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Ten-Year Trends of Persistent Mortality with Gallstone Disease: A Retrospective Cohort Study in New Jersey

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Mortality with Gallstone Disease over a Decade in New Jersey, 2009 to 2018

1,580 deaths with a diagnosis of gallstone disease	The trend of death with diagnosed gallstone disease did not change	Except in Latinos 65 years or older, it increased
0.2% (of 717,620 deaths in New Jersey)	1.61 → 1.65 (incidence of death per 100,000 New Jersey population)	0.11 → 0.23 (incidence of death per 100,000 New Jersey population)

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Title: Ten-Year Trends of Persistent Mortality with Gallstone Disease: A Retrospective Cohort Study in New Jersey.

Short Title: Persistent Mortality with Gallstone Disease.

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ABSTRACT

Background and Aims: Recent trends in mortality with gallstone disease remain scarce in the United States. Yet multiple changes in clinical management, such as rates of endoscopy, cholecystectomy, and cholecystostomy, and insurance access at the state level may have occurred. Thus, we evaluated recent secular trends of mortality with gallstone disease in New Jersey.

Methods: We performed a retrospective, cohort study of mortality from 2009 to 2018 using the National Center for Health Statistics, Restricted Mortality Files. The primary outcome was any death with an ICD-10-CM diagnosis code of gallstone disease in New Jersey. Simple linear regression was used to model trends of incidence of death.

Results: 1580 deaths with diagnosed gallstone disease occurred from 2009 to 2018. The annual trend of incidence of death was flat over 10 years. The incidence of death with diagnosed gallstone disease relative to all death changed only from 0.21% to 0.20% over 10 years. These findings were consistent also in 18 of 20 subgroup combinations, although the trend of death with diagnosed gallstone disease in Latinos 65 years or older, increased [slope estimate 0.93, 95% Confidence Limit 0.42 to 1.43, p=0.003].

Conclusions: The rate of death with diagnosed gallstone disease showed little change over a recent 10 years in New Jersey. This needs to be reproduced in other states and nationally. A closer examination of the changes in clinical care and insurance access is needed to help understand why they did not result in a positive change in this avoidable cause of death.

KEYWORDS: trends; epidemiology; cholelithiasis; gallstone disease; mortality

ABBREVIATIONS:
US – United States
dGD – diagnosed gallstone disease
NJ – New Jersey
NCHS – National Center for Health Statistics
ICD-10-CM – International Classifications of Disease, 10th edition, Clinical Modification

INTRODUCTION

Gallstone disease has been said to have reached epidemic proportions, with up to twenty percent of the total United States (US) population having asymptomatic disease, and 20 to 50 percent of those who are asymptomatic developing symptomatic gallstone disease in their lifetime. [1-3] Asymptomatic gallstone disease is known to be associated with very common health risks in the US including high-calorie diets, hyperinsulinism or insulin resistance, type 2 diabetes mellitus, dyslipidemia, obesity, and metabolic syndrome, which are associated with mortality. [4-7]

Symptomatic gallstone disease requiring treatment, increasing greater than 20 percent in the last three decades of the 20th century, results from progression of asymptomatic disease due to gallstone impaction of the physiologic drainage of the gallbladder, pancreas, liver, or intestine.[1, 2] Complications of gallstone disease include symptomatic cholelithiasis, e.g., biliary colic, cholecystitis, gallstone pancreatitis, choledocholithiasis, biliary cholangitis from choledocholithiasis, or gallstone ileus. [8-10] As a result, diagnosed symptomatic gallstone disease is one of the most common and costly gastrointestinal disorders spanning the entire life course with over 60% of related care requiring hospital stays, totaling 1.2 million inpatient admissions annually. [10, 11] Indeed, it is the most common and an increasing clinical digestive disease requiring surgery in the US. [12]

Gallstone disease has been thought to be an example of an 'ambulatory sensitive' disease, [13] i.e., one that, if appropriate outpatient care were made more available, emergency department presentation, hospital admission, and most importantly mortality, may all be avoidable. [14] Are we succeeding in this? Many recent changes in clinical management have occurred, such as rates of endoscopy and laparoscopic cholecystectomy, and cholecystostomy in the frail population, [15-17] as well as expansion of access to care with Medicaid expansion in 2014. [18] However, population-based data on recent US trends of death from gallstone disease are sparse. [11, 19, 20] Indeed, we are not aware of any US studies describing the trends of death from complications of gallstone disease. Thus, the aim of this study was to report on the recent mortality trends with diagnosed gallstone disease (dGD) in the highly diverse state population of New Jersey. [21] This report of the epidemiologic trends of the mortality with gallstone disease at the population level is necessary.

METHODS

Study Design and Period.

A 10-year retrospective population cohort study was conducted to determine the trends of mortality with diagnosed gallstone disease from 2009 to 2018.

Study Population.

The population selected for this study were residents of New Jersey (NJ).

Data Source(s).

