•	Inpatient	stays
characteristics	enrollees	disease	prevalence (%)	Number	Rate per 100000	Number	Rate per 100000	Number	Rate per 100000
Age (yr)									
0 to 11	1151595	74	0.01	166	14	1	0	21	2
12 to 24	1513615	1746	0.12	3130	207	89	6	319	21
25 to 44	2751143	12191	0.44	21940	797	703	26	1884	68
45 to 54	1522133	9860	0.65	16064	1055	773	51	1944	128
55 to 64	1683723	13626	0.81	20042	1190	1966	117	3776	224
65 to 74	2676036	27435	1.03	34291	1281	8425	315	9121	341
75+	2448780	31352	1.28	34847	1423	11055	451	14610	597
Sex									
Female	7184225	57525	0.80	83108	1157	12915	180	16716	233
Male	6562800	38759	0.59	47372	722	10097	154	14959	228
Race-ethnicity									
White	8855438	61929	0.70	83162	939	15179	171	20686	234
Black	1279712	10245	0.80	12817	1002	2912	228	3663	286
Hispanic	1562580	13974	0.89	20433	1308	2832	181	4140	265
Asian	623622	3392	0.54	4986	800	542	87	928	149
Unknown	1425673	6744	0.47	9082	637	1547	109	2258	158
Region									
Northeast	1512196	11049	0.73	14288	945	2738	181	4146	274
Midwest	3262384	19830	0.61	26775	821	5077	156	6714	206
South	5749137	44952	0.78	60159	1046	10882	189	14558	253
West	3223308	20453	0.63	29258	908	4315	134	6257	194
Total	13747025	96284	0.70	130480	949	23012	167	31675	230

Source: Optum Clinformatics® Data Mart.

#### Health care utilization - Medicaid data

Among Medicaid beneficiaries aged 19 to 64 years, rates (all-listed per 100000) were higher compared with national data for emergency department visits (577 vs 339 in 2019) and hospitalizations (202 vs 168 in 2019). Among Medicaid beneficiaries, health care utilization rates were highest among Hispanics and American Indians/Alaska natives, intermediate among Whites and Hawaiians/Pacific Islanders, and lowest among Blacks and Asians (Table 3).

# Mortality

Gallstones contributed to 2000 deaths in the United States (2019). Mortality rates were higher among men compared with women and much higher among persons 65+ years compared with younger adults. Rates were lower for Blacks compared with Whites and slightly lower for Hispanics compared with Whites after a steeper decline. From 2006 through 2019, the mortality rate (underlying or other cause per 100000) decreased by more than a quarter overall (0.63 to 0.45) and among each sex and racial-ethnic group, but primarily among adults 65+ years (Table 4, Figures 3J-L, 2J and K).

# Cholecystectomy - national data

In 2019, cholecystectomies performed in the United States included 605000 ambulatory laparoscopic, 280000 inpatient laparoscopic, 49000 inpatient open, and 1000 ambulatory open procedures. Rates (per 100000) were highest for ambulatory laparoscopic (178), followed by inpatient laparoscopic (78), inpatient open (13), and ambulatory open (0.4) pro-

Table 2 Number and age-adjusted rates of claims-based prevalence, ambulatory care visits, emergency department visits, and inpatient stays with gallstone disease (all-listed diagnosis) by age, sex, race, and region among Medicare beneficiaries in the United States, 2019

• .	Number of	Number of enrollees with	Claims-based	Ambulato visits	ory care	Emergency department visits		Inpatient	Stays
characteristics	enrollees	disease	prevalence (%)	Number	Rate per 100000	Number	Rate per 100000	Number	Rate per 100000
Age (yr)									
65 to 69	20237900	308820	1.53	423580	2093	141260	698	61100	302
70 to 74	13266460	267640	2.02	352280	2655	132480	999	58240	439
75 to 79	9036280	222320	2.46	281200	3112	117780	1303	52500	581
80 to 84	5891120	167340	2.84	195480	3318	99660	1692	47100	800
85+	5976720	173720	2.91	173100	2896	126000	2108	58040	971
Sex									
Female	29919040	601540	2.01	798340	2668	320720	1072	142000	475
Male	24489440	538300	2.20	627300	2562	296460	1211	134980	551
Race									
White	41376760	861180	2.08	1062720	2568	459580	1111	206300	499
Black	4973980	95700	1.92	105460	2120	61140	1229	25640	515
Other	8057740	182960	2.27	257460	3195	96460	1197	45040	559
Region									
Northeast	9949240	216300	2.17	274340	2757	111840	1124	48920	492
Midwest	11818160	231920	1.96	279940	2369	130720	1106	57740	489
South	20410320	437300	2.14	550700	2698	233980	1146	109480	536
West	12230760	254320	2.08	320660	2622	140640	1150	60840	497
Total	54408480	1139840	2.09	1425640	2620	617180	1134	276980	509

