Kidney Failure Attributed to Immunoglobulin A Nephropathy: A USRDS Retrospective Cohort Study of Epidemiology, Treatment Modalities, and Economic Burden

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Rationale & Objective: This study describes the epidemiology, characteristics, and outcomes of patients with immunoglobulin A nephropathy (IgAN)-attributed kidney failure in the US Renal Data System (USRDS) from 2008 to 2018, including health care resource utilization and costs among patients with Medicare-linked data.

Study Design: Retrospective cohort study.

Setting & Population: Patients with IgAN-attributed kidney failure in the USRDS.

Outcomes: Prevalence/incidence, clinical/demographic characteristics, time to kidney transplant, and health care resource utilization and costs.

Analytical Approach: Patients with IgAN as primary cause of kidney failure (IgAN cohort) were followed from USRDS registration (index date) until data end/death. Prevalence/incidence were calculated per 1,000,000 US persons. Demographic and clinical characteristics at index and treatment modality during follow-up were summarized. Time from index to kidney transplant was assessed using Kaplan-Meier and competing risk analyses. Health care resource utilization and health care costs were reported among patients with 1 year Medicare Part A+B coverage postindex, including or excluding those who died (Medicare Coverage and 1-year Medicare Coverage subgroups, respectively).

Results: The IgAN cohort, Medicare Coverage, and 1-year Medicare Coverage subgroups included 10,101, 1,696, and 1,510 patients, respectively. Mean annual period prevalence and incidence of IgAN-attributed kidney failure were 39.3 and 2.9 per 1,000,000 US persons, respectively. Initial treatment was in-center hemodialysis (63.1%) or kidney transplant (15.1%). Year 1 and 5 kidney transplant rates were 5% and 17%, respectively, accounting for competing risk of death. In the Medicare Coverage and 1-year Medicare Coverage subgroups, 74.4% and 72.3%, respectively, required inpatient admission, 67.3% and 64.4%, respectively, visited the emergency room, and mean total health care costs were \$6,293 (SD: \$6,934) and \$5,284 (\$3,455), respectively, per-patient-per-month in the year postindex.

Limitations: Drug costs may be underestimated as Medicare Part D coverage was not required; kidney acquisition costs were unavailable.

Conclusions: IgAN-attributed kidney failure is associated with substantial clinical and economic burdens. Novel therapies for IgAN that delay kidney failure are needed.

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Immunoglobulin A nephropathy (IgAN) is the glomerular accumulation of IgA-containing immune complexes in the kidneys.[1] IgAN-mediated inflammation may lead to damage of the glomerular filtration barrier, resulting in proteinuria, hematuria, and a progressive decline in the rate of glomerular filtration.[2] It is a rare disease, with annual incidence of approximately 1 per 100,000 individuals in the United States (US).[1] IgAN usually progresses slowly, and patients often remain undiagnosed until presenting with symptoms of kidney disease, such as proteinuria, decreased kidney function, gross hematuria, and hypertension.[3,4] Progression varies among populations, with 15% to 40% of patients eventually developing kidney failure within 10 to 20 years of diagnosis.[5-8] Kidney failure poses a substantial economic burden to health care systems worldwide, largely due to high costs associated with dialysis and transplantation.[4,9,10] In the US, kidney failure affects approximately 786,000 people, with estimated treatment costs of approximately \$51 billion for Medicare beneficiaries in 2019.[11,12] As IgAN progression is associated with greater patient and health care system burden, there is an urgent need to delay IgAN progression and prevent kidney failure.[4]

Although there is no cure for IgAN, certain therapies can slow its progression.[13] However, there are limited options specifically for the treatment of IgAN. Delayed release formulation budesonide (a corticosteroid) received accelerated approved by the US Food and Drug Administration to reduce proteinuria in adults with primary IgAN at risk of rapid disease progression.[14] Other commonly used treatments include angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers, which may be used in combination with dietary sodium restrictions to control proteinuria and blood pressure.[13] Immunosuppressive drugs are considered for patients who remain at high risk of progressive chronic kidney disease despite