Records came from the Centers for Disease Control (CDC) and Prevention, National Center for Health Statistics (NCHS), National Vital Statistics Data, Death (Mortality) – *Multiple Cause of Death, States and All Counties – Detailed*, NJ Files. [22] These restricted research files contain multiple-cause coding for cause of death by calendar year and month, i.e., geographical variables about the decedent down to the county level. The final analysis dataset included all deaths in NJ from 2009 to 2018 with ICD-10 mortality codes for gallstone disease. Gallstone disease occupied the 1st and 2nd up to the 13th death field known as the principal and contributory positions, respectively. We selected only codes indicating gallstones, such as biliary pancreatitis instead of pancreatitis alone, and cholangitis with common duct calculus instead of just cholangitis alone (Figure 1). All ICD-10 codes for death with diagnosed gallstone disease, such as cholelithiasis, cholecystitis, biliary pancreatitis, choledocholithiasis, biliary cholangitis secondary to choledocholithiasis, and gallstone ileus/fistula, were extracted from each calendar year file (Appendix Table 1).

The United States Census Bureau provided NJ population data. [23]

Study Measures.

Independent Variable.

The independent variable was calendar year between 2009 to 2018.

Outcome Variable.

A death with dGD was defined as any record with a relevant ICD-10 mortality code consistent with diagnosed gallstone disease.

Analysis.

Descriptive statistics and trends analyses.

Individual calendar year death counts were divided by the average of the 2010 and 2020 NJ Census population (i.e., 9,040,444) to compute a crude annual incidence of death with dGD per 100,000 NJ population. [23] The proportion of death with dGD was calculated each year by dividing deaths with dGD by all deaths in NJ. Annual incidences were plotted and analyzed for a temporal trend using line graphs and simple linear regression of incidence of death as a function of calendar year over the ten years. [24]

These analyses were repeated in 20 demographic subgroups; age less than and greater than or equal to 65 years, gender male and female, and race/ethnicity white, Black, Hispanic, Asian, and American Indian. "Hispanic" ethnicity was the description used by the NCHS and includes Asian Hispanic, Black Hispanic, and White Hispanic. We combined these groups and refer to them as Latino. [25]

P value < 0.05 was considered statistically significant. SAS 9.4 statistical software package was used for all analysis.

This research was classified as exempt by Rutgers Institutional Review Board.

RESULTS

Of the 717,620 deaths in NJ (Appendix Figure 1), 1580 (0.2%) were deaths with a diagnosis of gallstone disease (Table 1). Cholecystitis (68.7%, N=1085) and cholelithiasis / gallbladder disease (25.4%, N=402) totaled together 94.1% of the gallstone disease death codes (N=1487). The median age of death with dGD was 83 years [interquartile range; 73, 89]. Of these, 12.7%, 58.4%, and 10.8% of deaths with dGD were among those who were less than 65 years of age, female, and black, respectively.

57.5% (n=908) of the 1,580 deaths with gallstone disease included gallstone disease codes in the principal position (Table 2). Gallstone disease occupied the principal through 5th position in 87.1%. After removing death records including duodenal, gallbladder, pancreas, biliary tract, or liver cancer diagnoses, gallstone disease occupied the principal position in 58.1% (n=905) of the 1557 deaths and principal through 5th contributory positions in 85.5% (N=1332).

The trend of counts of death with dGD over 10 years' time did not change overall [p=0.58; slope parameter estimate, - 0.009, 95% CL, - 0.05 to + 0.03] (Figure 2) (Table 3). The incidence of death with dGD relative to all death in NJ also did not change [p=0.14; slope estimate, - 0.000034; 95% CL, - 0.000081 to + 0.000014] (Figure 3) (Table 3).

The most deaths with dSGD, 40.4% and 29.2% of total deaths, were in white females and males, respectively. Further, the most death with dGD, 5.4% and 3.8% of total deaths, were in Black and Latina females equal to or greater than 65 years of age. However, 18 of the 20 subgroups (using binary gender, binary age <65 and >=65, and five NCHS race/ethnicity classifications) had similarly flat 10-year trends individually (Appendix Figure 2, 3, and 4) (Table 3), except Latinos 65 years or older, where the slope increased [slope estimate 0.93, 95% CL 0.42 to 1.43, p=0.003].

DISCUSSION

The US has seen many changes in the care of patients with dGD, as well as expansion of access to Medicaid starting in 2014. Yet, our retrospective population study of death with dGD in a population in the diverse northeast US state of New Jersey found an unchanged, persistent incidence of mortality from 2009 to 2018. Deaths with dGD relative to all deaths in NJ were also unchanged over this time. Despite deaths with dGD being level overall, and in 18 demographic subgroups, mortality rose with dGD over the last 10 years among Latinos age 65 years or older, although this was not an a priori hypothesis and may have been due to random error.

Population-based studies are essential to understanding the impact of a disease on an entire population, rather than just a clinical population. [26] To our knowledge this is the first study to identify recent population trends in mortality rate with dGD, a potentially avoidable cause of death. We know of only one group, Perry et al., using the Centers for Disease Control Wide-ranging Online Data for Epidemiologic Research, [27] who individually reported single year 2012,

[19] 2016, [20] and 2019 [11] US mortality data on cholecystitis, acute pancreatitis, and cholangitis. Similar to our finding of persistent mortality with gallstone disease, crude mortality rates across the three years for cholecystitis appeared to be increasing from 0.7 to 0.8 per 100,000 and acute pancreatitis and cholangitis appeared flat at 0.9 and 0.3 per 100,000, respectively. One possibility therefore is that this level mortality rate in NJ might be a combination of a steady or even increasing incidence of non-complicated symptomatic gallstone disease with prevention of progression to high-risk complicated emergency symptomatic disease. Asmar et al. highlight a more recent shift away from cholecystectomy to cholecystostomy. [17] An associated increasing mortality as this non-surgical procedure becomes more utilized now first in the frail, combined with a decreasing case fatality of traditional cholecystectomy if present, could also possibly explain a lack of improvement in mortality with gallstone disease over time. With this may come lower procedural or surgical case fatality rates [28]; that remains to be studied.