Source: Centers for Medicare and Medicaid Services.

cedures. Laparoscopic cholecystectomy rates were higher among women compared with men. Inpatient laparoscopic procedure rates were higher among Hispanics and lower among Blacks compared with Whites. Ambulatory laparoscopic cholecystectomy rates were highest among middle-aged adults, followed by young adults and older adults. In contrast, both inpatient laparoscopic and open rates increased with age. From 2005 to 2019, inpatient cholecystectomy rates decreased overall by 30% for laparoscopic (112 to 78) and 60% for open (32 to 13) procedures and by sex, race-ethnicity, and age groups (Table 5, Figure 4A-D).

# Cholecystectomy - commercial insurance data

Among commercial insurance enrollees, rates (per 100000 in 2019) were higher compared with national data for ambulatory laparoscopic (223 vs 178) and inpatient laparoscopic (96 vs 78) cholecystectomies, and similar for inpatient open procedures (12 vs 13). Among commercial insurance enrollees, laparoscopic cholecystectomy rates were highest among Hispanics and lowest among Asians. Ambulatory laparoscopic rates were higher among Whites compared with Blacks. In contrast to national cholecystectomy rates that declined over the years studied, a decline was seen only for ambulatory laparoscopic procedures among commercial insurance enrollees, and only for women, Whites, and Blacks while rates increased among men and Hispanics (Table 6, Figure 4E-K).

#### Cholecystectomy - Medicare data

Among Medicare beneficiaries, rates (per 100000 in 2019) were higher compared with national data for ambulatory laparoscopic (204 vs 178), inpatient laparoscopic (158 vs 78), and inpatient open (25 vs 13) cholecystectomies. Ambulatory laparoscopic cholecystectomy rates were higher among women, but in contrast to national data inpatient laparoscopic and open cholecystectomy rates were higher among male compared with female Medicare beneficiaries. Among Medicare beneficiaries, laparoscopic cholecystectomy rates were higher among Whites compared with Blacks, especially for ambulatory procedures (Table 7, Figure 4L-P).