PLAIN-LANGUAGE SUMMARY

This study of patients in the United States Renal Data System (USRDS) observed fluctuating incidence and increasing prevalence of immunoglobulin A nephropathy (IgAN)-attributed kidney failure from 2008 to 2018. Patients experienced a high clinical burden, with 63% receiving in-center dialysis and over 15% receiving transplantation as initial therapy. In the first year after USRDS registration, nearly three-quarters of patients with Medicare coverage required hospitalization, and around two-thirds visited the emergency room. The total annual health care costs were >$63,000 per patient with IgAN-attributed kidney failure, underscoring the high economic burden of this disorder and currently available treatments. Novel therapies for IgAN are needed to delay or prevent the need for costly dialysis and transplantation after kidney failure.

maximal supportive therapy.[15] However, the value of even short-term systemic immunosuppression remains controversial due the lack of high quality evidence of its efficacy and the multiple side effects caused by glucocorticoids, particularly as glomerular filtration rate (GFR) declines.[13]

A detailed understanding of the epidemiology and treatment landscape of IgAN-attributed kidney failure is crucial to meeting the unmet medical needs of this patient population. However, there is a lack of real-world evidence on the US epidemiology, patient characteristics, treatment modalities, clinical outcomes, and health care resource utilization (HRU) related to patients with IgAN and in particular those who progress to kidney failure. To address this gap, this retrospective observational study aimed to characterize patients with IgAN-attributed kidney failure, including estimates of prevalence and incidence and descriptions of patient characteristics, treatment modalities, and clinical outcomes, using the US Renal Data System (USRDS) database. Additionally, HRU and direct health care costs were described for the subgroup of patients with IgAN-attributed kidney failure with linked Medicare claims data.

METHODS

Data Source

This study used data from the USRDS spanning from 2008 to 2018.[16] The USRDS is the national data registry that collects, analyzes, and distributes information on the kidney failure population in the US, including treatments and outcomes. In the database, kidney failure is defined as chronic kidney failure requiring maintenance with kidney replacement treatment (ie, dialysis or kidney transplant) to sustain life. All patients with kidney failure in the US, regardless of insurance coverage and age, are included in the USRDS database. Kidney health care providers must immediately complete a Medical Evidence Report (MER) form for kidney failure patients to register them in the Centers for Medicare & Medicaid Services end-stage kidney disease database and to apply for Medicare eligibility if not previously eligible. Medicare is the US federal program providing health care coverage to persons aged 65 years or those of any age with certain medical conditions, including kidney failure. Linked Medicare claims data are available for kidney failure patients with Medicare coverage, allowing analysis of HRU and direct health care costs. The Medicare claims data include information from Part A (hospital insurance available to all beneficiaries), Part B (optional coverage for physician services, outpatient care, physical therapy, and some home health), and Part D (optional prescription drug coverage for Medicare enrollees). Medicare Parts B and D require monthly premiums.

This study received an exemption from ethical review by the WCG Institutional Review Board on March 20, 2021 (IRB # 17-1409204-1).

Study Design and Sample Selection

In this retrospective cohort study, patients with IgAN-attributed kidney failure (IgAN cohort) were identified as those whose primary cause of kidney failure, as recorded in the MER form by the attending physician at registration, was IgAN. The MER form includes a field for the primary cause of kidney failure using International Classification of Diseases 9th (ICD-9-CM; 1995-2014) or 10th edition (2015 onward) diagnosis codes; patients with IgAN as the primary cause of kidney failure were identified using codes 583.81 and N02.8, respectively.

The *index date* was defined as the date of registration in the USRDS data (ie, the earliest date of first dialysis or transplant). The *follow-up period* was defined as the period from the index date until the first date of death, loss to follow-up, or end of data availability.