Several other known mechanisms may exist, e.g., prevention of smoking, obesity, metabolic syndrome, dyslipidemia, alcohol intake, and sedentary lifestyle, by which the population’s overall mortality from dGD could be reduced significantly; yet we did not find this. [1, 2, 5, 6, 29] Further exploration of current factors like cholecystectomy that may impact natural trends of death with dGD within and among multiple states is necessary. [30] For example, hospital admissions with cholecystitis, the most common severe complication of gallstones and indication for cholecystectomy, increased 44% from 1997 to 2012 in the US [12]; might this explain a lack of change in death despite perhaps worse (or better) outcomes from each case? Trends in emergency cholecystectomy, and concurrent other approaches to tertiary prevention of mortality with dGD like antecedent endoscopic clearance of the pancreatic or common bile duct of stones in acute gallstone pancreatitis or cholangitis, and relative trends in complications, require analysis of surgical with these non-surgical and medical populations treated for symptomatic gallstone disease. [31, 32] Alternatively, if efforts between gastroenterology and primary care and other specialists together can predict how, why, and which patients require invasive treatments before they do, population health facilitators of primary and secondary prevention targets at the primary care level may help to avoid higher risk tertiary prevention efforts altogether. [26, 33] This may be especially important given the increased proportion of gallbladder disease and pancreatitis presenting to emergency departments in the US, increased endoscopic ultrasound but decreasing endoscopic retrograde cholangiopancreatography rates treating choledocholithiasis, the high 30-day readmission rates that are due to gallbladder diseases, and the fivefold higher mortality associated with inpatient emergency versus outpatient elective cholecystectomy reported in at least one northern region US state. [20, 34] Better understanding and consensus on patient-centered outcomes of importance across the stages and complications of gallstone disease may guide such concerted and complementary approaches to preventing and modifying the persistent metabolic, biologic, behavioral, structural, social, and economic etiologies upstream from the preventable clinical etiologies of morbidity, mortality, and disability with dGD. [35-37]

Understanding how and why deaths with dGD occur inside the hospital on index admission for non-emergency or emergency symptomatic gallstone disease, inside the hospital on readmission to the same hospital after antecedent non-treatment or treatment of symptomatic gallstone disease, inside the hospital on readmission to a different hospital, or outside the hospital and during rehabilitation, might help to form a more systematic construct of zero preventable death with dGD. [26] Thus, in summary, we propose some of the possible mechanistic hypotheses about why we are seeing a persistent risk of death with diagnosed gallstone disease:

1. Changes (or lack of changes) in the etiology of developing gallstone disease, e.g., due to pathogenic cholesterol metabolism and individual / family microbiome factors, or access to healthy diet, weight loss, or beneficial pharmacologic prevention.
2. Changes (or lack of changes) in the rates of uncomplicated vs. complicated gallstone disease, e.g., changes affecting the pathologic composition and size of gallstones.
3. Changes (or lack of changes) in the etiology of developing gallstone disease from changes in exposure to harmful pharmacologic or environmental agents.
4. Changes (or lack of changes) in the rates of asymptomatic gallstone disease becoming symptomatic gallstone disease, e.g., evolution of gallbladder sludge into precipitate, and then into gallstones, from changes in #1 - 3 above.
5. Changes (or lack of changes) in the proportion of symptomatic disease that presents early enough for medical vs. procedural or surgical intervention, e.g., patient attitudes, beliefs, and skills affecting their response to the first symptoms of abdominal pain.
6. Changes (or lack of changes) in the balance of elective and emergency endoscopic or surgery interventions, e.g., particular communities conditioned or facilitated in their access to hospital rather than ambulatory care based on out-of-pocket costs or insurance.
7. Changes (or lack of changes) in non-operative, endoscopic, or surgical techniques and outcomes, e.g., patient, primary care, and specialists' decision making toward surgery, or no surgery.
8. Changes (or lack of changes) in the non-operative, endoscopic, or surgical techniques and outcomes, e.g., endoscopic, procedural, and surgical case fatality rates over time due to clinical training or facility and workforce capacity.

9. Changes (or lack of changes) in the approaches to and outcomes among different demographic subgroups, e.g., institutional bias or racism.
10. Changes (or lack of changes) in the approaches to and outcomes among different demographic subgroups, e.g., provider and organizational incentives related to utilization of health care services rather than preventive services.
11. Changes (or lack of changes) in the approaches to and outcomes among different demographic subgroups, e.g., lack of policy toward increasing health and preventive services rather than health care services.