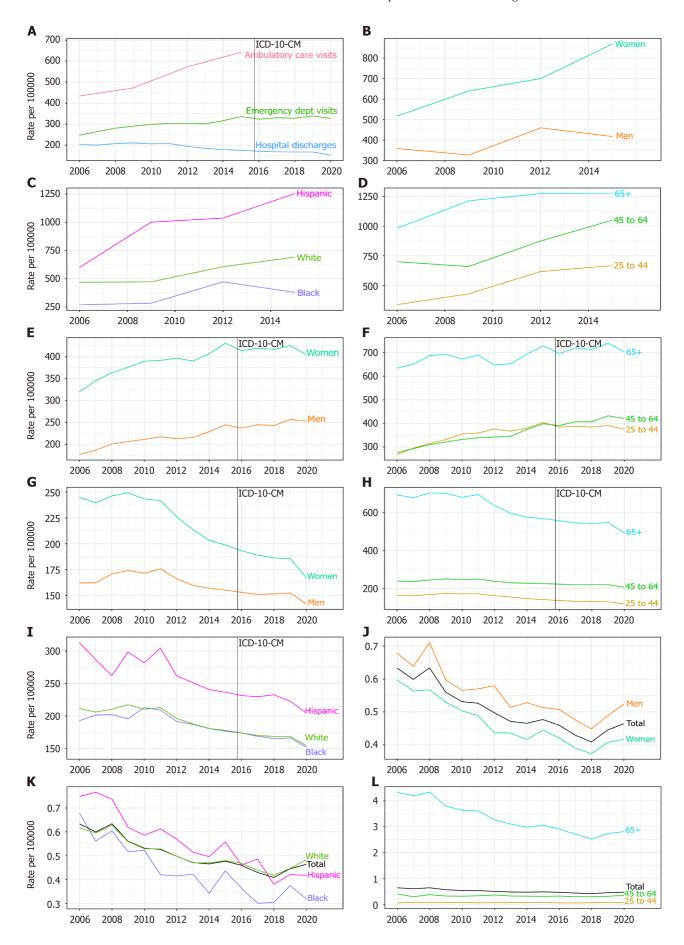
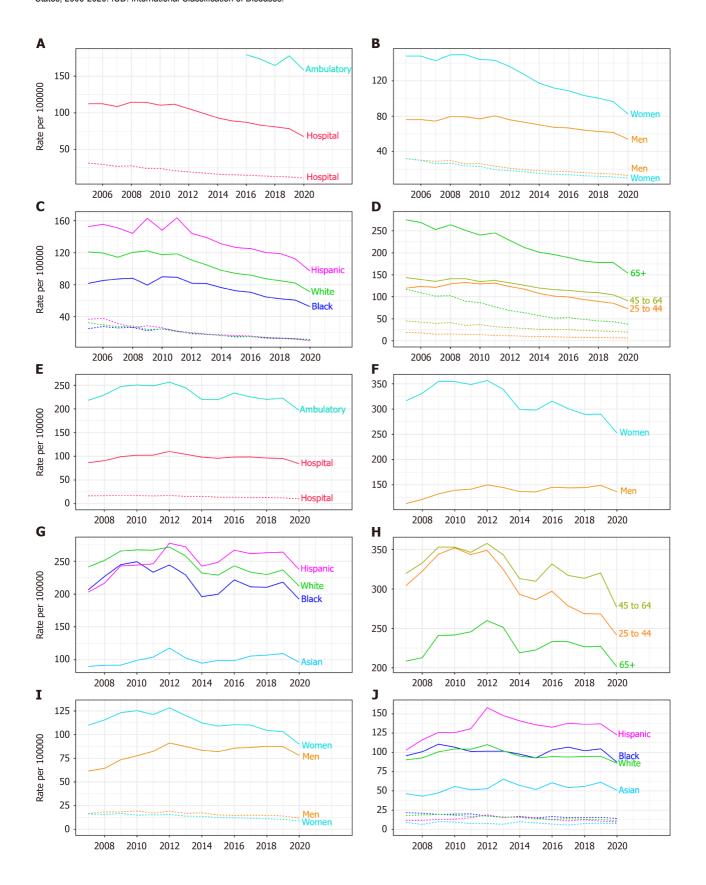


Figure 3 Age-adjusted rates with all-listed gallstone disease diagnoses in the United States. A: Total visits; B: Ambulatory care visits by sex; C: Ambulatory care visits by race-ethnicity; D: Ambulatory care visits by age; E: Emergency department visits by sex; F: Emergency department visits by age; G:

Hospital discharges by sex; H: Hospital discharges by age; I: Hospital discharges by race-ethnicity; J: Mortality by sex; K: Mortality by race-ethnicity; L: Mortality by age. Source: National Ambulatory Medical Care Survey, 2005-2016 (3-year averages, 2005-2007, 2008-2010, 2011-2013, 2014-2016); Healthcare Cost and Utilization Project (HCUP) Nationwide Emergency Department Sample, 2006-2020; HCUP National Inpatient Sample, 2006-2020; and Vital Statistics of the United States, 2006-2020. ICD: International Classification of Diseases.