Among patients in the IgAN cohort, a *Medicare Coverage subgroup* was constructed of individuals with ≥1 year of continuous Medicare Part A and B coverage following the index date or until death, if death occurred within 1 year postindex. The *1-year Medicare Coverage subgroup* was constructed to include only patients with ≥1 year of continuous Medicare Part A and B coverage following the index date (ie, excluding patients who died within 1 year of the index date). For both subgroups, cardiovascular events, HRU, and direct health care costs during the 1-year period following the index date were reported, as they had the linked Medicare claims required for these analyses.

Study Measures

Epidemiology

Estimates of the US prevalence and incidence of IgAN-attributed kidney failure were calculated per 1,000,000 persons per year from 2008 to 2018, overall and by age groups (<18 and ≥18 years). Incidence was estimated as the number of IgAN-attributed kidney failure patients whose index dates occurred during the reporting year, divided by the size of the US population during the corresponding year.[17,18] Prevalence was estimated as the number of IgAN-attributed kidney failure patients who were alive and whose index dates occurred before the reporting year, divided by the size of the US population during the corresponding year.[17,18]

Patient Characteristics

Demographics, laboratory values of estimated GFR, and selected comorbid conditions (hypertension, diabetes, and congestive heart failure) as reported at USRDS registration were summarized overall and among the Medicare subgroups.

Treatment Modalities

The types of dialysis (ie, hemodialysis or peritoneal) and/or kidney transplant received by IgAN-attributed kidney failure patients as of the index date, during the first-year postindex, and during the entire follow-up period were described as recorded in the USRDS. Time on dialysis during the follow-up period was summarized.

Clinical Outcomes

Patient clinical outcomes included time to kidney transplant, time to death, and the 10 most common causes of death among the overall cohort. Additionally, rates of cardiovascular events were assessed for the Medicare subgroups during the 1-year period postindex.

Health Care Resource Utilization and Health Care Costs

Among the Medicare subgroups, HRU and direct health care costs were summarized in the 1-year period postindex, stratified by place of service (outpatient, inpatient, emergency room [ER], home health agency, skilled nursing facility, hospice, or other). "Other" costs comprised those incurred at places of service outside of the other categories and includes some kidney failure treatment facilities. For patients with an inpatient stay, the total number of inpatient days was summarized. Prescription drug costs were summarized. Direct health care costs were also separately reported for subgroups defined by treatment received, considering the following 4 mutually exclusive groups: kidney transplant, in-center hemodialysis only, peritoneal dialysis only, and other/mixed dialysis.

Statistical Analyses

Incidence and prevalence of IgAN-associated kidney failure were reported using counts and rates per 1,000,000 persons in the US population. Continuous variables were described using means, medians, and standard deviations (SD); categorical variables were described using frequencies and percentages.

The time from index to kidney transplant and to death was assessed using Kaplan-Meier (KM) analyses with patients censored at the earliest date of death, loss to follow-up, or data end. The median times to kidney transplant and death were reported, as well as rates at 1, 3, 5, and 10 years with 95% confidence intervals (CIs). Time to kidney transplant and to death were also assessed using competing risk estimators, with death and kidney transplant as the respective competing risks.

HRU and health care costs for the Medicare subgroups were estimated per-patient-per month (PPPM) to account for different follow-up times across patients. Health care costs were adjusted to 2020 US dollars. Annual results for the 1-year Medicare Coverage subgroup are presented in Tables S1-S4.

All analyses were conducted using SAS Enterprise Guide Software v7.1 (SAS Institute, Inc., Cary, NC, US) and R software v4.0.3 (R Foundation for Statistical Computing, Vienna, Austria), including the cmprsk package for competing risk analysis.

RESULTS

Sample Selection

Of the 3,135,443 patients in the USRDS database, 10,101 were included in the IgAN cohort while 1,696 and 1,510 were included in the Medicare Coverage and 1-year Medicare Coverage subgroups, respectively (Fig 1).