We have also organized these factors into an adapted research framework that addresses the complex and multifaceted nature of digestive health (Figure 4). [38] Because some of these may have gotten better or worse, we need to understand what etiologic factors and combination of different trends were involved, i.e., how the mixing of effects of one or more of the above changes mortality from diagnosed gallstone disease and led to an overall unchanging trend in the risk of death in the population.

There are several limitations of this study to consider. First, potentially biasing the measurement of counts of death with dGD in this study are the coding practices of persons completing death certificates in NJ, if those changed over that decade. We know of no reason to think this happened, however. Second, the validity of death certificate coding of *principal* versus *contributing causes of death* and its impact on trends data may have very different implications depending on the specific a priori hypotheses and data interpretation. For example, others have delineated '*contributing'* from *'underlying' cause of death* and differentiated death with and without cancer in trends analyses. [11, 39] Our use of *principal* and *contributory cause of death* positions together, established on the death record as the *underlying* cause or any of the thirteen additional diseases leading to death in the *contributory* position, should not necessarily be regarded as a more or less accurate measure than using only the *underlying cause of death*, a disease that initiated the sequence of events leading to death, but as a measure that we used to capture the natural epidemiology of dGD. Third, we may have overestimated death with dGD by not excluding 23 of our 1580 deaths with a concomitant ICD-10 code of duodenal, gallbladder, pancreas, biliary tract, or liver cancer, but this small number is not likely to have changed overall trends. Finally, it is not clear, for example, if the increasing death rates from 2009 to 2018 in Latinos aged 65 or older are a false positive secondary to the greatest increase of the share of the population being Latino (17.3% to 20.4%) or age 65 and older (increased 22.9%) (see Supplement Table 1 and Table 2). [40-44] Age, sex, and race/ethnicity were each controlled for in the analysis. Our positive findings, about Latinos, and negative findings about non-Latino race/ethnic groups, however, may result from multiple sub-analyses and requires additional investigation in other settings with a priori hypotheses given the important health and healthcare equity implications of each.

CONCLUSION

Death with dGD is avoidable, but based on these NJ data, we are not achieving this, despite many changes in clinical care and marked expansion in insurance access during this time window. These results need to be confirmed elsewhere. However, additional studies are needed to try to understand why we are not succeeding in avoiding death with dGD. This will provide a foundation of achieving zero preventable death with dGD in the US.

Table 1. Death in New Jersey with symptomatic gallstone disease, 2009 to 2018. [1, 2, 3, 4]

Deaths [1]	N = 1580 (100)
Cholecystitis	1085 (68.7)
Cholelithiasis / gallbladder disease	402 (25.4)
Choledocholithiasis	63 (4.0)
Cholangitis, with Choledocholithiasis	17 (1.1)
Gallstone ileus / gallbladder fistula	11 (0.7)
Gallstone pancreatitis	2 (0.1)
Gender	
Female	922 (58.4)
Male	658 (41.6)
Age [2]	
<25	3 (0.2)
26-34	3 (0.2)
35-49	35 (2.2)
50-64	160 (10.1)
65-84	691 (43.7)
>= 85	688 (43.6)
Race and ethnicity [3]	
White	1214 (76.8)
Black	171 (10.8)
Latino [4]	137 (8.7)
Asian	57 (3.6)
American Indian	1 (0.1)

[1] Gallstone disease occupies any position, principal or contributing, on the NJ death certificate. Data indicated by N (%).
[2] Median age (IQR) is 83 (73, 89). 87.3% (n=1379) of deaths were in people >=65. 12.7% (n=201) of deaths were in people < 65.
[3] Zero deaths were recorded for Pacific Islanders and Native Americans.
[4] Latino includes Asian Hispanic, White Hispanic, and Black Hispanic.

Table 2. Gallstone disease diagnosis on a NJ Death Certificate, 2009 to 2018. [Ŷ, †, ¤, ‡, §]

Position on death certificate	Death with symptomatic gallstone disease (SGD) [Ŷ] All SGD n = 1,580	Death with symptomatic gallstone disease (SGD) [Ŷ] With cancers omitted [†] n = 1,557 [¤]
1 [‡]	908 (57.5%)	905 (58.1%)
2	62	55
3	135	122
4	144	130
5	127	117
6	79	73
7	65	60
8	46	44
9	31	28
10	17	16
11	4	4
12	1	1
13	2	2
>1 position occupied	N = 1621[§]	N = 0

[Ŷ] Symptomatic gallstone disease includes cholelithiasis / other gallbladder disease, cholecystitis, gallstone pancreatitis, choledocholithiasis, cholangitis, with choledocholithiasis, gallstone ileus / gallbladder fistula.

[†] Select cancers removed includes duodenal, gallbladder, pancreas, biliary tract, or liver.

[¤] N=1557 reflects SGD diagnoses in the earliest position for records with >1 diagnosis.

[‡] Position 1 is the 'principal' position; the others are considered 'contributing'.

[§] N=1621 is greater than 1,580 because gallstone disease occupies more than one position on some death certificates.