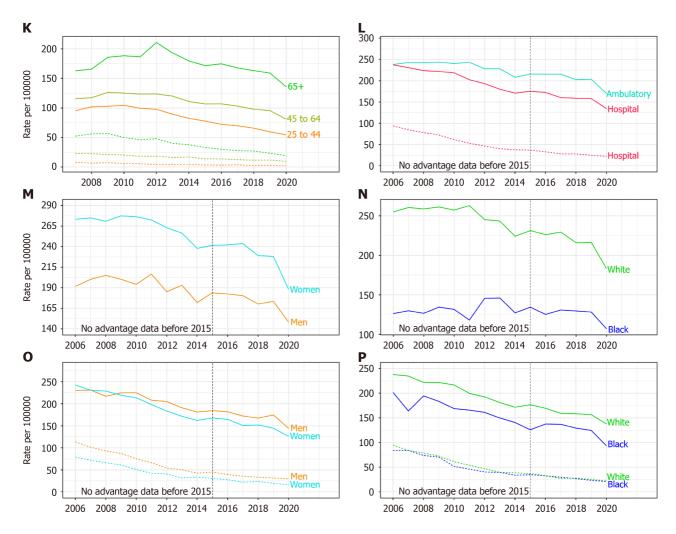


Figure 4 Cholecystectomy rates in the United States. A: National total cholecystectomies; B: National hospital cholecystectomy by sex; C: National hospital cholecystectomy by race-ethnicity; D: National hospital cholecystectomy by age; E: Optum total cholecystectomies; F: Optum ambulatory laparoscopic cholecystectomy by sex; G: Optum ambulatory laparoscopic cholecystectomy by race-ethnicity; H: Optum ambulatory laparoscopic cholecystectomy by age; I: Optum hospital cholecystectomy by sex; J: Optum hospital cholecystectomy by race-ethnicity; K: Optum hospital cholecystectomy by age; L: Medicare total cholecystectomies; M: Medicare ambulatory laparoscopic cholecystectomy by sex; N: Medicare ambulatory laparoscopic cholecystectomy by race; O: Medicare hospital cholecystectomy by sex; P: Medicare hospital cholecystectomy by race. Source: Healthcare Cost and Utilization Project (HCUP) Nationwide Ambulatory Surgery Sample, 2016-2020; HCUP National Inpatient Sample, 2006-2020; Optum Clinformatics® Data Mart, 2007-2020; Medicare 5% file, 2006-2020.

#### Cholecystectomy - Medicaid data

Among Medicaid beneficiaries, rates (per 100000 in 2019) were higher compared with national data for ambulatory laparoscopic (261 vs 178) and inpatient laparoscopic (112 vs 78) cholecystectomies, but lower for inpatient open procedures (9 vs 13). Among Medicaid beneficiaries, laparoscopic cholecystectomy rates were highest among American Indians/Alaska natives, intermediate among Whites and Hawaiians/Pacific Islanders, and lowest among Blacks and Asians (Table 8).

# DISCUSSION

In this report, we expanded on earlier findings and investigated current trends in the gallstone disease burden in the United States using national survey and claims databases[18]. We found that the gallstone disease burden in the United States is substantial and increasing, particularly among women, Hispanics, and older adults. The prevalence of gallstone disease has increased, especially among older adults, based on claims diagnoses among both commercial insurance and Medicare enrollees. This is consistent with our previous findings using data from the National Health and Nutrition Examination Survey of a doubling of the gallstone disease prevalence in the United States population over the past three decades, possibly because of the worsening of metabolic risk factors and growth of laparoscopic cholecystectomy[4]. In the current report, prevalence was higher among older adults, women, American Indians/Alaska natives and Hispanics, and lower among Blacks (except among commercial insurance enrollees) and Asians, consistent with known risk factors. Among the three claims data sources used in the current analysis, prevalence was highest among Medicare beneficiaries (2.09%) as expected given that older age is a risk factor for gallstone disease. Prevalence was higher among Medicaid

Table 3 Number and age-adjusted rates of claims-based prevalence, ambulatory care visits, emergency department visits, and inpatient stays with gallstone disease (all-listed diagnosis) by age, sex, race-ethnicity, and region among Medicaid beneficiaries in the United **States**, 2019

Demographic	Number of	Number of enrollees with	Claims-based	Ambulato visits	ory care	Emergency department visits		Inpatient	stays
characteristics	enrollees	disease	prevalence (%)	Number	Rate per 100000	Number	Rate per 100000	Number	158 191 247 289 233 158 189 172 308 122 358 182 178
Age (yr)									
19 to 34	18016135	138819	0.77	169416	940	100163	556	28456	158
35 to 44	8135908	80155	0.99	88679	1090	46780	575	15519	191
45 to 54	6837507	86815	1.27	88868	1300	41658	609	16890	247
55 to 64	6606519	102452	1.55	96526	1461	39721	601	19125	289
Sex									
Female	23368766	286708	1.23	341646	1462	170220	728	54372	233
Male	16227303	121533	0.75	101843	628	58102	358	25618	158
Race-ethnicity									
White	16266919	173456	1.07	196304	1207	91310	561	30701	189
Black	7392713	62358	0.84	57154	773	37617	509	12727	172
Hispanic	6279192	84023	1.34	95940	1528	54029	860	19315	308
Asian	1800629	13259	0.74	16320	906	4911	273	2202	122
American Indian/Alaska native	571976	7821	1.37	8035	1405	4041	706	2050	358
Hawaiian/Pacific Islander	207441	2033	0.98	1940	935	1286	620	378	182
Multiracial/unknown	7077199	65291	0.92	67796	958	35128	496	12617	178
Region									
Northeast	8712132	82116	0.94	87273	1002	40923	470	17035	196
Midwest	7836180	80735	1.03	94764	1209	43962	561	13226	169
South	11095989	114258	1.03	115694	1043	64653	583	22782	205
West	11951768	131132	1.10	145758	1220	78784	659	26947	225
Total	39596069	408241	1.03	443489	1120	228322	577	79990	202

Source: Centers for Medicare and Medicaid Services.

beneficiaries compared with commercial insurance enrollees (1.03% vs 0.70%). This may be because Medicaid beneficiaries represent a lower income group compared with persons with commercial insurance and gallstone disease was associated with lower socioeconomic status in the United States[4].