Incidence and Prevalence of IgAN-Attributed Kidney Failure

During 2008 to 2018, the mean annual period prevalence and incidence rates of IgAN-attributed kidney failure were 39.3 and 2.9 per million US persons, respectively (Fig 2). The mean period prevalence of IgAN-attributed kidney failure was lower among patients aged <18 years compared to adults aged ≥18 years (3.8 vs. 50.2 per million, respectively) and higher among males than females (52.3 vs 26.7 per million) (Table S1). Native Hawaiian/Pacific Islanders experienced the highest mean period prevalence (380.5 per million), followed by Asians (107.1 per million) (Table S2).

Patient Baseline Characteristics

Baseline demographic and clinical characteristics of the overall IgAN cohort and Medicare subgroups are shown in Table 1.[19] Among the IgAN cohort, the mean (SD) age at USRDS registration was 47.7 (15.9) years, and the proportion of males was 65.8%. Most patients were White (75.8%) or Asian (14.3%). The most common individual comorbid condition was history of hypertension (87.5%), followed by diabetes (12.9%).

Among the Medicare Coverage subgroup, the mean (SD) age at USRDS registration was 59.7 (17.1) years, with 66.6% male. The majority of patients were White (80.9%), and the most common comorbid condition was history of hypertension (88%), followed by diabetes (23.3%). Among the 1-year Medicare Coverage subgroup, mean (SD) age was 58.2 (17.1) years, and the proportion

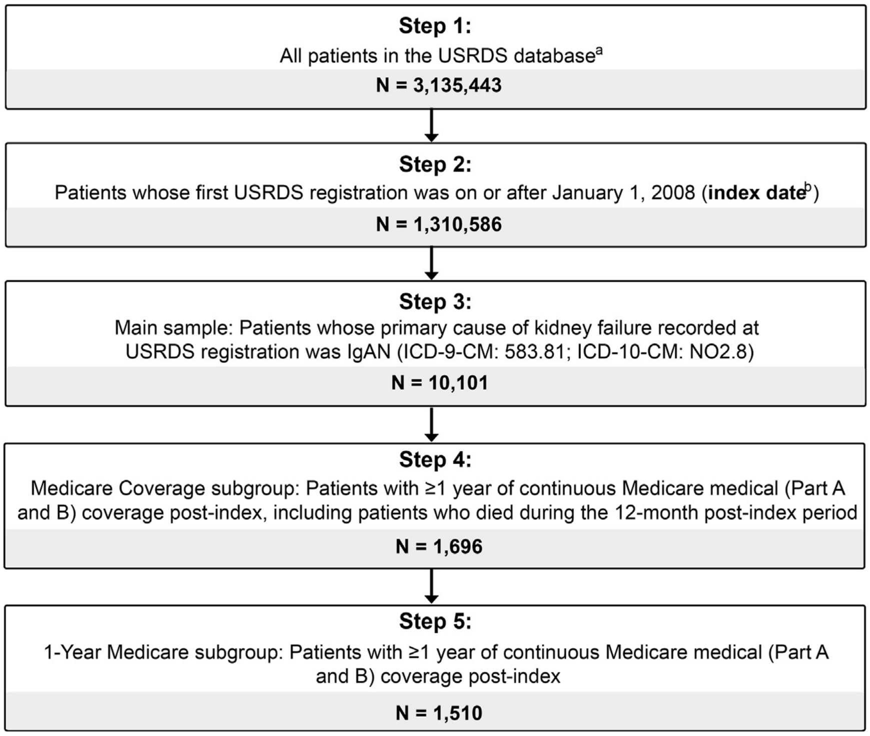


Figure 1. Sample selection. *Notes*: [a]Included patients with a record in both the patient's file and in the medical evidence form file. The patient's file was used to collect their USRDS registration date. The medical evidence form file was used to collect their demographics and additional information from their kidney failure registration. [b]The index date was defined as the date of first USRDS registration. Abbreviations: ICD-9-CM, International Classification of Diseases, 9th Revision, Clinical Modification; ICD-10-CM, International Classification of Diseases, 10th Revision, Clinical Modification; IgAN, immunoglobulin A nephropathy; USRDS, United States Renal Data System.

of males was 66.5%. Most patients (80.1%) were White, and the most common comorbid condition was history of hypertension (89.5%).