Table 3. Annual Incidence of Diagnosed Gallstone Disease and All Deaths in New Jersey, with dGD incidence of death adjusted for age, sex, and race/ethnicity, individually, 2009 to 2018. [i, ii, iii, iv, v, vi]

	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	Total
dGD											
counts	146	154	181	179	150	148	166	150	157	149	1580
incidence [i]	1.61	1.7	2	1.98	1.65	1.64	1.84	1.66	1.73	1.65	17.48
monthly incidence [ii]	0.134 (.034)	0.142 (.055)	0.167 (.055)	0.165 (.034)	0.138 (.047)	0.136 (.049)	0.153 (.037)	0.138 (.050)	0.145 (.029)	0.137 (.038)	1.74 [iii] (0.045)
All death											
counts	68277	69495	70558	70534	71403	71316	72271	73155	74846	75765	717620
incidence [i]	755.23	768.71	780.47	780.20	789.81	788.42	799.42	809.20	827.90	828.06	7,937.88
Rate of dGD death relative to All deaths [iv]											
proportion	.00213	.00221	.00256	.00254	.00209	.00208	.00230	.00205	.00209	.00197	0.0022
dGD incidence of death adjusted for age											
< 65 years	.22123	.24335	.19910	.30972	.12168	.19911	.25441	.19911	.26547	.21017	2.23
>= 65 years	1.39	1.46	1.80	1.67	1.54	1.44	1.58	1.46	1.47	1.44	15.25
dGD incidence of death adjusted for sex											
Female	1.07	1.02	1.27	1.08	0.88	0.94	1.03	0.97	0.96	0.96	10.20
Male	0.54	0.69	0.73	0.90	0.77	0.70	0.81	0.69	0.77	0.69	7.28
dGD incidence of death adjusted for race/ethnicity [v]											
Black	0.19	0.17	0.22	0.19	0.19	0.13	0.23	0.23	0.21	0.13	1.89
Latino [vi]	0.11	0.09	0.10	0.15	0.17	0.18	0.19	0.14	0.15	0.23	1.51
Asian	0.01	0.07	0.06	0.09	0.08	0.09	0.04	0.07	0.06	0.08	0.65
White	1.30	1.38	1.62	1.55	1.23	1.23	1.37	1.22	1.32	1.21	13.43

[i] Incidence is calculated per 100,000 NJ population using the average of the 2010 and 2020 annual populations from the United States Census Bureau, New Jersey, i.e., 9,040,444.
[ii] Monthly incidences means and standard errors (SEs); SEs in parentheses.
[iii] Total annual incidence mean with SE.
[iv] Proportion of death is calculated using a numerator of incidence of death with diagnosed gallstone disease and a denominator of incidence of all death.
[v] < 0.01 incidence in 2014 is not shown for American Indian subgroup.
[vi] Latino includes Asian Hispanic, White Hispanic, and Black Hispanic.

Figure 1. Study Population and Total New Jersey Deaths with diagnosed Gallstone Disease [i, ii]

[i] All death records data were according to the Centers for Disease Control and Prevention, National Center for Health Statistics Detailed Mortality – All Counties files in NJ for calendar years 2009 to 2018.

[ii] Records indicating an ICD-10-CM mortality code of gallstone disease in principal and contributory positions on the death certificate. See Appendix Table 1 for full list of ICD-10-CM codes.

Figure 2. Trend of the Incidence of Death with Diagnosed Gallstone Disease in NJ, 2009 to 2018.[i, ii, iii]

[i] Incidence calculated per 100,000 NJ population using the average of the 2010 and 2020 populations from the United States Census Bureau in New Jersey (n = 9,040,444).

[ii] Annual incidences are the sum of 12 monthly incidences in each year. See Table 3 for each year's mean monthly incidences and standard errors.

[iii] Ten-year trend slope parameter estimate, -0.009, SE 0.02, p=0.58; 95% CL, - 0.05 to + 0.03.

Figure 3. Trend of the Incidence of Diagnosed Gallstone Disease as a Proportion of All Deaths in NJ, 2009 to 2018. [i, ii, iii]

[i] The proportion of incidence of deaths with dSGD to All Deaths was calculated by dividing incidence of deaths with dSGD by incidence of all death.

[ii] Standard errors of proportions indicated by error bars.

[iii] Ten-year trend slope parameter estimate, -0.000034, SE 0.000021, p=0.14, 95% CL, -0.000081 to + 0.000014.

Figure 4. Framework to assess progress, gaps, and opportunities for improving mortality with diagnosed gallstone disease.[1]

[1] Adapted from the National Institute on Minority Health and Health Disparities, 2018.

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Table 1. Death in New Jersey with symptomatic gallstone disease, 2009 to 2018. [1, 2, 3, 4]

Deaths [1]	N = 1580 (100)
Cholecystitis	1085 (68.7)
Cholelithiasis / gallbladder disease	402 (25.4)
Choledocholithiasis	63 (4.0)
Cholangitis, with Choledocholithiasis	17 (1.1)
Gallstone ileus / gallbladder fistula	11 (0.7)
Gallstone pancreatitis	2 (0.1)
Gender	
Female	922 (58.4)
Male	658 (41.6)
Age [2]	
<25	3 (0.2)
26-34	3 (0.2)
35-49	35 (2.2)
50-64	160 (10.1)
65-84	691 (43.7)
>= 85	688 (43.6)
Race and ethnicity [3]	
White	1214 (76.8)
Black	171 (10.8)
Latino [4]	137 (8.7)
Asian	57 (3.6)
American Indian	1 (0.1)

[1] Gallstone disease occupies any position, principal or contributing, on the NJ death certificate. Data indicated by N (%).
[2] Median age (IQR) is 83 (73, 89). 87.3% (n=1379) of deaths were in people >=65. 12.7% (n=201) of deaths were in people < 65.
[3] Zero deaths were recorded for Pacific Islanders and Native Americans.
[4] Latino includes Asian Hispanic, White Hispanic, and Black Hispanic.