The mortality rate associated with gallstone disease is low, but the economic burden on the health care system is high. Because cholecystectomy is one of the most common procedures in the United States, gallstone disease and other biliary tract diseases are the most expensive digestive condition. According to a recent report, biliary tract diseases accounted for the highest health care expenditure (\$16.9 billion) out of 23 digestive conditions that resulted in a total expenditure of \$119.6 billion in 2018[9]. Gallstone disease mortality has continued to decline in recent years resulting in an approximately 80% lower mortality rate over the past four decades, primarily due to a decrease among older adults [6]. Although gallstone disease is more common among women and women had higher medical care rates, the mortality rate was higher among men. Sex differences in gallbladder disease severity may be a factor. Men were found more likely to present with complicated gallbladder disease suggesting a more advanced stage of disease while women were more likely to present with uncomplicated gallbladder disease[19]. Hispanics had higher ambulatory care visit and hospital discharge rates compared with Whites, but not mortality rates. The Hispanic population in the United States is younger compared with the non-Hispanic White population. Hispanics experience lower mortality than non-Hispanic Whites overall[20]. In addition, Hispanics may die of other causes first and gallstone disease may not be captured even among all-listed causes of death.

Table 4 Number and age-adjusted rates of ambulatory care visits, emergency department visits, hospital discharges, deaths, and years of potential life lost (to age 75) with gallstone disease (all-listed diagnosis) by age, sex, race, and ethnicity in the United States

Demographic	Ambulatory ca (2015)	re visits	Emergency dep	partment	Hospital discha	arges (2019)	Mortality (20	19)
characteristics	Number in thousands	Rate per 100000	Number in thousands	Rate per 100000	Number in thousands	Rate per 100000	Number of deaths	Rate per 100000
Age (yr)								
0 to 11	2	4	2	5	2	3	0	0
12 to 24	148	263	95	172	28	51	3	0
25 to 44	565	669	343	392	114	130	61	0.1
45 to 54	467	1084	170	417	75	185	66	0.2
55 to 64	414	1015	190	447	109	256	190	0.5
65 to 74	389	1415	179	570	126	399	307	1.0
75+	218	1080	221	977	171	759	1169	5.2
Sex								
Female	1466	870	756	426	356	186	959	0.4
Male	738	418	444	257	269	152	837	0.5
Race								
White	1901	691	-	-	508	169	1517	0.5
African American	172	380	-	-	74	166	154	0.4
Other	131	519	-	-	49	190	125	0.5
Hispanic origin								
Hispanic	600	1254	-	-	111	223	157	0.4
Not Hispanic	1604	554	-	-	521	159	1639	0.5
Total	2204	642	1200	339	625	168	1796	0.5

Source: National Ambulatory Medical Care Survey (3-year average, 2014-2016), Healthcare Cost and Utilization Project Nationwide Emergency Department Sample and National Inpatient Sample, and Vital Statistics of the United States. The Nationwide Emergency Department Sample does not include information on race-ethnicity.

# Table 5 Number and age-adjusted rates of ambulatory and inpatient laparoscopic and open cholecystectomy by age, sex, race, and ethnicity in the United States, 2019

Demographic	Ambulatory				Inpatient			
characteristics	Number in thousands <sup>1</sup>	Rate per 100000 <sup>1</sup>	Number in thousands <sup>2</sup>	Rate per 100000 <sup>2</sup>	Number in thousands <sup>1</sup>	Rate per 1000001	Number in thousands <sup>2</sup>	Rate per 100000 <sup>2</sup>
Age (yr)								
0 to 11	720	2	0	0	615	1	395	1
12 to 24	57257	104	83	0.1	20435	37	1020	2
25 to 44	217271	248	365	0.4	74860	86	6005	7
45 to 54	109649	268	294	0.7	40125	98	6485	16
55 to 64	105287	248	301	0.7	47175	111	11440	27
65 to 74	78051	248	246	0.8	48685	155	13585	43
75+	37144	165	168	0.7	47655	211	9995	44
Sex								

Female	440796	260	872	0.5	172020	96	22265	11
Male	164542	96	584	0.3	107520	62	26660	15
Race								
White	-	-	-	-	232640	82	40298	13
African American	-	-	-	-	27545	61	5485	12
Other	-	-	-	-	21967	82	3626	14
Hispanic origin								
Hispanic	-	-	-	-	60436	112	5893	12
Not Hispanic	-	-	-	-	221716	72	43516	13
Total	605379	178	1456	0.4	279550	78	48925	13

 $<sup>^{1}</sup>$ Laparoscopic.