Treatment Modalities

The mean follow-up time for the overall cohort with IgAN-attributed kidney failure was 64.0 (36.4) months. The most common initial treatment modalities (ie, treatment received at USRDS registration) were in-center hemodialysis (63.1%) and peritoneal dialysis (21.5%), while 15.1% of patients received a kidney transplant as their initial treatment and 0.3% received home hemodialysis (Fig 3). In the first year after the index date, the proportion of IgAN-attributed kidney failure patients receiving a kidney transplant increased nearly 2-fold to 28.2%, and, across the entire study period, over half (53.2%) of patients received a kidney transplant. The mean time spent on dialysis of any type was 3.2 (2.5) years. On average, patients spent over 2 years on in-center hemodialysis and peritoneal dialysis.

Clinical Outcomes

Kidney Transplant and Death

A total of 5,376 patients had a kidney transplant during the follow-up period, and the median time to transplant was 3.8 years. Kidney transplant rates from the KM analysis were 29% at 1 year and 57% at 5 years (Fig 4). A total of 2,133 patients died during the follow-up period, and the median time to death was not reached. Mortality rates at 1 and 5 years from the KM analysis were 5% and 17%, respectively (Fig 4). After accounting for death as a competing risk of kidney transplant, transplant rates decreased from 75% to 63% at 10 years postindex. The most common specified causes of death were cardiac arrest (4.7%) and withdrawal from dialysis/uremia (2.7%); the second most common cause of death was undefined/unknown (3.1%) (Table 2).

Rates of Cardiac Events

Among the Medicare Coverage and 1-year Medicare Coverage subgroups, 42.6% and 37.8%, respectively, had a cardiovascular event of any type during the 1-year period following the index date (Table S3). The most common cardiovascular events in both subgroups were heart failure (26.8% and 22.6%, respectively) and atrial fibrillation (19.5% and 16.0%).

Health Care Resource Utilization

In the 12-month period following USRDS registration, 74.4% of the Medicare Coverage subgroup required