Table 2. Gallstone disease diagnosis on a NJ Death Certificate, 2009 to 2018. [Ÿ, †, ¤, ‡, §]

Position on death certificate	Death with symptomatic gallstone disease (SGD) [Ÿ]	
	All SGD n = 1,580	**With cancers omitted [†] n = 1,557 [¤]**
1 [‡]	908 (57.5%)	905 (58.1%)
2	62	55
3	135	122
4	144	130
5	127	117
6	79	73
7	65	60
8	46	44
9	31	28
10	17	16
11	4	4
12	1	1
13	2	2
>1 position occupied	N = 1621[§]	N = 0

[Ÿ] Symptomatic gallstone disease includes cholelithiasis / other gallbladder disease, cholecystitis, gallstone pancreatitis, choledocholithiasis, cholangitis, with choledocholithiasis, and gallstone ileus / gallbladder fistula.

[†] Select cancers removed includes duodenal, gallbladder, pancreas, biliary tract, or liver.

[¤] N=1557 reflects SGD diagnoses in the earliest position for records with >1 diagnosis.

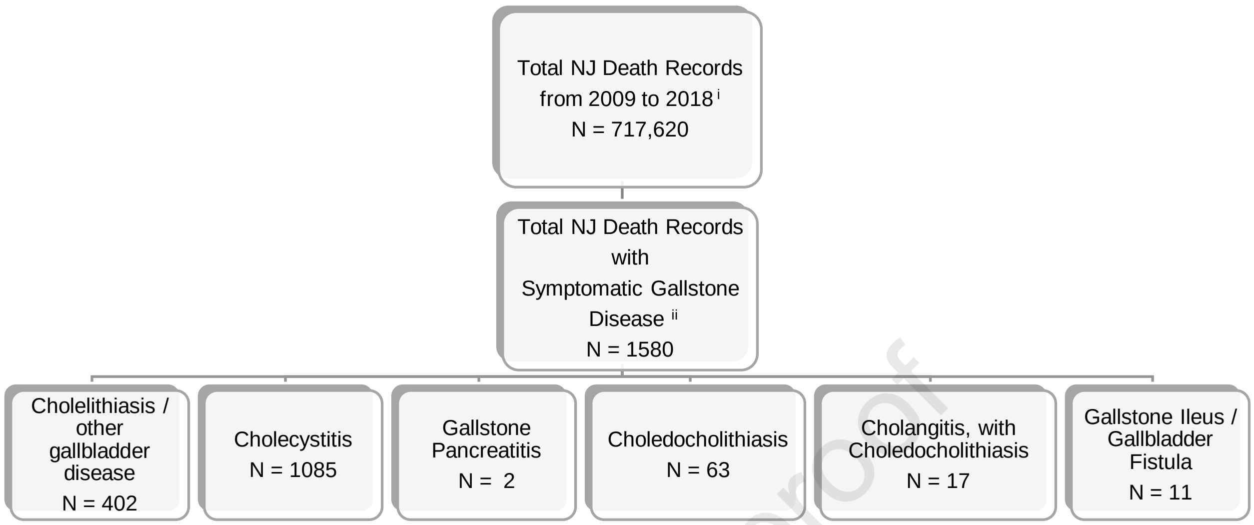
[‡] Position 1 is the 'principal' position; the others are considered 'contributing'.

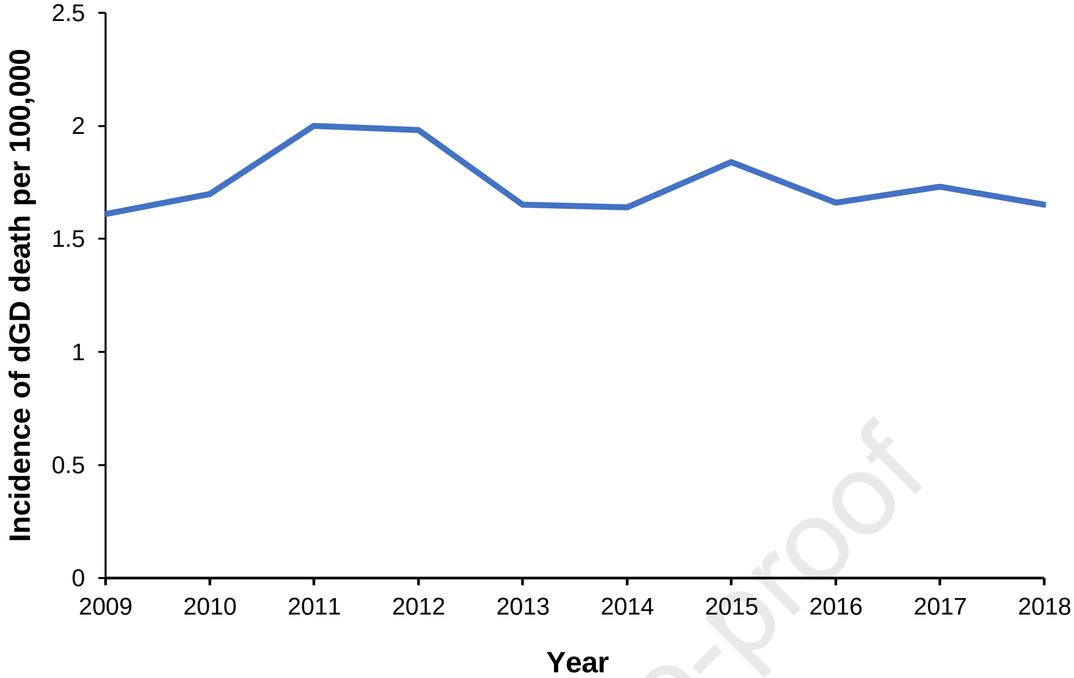
[§] N=1621 is greater than 1,580 because gallstone disease occupies more than one position on some death certificates.