Source: Healthcare Cost and Utilization Project Nationwide Ambulatory Surgery Sample and National Inpatient Sample. The Nationwide Ambulatory Surgery Sample does not include information on race-ethnicity.

Table 6 Number and age-adjusted rates of ambulatory and inpatient laparoscopic and open cholecystectomy by age, sex, raceethnicity, and region among persons with commercial insurance in the United States, 2019

Demographic	Ambulatory				Inpatient			
characteristics	Number in thousands <sup>1</sup>	Rate per 100000 <sup>1</sup>	Number in thousands <sup>2</sup>	Rate per 100000 <sup>2</sup>	Number in thousands <sup>1</sup>	Rate per 100000 <sup>1</sup>	Number in thousands <sup>2</sup>	Rate per 100000 <sup>2</sup>
Age (yr)								
0 to 24	1306	49	2	0.1	293	11	10	0
25 to 44	7383	268	22	0.8	1641	60	85	3
45 to 64	10270	320	62	1.9	3059	95	380	12
65+	11646	227	137	2.7	8147	159	1202	24
Sex								
Female	20830	290	111	1.5	7410	103	756	11
Male	9775	149	112	1.7	5730	87	921	14
Race-ethnicity								
White	20966	237	151	1.7	8406	95	1147	13
Black	2791	218	27	2.1	1339	105	201	16
Hispanic	4125	264	22	1.4	2140	137	168	11
Asian	680	109	7	1.1	382	61	50	8
Unknown	2043	143	16	1.1	873	61	111	8
Region								
Northeast	2383	158	22	1.5	1364	90	182	12
Midwest	7787	239	43	1.3	2697	83	413	13
South	14904	259	123	2.1	6277	109	775	14
West	5531	172	35	1.1	2802	87	307	10
Total	30605	223	223	1.6	13140	96	1677	12

 $<sup>^{1}{\</sup>rm Laparoscopic}.$ 

<sup>2</sup>Open.

Source: Optum Clinformatics® Data Mart.

<sup>&</sup>lt;sup>2</sup>Open.

Table 7 Number and age-adjusted rates of ambulatory and inpatient laparoscopic and open cholecystectomy by age, sex, race, and region among Medicare beneficiaries in the United States, 2019

Demographic	Ambulatory				Inpatient			
characteristics	Number in thousands <sup>1</sup>	Rate per 100000 <sup>1</sup>	Number in thousands <sup>2</sup>	Rate per 100000 <sup>2</sup>	Number in thousands <sup>1</sup>	Rate per 100000 <sup>1</sup>	Number in thousands <sup>2</sup>	Rate per 100000 <sup>2</sup>
Age (yr)								
65 to 69	44920	222	240	1.2	23360	115	4060	20
70 to 74	31080	234	300	2.3	21260	160	3380	26
75 to 79	19840	220	-	-	17720	196	2480	27
80 to 84	9640	164	-	-	12600	214	1840	31
75+	5280	88	-	-	11060	185	1760	29
Sex								
Female	68280	228	460	1.5	43220	145	5780	19
Male	42480	174	460	1.9	42780	175	7740	32
Race								
White	89580	217	740	1.8	64800	157	10480	25
Black	6380	128	-	-	6200	125	1160	23
Other	14800	184	-	-	15000	186	1880	23
Region								
Northeast	15480	156	-	-	12720	128	2480	25
Midwest	25100	212	280	2.4	17620	149	3020	26
South	49260	241	280	1.4	36280	178	5860	29
West	20920	171	-	-	19380	159	2160	18
Total	110760	204	920	1.7	86000	158	13520	25

<sup>&</sup>lt;sup>1</sup>Laparoscopic.

Source: Centers for Medicare and Medicaid Services 5% file. Counts less than 200 are not reported.