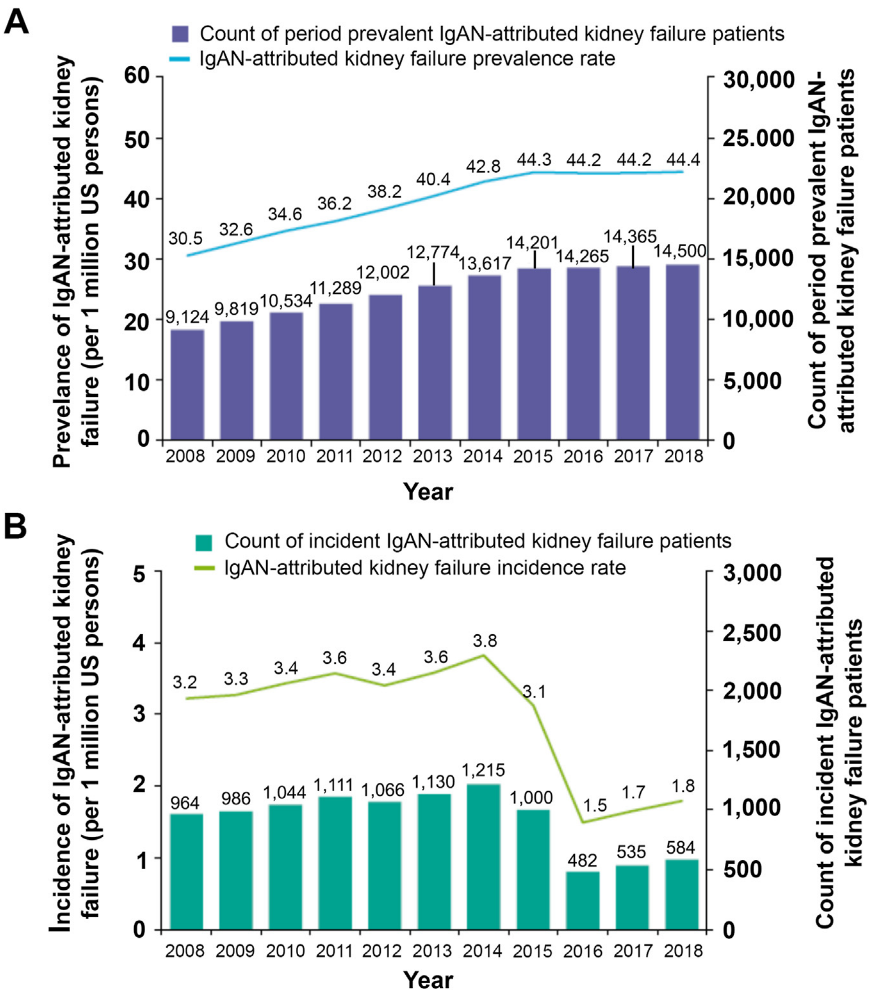


Figure 2. Prevalence and incidence of IgAN-attributed kidney failure. Abbreviations: IgAN, immunoglobulin A nephropathy; US, United States.

inpatient admission, with an average of 3.6 inpatient days PPPM, and 67.3% visited the emergency room (Table 3). Additionally, 54.0% of patients had home health visits, and 13.1% required visits to skilled nursing facilities. Among the 1-year Medicare Coverage subgroup, 72.3% required inpatient admission, with an average of 2.4 inpatient days PPPM, and 64.4% visited the emergency room (ER). The mean number of outpatient visits in both Medicare Coverage subgroups was 2.5 PPPM.

Health Care Costs

In the Medicare Coverage subgroup, the mean (SD) monthly health care costs were $6,293 ($6,934), driven by inpatient ($2,592 [$6,685]) and outpatient ($2,206 [$1,761]) costs (Table 4). The analysis of health care costs by treatment type during the follow-up period revealed that patients with in-center hemodialysis incurred the highest costs ($7,779 [$8,825] PPPM), followed by other/mixed dialysis ($6,047 [$4,198] PPPM). Total annual health care costs for this population were estimated at $107 million.

In the 1-year Medicare Coverage subgroup, which excluded patients who died during the first year postindex, the mean (SD) total health care costs PPPM during the 1-year period following USRDS registration were $5,284 ($3,455), comprised of medical ($5,040 [$3,348]) and pharmacy ($244 [$498]) costs (Table 4). Outpatient visits constituted most of these costs ($2,215 [$1,738]), followed by inpatient visits ($1,666 [$2,774]). In this sample, patients with in-center hemodialysis incurred the highest mean (SD) total PPPM health care costs ($6,087 [$3,555]), followed by those with other/mixed dialysis ($5,761 [$3,968]). Patients with kidney transplant incurred the highest mean (SD) inpatient costs ($2,723 [$2,879]). Because all patients in the 1-year Medicare Coverage subgroup had a full year of follow-up postindex, annual costs are presented in Table S4. The mean (SD) total annual health care costs were $63,403 ($41,462), driven by outpatient ($26,584 [$20,852]) and inpatient ($19,995 [$33,290]) costs. The total health care costs were estimated at $95.7 million for this subgroup during the 1-year follow-up period.