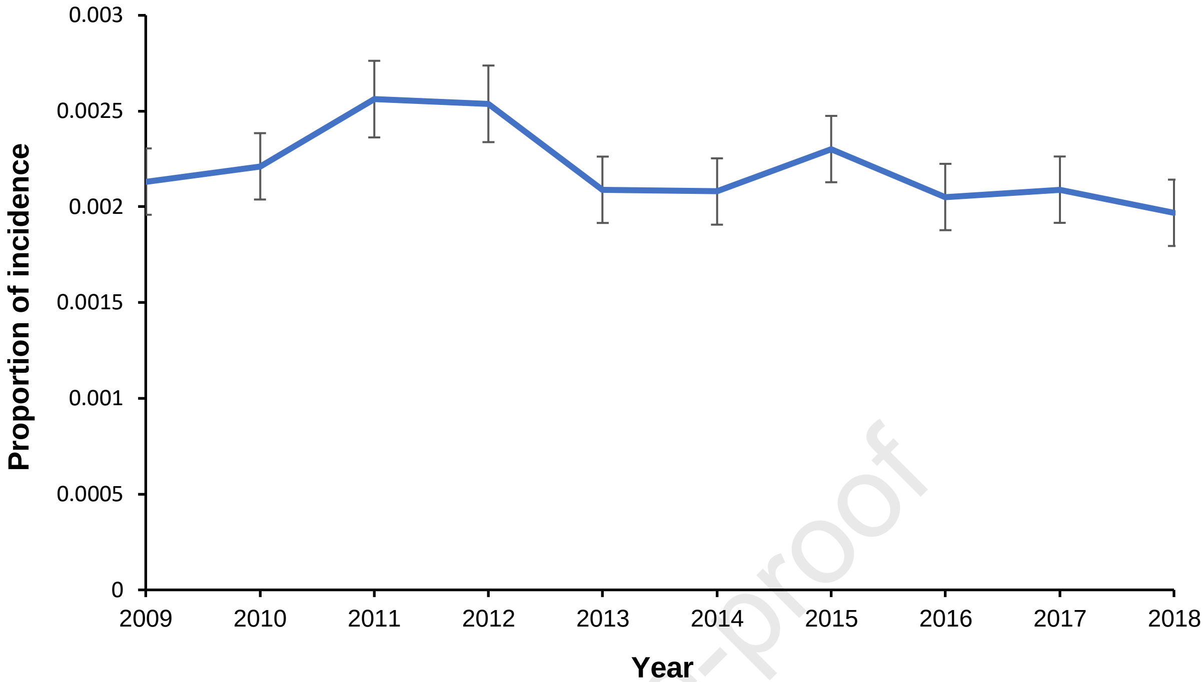
Table 3. Annual Incidence of Diagnosed Gallstone Disease and All Deaths in New Jersey, with dGD incidence of death adjusted for age, sex, and race/ethnicity, individually, 2009 to 2018. [i, ii, iii, iv, v, vi]