In contrast to mortality, rates of both ambulatory care visits to physicians' offices and emergency department visits with gallstone disease increased since the mid-2000s. Hospital discharge rates declined beginning in the early 1990s due to the shift to outpatient laparoscopic cholecystectomy, then stabilized between 2000 and 2011, after which they again decreased[5]. The decline in recent years was primarily among older adults (Figure 3H) and may be the result of two decades of widespread use of laparoscopic cholecystectomy. Hospital discharge rates underestimate the actual burden because most hospitalizations with gallstones were for cholecystectomy and a high proportion of cholecystectomies were performed laparoscopically without an overnight stay, and therefore, were not included in hospitalization statistics. In contrast to national hospitalization data, among commercial insurance enrollees hospitalization rates increased. Blacks had lower ambulatory care visit and mortality rates, but similar hospital discharge rates compared with whites. Blacks may be in lower socioeconomic groups and have less access to care. They may also receive care in later stages of gallstone disease that may require inpatient hospitalization.

Most cholecystectomies are now performed laparoscopically in an ambulatory setting. Ambulatory laparoscopic cholecystectomy rates varied by race-ethnicity and were generally highest in Hispanics, lower in Blacks compared with Whites, and lowest in Asians. These rate differences are consistent with gallstone disease prevalence among racial-ethnic groups. Ambulatory cholecystectomy rate differences could also reflect disparities in access to care. Racial and ethnic minorities may have a higher likelihood of receiving inpatient as compared to ambulatory cholecystectomy [21]. This may contribute to lower ambulatory laparoscopic cholecystectomy rates among Blacks compared with Whites. It may also help to explain lower ambulatory and higher inpatient laparoscopic cholecystectomy rates among Hispanic compared with White Medicaid beneficiaries. Because ambulatory cholecystectomy is associated with lower morbidity and costs relative to inpatient cholecystectomy, continued monitoring of practice patterns among racial-ethnic groups is warranted for better health care access and optimizing surgical care for gallstone disease. Ambulatory laparoscopic cholecystectomy rates also differed by sex. They were higher among women compared with men, reflecting the higher prevalence of gallstone disease among women. Sex differences in gallbladder disease complexity may also be a factor. Women were found more likely to present with uncomplicated gallbladder disease while men were more likely to present with com-

<sup>&</sup>lt;sup>2</sup>Open.

Table 8 Number and age-adjusted rates of ambulatory and inpatient laparoscopic and open cholecystectomy by age, sex, raceethnicity, and region among Medicaid beneficiaries in the United States, 2019

Demographic	Ambulatory				Inpatient			
characteristics	Number in thousands <sup>1</sup>	Rate per 1000001	Number in thousands <sup>2</sup>	Rate per 100000 <sup>2</sup>	Number in thousands <sup>1</sup>	Rate per 1000001	Number in thousands <sup>2</sup>	Rate per 100000 <sup>2</sup>
Age (yr)								
19 to 34	48231	268	-	-	19107	106	712	4.0
35 to 44	22854	281	-	-	9345	115	704	8.7
45 to 54	17784	260	-	-	8105	119	950	13.9
55 to 64	14468	219	-	-	7698	117	1235	18.7
Sex								
Female	84647	362	-	-	33167	142	1825	7.8
Male	18690	115	-	-	11088	68	1776	10.9
Race-ethnicity								
White	52396	322	252	1.5	17112	105	1690	10.4
Black	11598	157	-	-	6005	81	600	8.1
Hispanic	17567	280	-	-	11268	179	484	7.7
Asian	1892	105	-	-	1182	66	-	-
American Indian/Alaska native	2173	380	-	-	1038	182	-	-
Hawaiian/Pacific Islander	459	221	-	-	233	112	-	-
Multiracial/unknown	17252	244	-	-	7417	105	631	8.9
Region								
Northeast	17392	200	-	-	8986	103	617	7.1
Midwest	25378	324	-	-	7661	98	887	11.3
South	33066	298	237	2.1	11824	107	1133	10.2
West	27501	230	-	-	15784	132	964	8.1
Total	103337	261	521	1.3	44255	112	3601	9.1

<sup>&</sup>lt;sup>1</sup>Laparoscopic.

Source: Centers for Medicare and Medicaid Services. Counts less than 200 are not reported.

plicated gallbladder disease suggesting a more advanced stage of disease[19].

The data used in this report have limitations. For national data sources, ambulatory care numbers and rates represent visits, not persons with a visit and hospital numbers and rates represent discharges, not persons with an inpatient stay. National health care data do not include care in federal facilities and NEDS and NASS include only hospital-owned emergency departments and ambulatory surgery facilities, respectively; therefore, rates based on the United States population are underestimates. The NAMCS sample is limited to office-based physicians, a group that has become a less inclusive source for ambulatory care and samples are small, so estimates are less statistically reliable. HCUP data sources do not include all states and not all participating states collect data on race-ethnicity. Mortality data are dependent on the accuracy of death certificates. This may vary by condition and chronic diseases that contribute to mortality are frequently underreported.