	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	Total
dGD											
counts	146	154	181	179	150	148	166	150	157	149	1580
incidence [i]	1.61	1.7	2	1.98	1.65	1.64	1.84	1.66	1.73	1.65	17.48
monthly incidence [ii]	0.134 (.034)	0.142 (.055)	0.167 (.055)	0.165 (.034)	0.138 (.047)	0.136 (.049)	0.153 (.037)	0.138 (.050)	0.145 (.029)	0.137 (.038)	1.74 [iii] (0.045)
All death											
counts	68277	69495	70558	70534	71403	71316	72271	73155	74846	75765	717620
incidence [i]	755.23	768.71	780.47	780.20	789.81	788.42	799.42	809.20	827.90	828.06	7,937.88
Rate of dGD death relative to All deaths [iv]											
proportion	.00213	.00221	.00256	.00254	.00209	.00208	.00230	.00205	.00209	.00197	0.0022
dGD incidence of death adjusted for age											
< 65 years	.22123	.24335	.19910	.30972	.12168	.19911	.25441	.19911	.26547	.21017	2.23
>= 65 years	1.39	1.46	1.80	1.67	1.54	1.44	1.58	1.46	1.47	1.44	15.25
dGD incidence of death adjusted for sex											
Female	1.07	1.02	1.27	1.08	0.88	0.94	1.03	0.97	0.96	0.96	10.20
Male	0.54	0.69	0.73	0.90	0.77	0.70	0.81	0.69	0.77	0.69	7.28
dGD incidence of death adjusted for race/ethnicity [v]											
Black	0.19	0.17	0.22	0.19	0.19	0.13	0.23	0.23	0.21	0.13	1.89
Latino [vi]	0.11	0.09	0.10	0.15	0.17	0.18	0.19	0.14	0.15	0.23	1.51
Asian	0.01	0.07	0.06	0.09	0.08	0.09	0.04	0.07	0.06	0.08	0.65
White	1.30	1.38	1.62	1.55	1.23	1.23	1.37	1.22	1.32	1.21	13.43

[i] Incidence is calculated per 100,000 NJ population using the average of the 2010 and 2020 annual populations from the United States Census Bureau, New Jersey, i.e., 9,040,444.
[ii] Monthly incidences means and standard errors (SEs); SEs in parentheses.
[iii] Total annual incidence mean with SE.
[iv] Proportion of death is calculated using a numerator of incidence of death with diagnosed gallstone disease and a denominator of incidence of all death.
[v] < 0.01 incidence in 2014 is not shown for American Indian subgroup.
[vi] Latino includes Asian Hispanic, White Hispanic, and Black Hispanic.


Total NJ Death Records from 2009 to 2018 i
N = 717,620
Total NJ Death Records with Symptomatic Gallstone Disease ii
N = 1580
Cholelithiasis / other gallbladder disease
N = 402
Cholecystitis
N = 1085
Gallstone Pancreatitis
N = 2
Choledocholithiasis
N = 63
Cholangitis, with Choledocholithiasis
N = 17
Gallstone Ileus / Gallbladder Fistula
N = 11


Incidence of dGD death per 100,000
2.5
2
1.5
1
0.5
0
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
Year


0.003
0.0025
0.002
0.0015
0.001
0.0005
0
Proportion of incidence
2009
2010
2011
2012
2013
2014
2015
2016
2017
2018
Year

Life course

Diagnosed gallstone disease	Levels of Influence			
Domains of Influence	**Individual**	**Interpersonal**	**Community**	**Societal**
Biological	• Cholesterol metabolism and microbiome (individual) • Changes affecting the pathologic composition and size of gallstones • Biomarkers	• Cholesterol metabolism and microbiome (familial) • Genetic predisposition / mutations	• Access to healthy diet or weight loss • Exposure to harmful pharmacologic or environmental agents	• Access to beneficial pharmacologic prevention • Exposure to harmful pharmacologic or environmental agents • Big data on metabolomics
Behavioral	• Patient attitudes, beliefs, skills affecting their response to the first symptoms of abdominal pain • Use of emergency vs. non-emergency care networks • Patient decision making toward surgery or no surgery	• Family response or support of patients in their response to the first symptoms of abdominal pain • Primary care and specialists' decision making toward surgery or no surgery	• Local access to education on healthy diet or weight loss interventions • Local conditioning or facilitation of access to ambulatory rather than hospital care based on cost / reimbursement	• Regional access to education on healthy diet or weight loss interventions • Regional conditioning or facilitation of access to ambulatory rather than hospital care based on insurance
Physical Built Environ.	• Microbiome • Home availability of and proximity to recreation facilities	• Microbiome • Occupational availability of and proximity to recreation facilities • Endoscopic, procedural, and surgical case fatality rate due to clinical provider ethics / training	• Local endoscopic, procedural, and surgical case fatality rate due to facility and workforce capacity • Rural / urban geo-density of fast-food establishments	• Regional endoscopic, procedural, and surgical case fatality rate due to facility and workforce capacity • Policy on air/water quality • Incentives for active transport
Sociocultural Environment	• Intrapersonal bias or racism • Limited English proficiency • Sociodemographic norms / predisposition / protection	• Interpersonal bias or racism • Limited non-English proficiency • Use of emergency vs. non-emergency care networks	• Local institutional bias or racism • Limited institutional interpreters for non-English proficiency • Provision of emergency vs. non-emergency care networks	• Regional institutional bias or racism • Geopolitical variation in multi-disciplinary action and policy making
Health Care System	• Limited English proficiency • Insurance coverage • Distrust or trust in diagnosis/treatment	• Primary care and specialists' decision making toward surgery or no surgery • Provider incentives related to utilization of health care services vs. preventive services • Disparities in clinical / preventive workforce • Patient-centered value-based outcomes	• Local institutional incentives related to utilization of health care services vs. preventive services • Limited institutional interpreters for non-English proficiency • Safety-net preventive health services	• Policy toward preventive services that decrease health care services • Regional institutional incentives related to utilization of health care services vs. preventive services • Quality of primary / procedural / surgical care
Health Outcome	**Individual Health**	**Family / Organizational Health**	**Community Health**	**Population Health**