The limitations are offset by the following strengths. NAMCS data were obtained from provider records. HCUP data sources are the largest all-payer inpatient, emergency department, and ambulatory surgery databases in the United States. National health care and Medicare data were weighted to provide national estimates, and mortality data include all deaths occurring in the United States. CDM, Medicare, and Medicaid data are person-level and claim-based prevalence can be calculated. Medicare covers approximately 96 percent of all United States citizens aged 65 years and over permitting generalization to the United States older adult population[22]. CDM includes information on Asians and Medicaid on Asians, American Indians/Alaska natives, and Hawaiians/Pacific Islanders, groups for which data are less commonly available.

<sup>&</sup>lt;sup>2</sup>Open.

Because of potential short-term effects of the COVID-19 pandemic on gallstone disease healthcare utilization and mortality, we calculated trends using rates for 2019, while figures present data through 2020. Between 2019 and 2020, there were generally small decreases in medical care use with gallstone disease and increases in gallstone disease mortality. Whether these changes represent only temporary fluctuations will become clearer when additional years of data are available.

# CONCLUSION

The burden of gallstone disease in the United States is considerable and rising. Although the gallstone disease mortality rate has decreased over the past four decades leading to a low case fatality rate, medical care devoted to gallstone disease is significant. Cholecystectomy is one of the most common digestive disease surgical procedures. Gallstone disease prevalence (claims based), ambulatory care visit, and emergency department visit rates are increasing, and the appearance of decreasing hospitalization rates is deceptive because of the shift from inpatient open cholecystectomy to ambulatory laparoscopic procedures. Significant disparities exist with a disproportionately high gallstone disease burden among women, Hispanics, American Indians/Alaska natives, and older adults. Current practice patterns should be monitored post-pandemic for better health care access. Public health measures are needed to address the substantial and increasing gallstone disease burden.

# **ACKNOWLEDGEMENTS**

The authors thank Bryan Sayer, MHS, for statistical analysis and Helen Corns, MPH, for statistical programming and figure creation. The work was supported by a contract from the National Institute of Diabetes and Digestive and Kidney Diseases, No. 75N94022F00050.

# **FOOTNOTES**

Author contributions: Unalp-Arida A and Ruhl CE conceived and designed the study and analyzed and interpreted the data; Ruhl CE drafted the manuscript; Unalp-Arida A critically revised the manuscript for important intellectual content; both authors have read and approved the final manuscript.

Institutional review board statement: The study used only secondary de-identified data. Because there were no experimental protocols including human subjects, our study does not qualify as human subjects research. Consequently, there were no institutional approval requirements.

Informed consent statement: The study used only secondary de-identified data. Because there were no experimental protocols including human subjects, our study does not qualify as human subjects research. Consequently, there were no individual patient consent requirements.

**Conflict-of-interest statement:** All the authors report no relevant conflicts of interest for this article.

Data sharing statement: Vital Statistics of the United States data are publicly available at https://www.nber.org/research/data/ mortality-data-vital-statistics-nchs-multiple-cause-death-data. The National Ambulatory Medical Care Survey data are available at https://www.cdc.gov/nchs/ahcd/index.htm. Restricted data are available through the National Center for Health Statistics Research Data Center (http://www.cdc.gov/rdc). Healthcare Cost and Utilization Project National Inpatient Sample, Nationwide Emergency Department Sample, and Nationwide Ambulatory Surgery Sample data were purchased from the Agency for Healthcare Research and Quality with a data use agreement and cannot be made available to other researchers (https://hcup-us.ahrq.gov/). The Medicare 5% Sample and Medicaid data were used through a data use agreement with the Centers for Medicare and Medicaid Services and cannot be made available to other researchers (https://resdac.org/). Optum Clinformatics® Data Mart data were used through a contract between the National Institute of Diabetes and Digestive and Kidney Diseases and Optum and a third-party agreement with DLH. Optum electronic health records are proprietary and cannot be made available to other researchers. https://www.optum.com/content/dam/ optum/resources/productSheets/Clinformatics\_for\_Data\_Mart.pdf.

STROBE statement: The authors have read the STROBE Statement-checklist of items, and the manuscript was prepared and revised according to the STROBE Statement-checklist of items.

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Country/Territory of origin: United States



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S-Editor: Wang JJ L-Editor: A P-Editor: Xu ZH

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