Table 1. Patient Characteristics

	IgAN-attributed kidney failure patients (n=10,101)	Medicare Coverage subgroup (n=1,696)	1-y Medicare Coverage subgroup (n=1,510)
Demographic Characteristics			
Age at index, mean (SD) [median]	47.7 (15.9) [47.0]	59.7 (17.1) [65.0]	58.2 (17.1) [62.7]
Male, n (%)	6,650 (65.8%)	1,130 (66.6%)	1,004 (66.5%)
Race, n (%)			
White	7,661 (75.8%)	1,372 (80.9%)	1,209 (80.1%)
Asian	1,446 (14.3%)	155 (9.1%)	149 (9.9%)
Black	644 (6.4%)	108 (6.4%)	97 (6.4%)
Native Hawaiian or Other Pacific Islander	168 (1.7%)	22 (1.3%)	20 (1.3%)
Other	182 (1.8%)	39 (2.3%)	35 (2.3%)
Medical coverage at index[a] (%)			
Employer group health insurance	5,185 (51.3%)	260 (15.3%)	237 (15.7%)
Medicare coverage	2,237 (22.1%)	1,228 (72.4%)	1,051 (69.6%)
Other medical insurance	1,748 (17.3%)	495 (29.2%)	437 (29.0%)
Medicaid coverage	1,682 (16.7%)	406 (23.9%)	366 (24.2%)
No medical insurance	758 (7.5%)	114 (6.7%)	114 (7.5%)
Medicare Advantage	299 (3.0%)	24 (1.4%)	19 (1.3%)
Clinical Characteristics			
eGFR (mL/min/1.73m^2),[b] mean (SD) [median]	9.1 (5.3) [8.2]	9.8 (6.0) [8.8]	9.6 (6.0) [8.7]
Comorbidities, n (%)[c]			
History of hypertension	8,843 (87.5%)	1,506 (88.8%)	1,352 (89.5%)
Diabetes	1,301 (12.9%)	395 (23.3%)	321 (21.3%)
Congestive heart failure	736 (7.3%)	276 (16.3%)	215 (14.2%)
Follow-up duration (mo),[d] mean (SD) [median]	64.0 (36.4) [62.7]	55.6 (35.1) [52.9]	61.9 (32.0) [57.7]

Notes: [a]Patients may have had multiple types of medical coverage. [b]eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation and reported directly in the Medical Evidence file of the USRDS data.[19] [c]The top 3 comorbidities recorded in the Medical Evidence file are shown. [d]Follow-up duration was calculated as the time from the index date until the earliest of death, loss to follow-up, or end of data availability.
Abbreviations: eGFR, estimated glomerular filtration rate; IgAN, immunoglobulin A nephropathy; SD, standard deviation; USRDS, United States Renal Data System.

DISCUSSION

This retrospective cohort study of patients with IgAN-attributed kidney failure in the USRDS found evidence that the prevalence of IgAN-attributed kidney failure in the US has been increasing over time and that the disorder imposes a substantial clinical and economic burden on patients and the health care system. This study observed that the US incidence of IgAN-attributed kidney failure increased steadily from 2008 to 2014, from 3.2 to 3.8 persons per million, while the prevalence continued rising

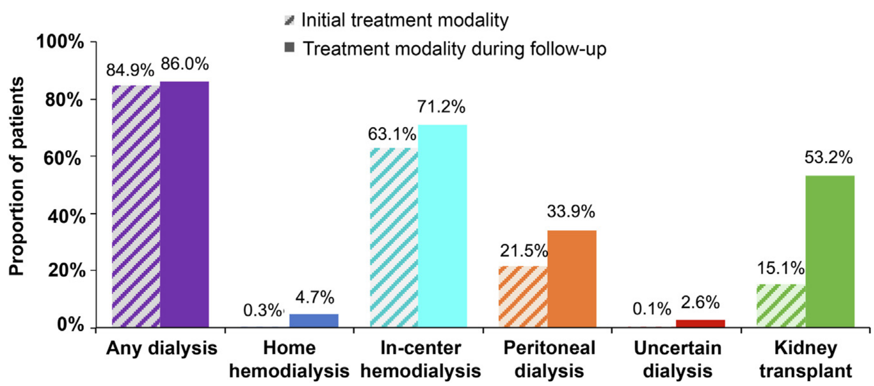
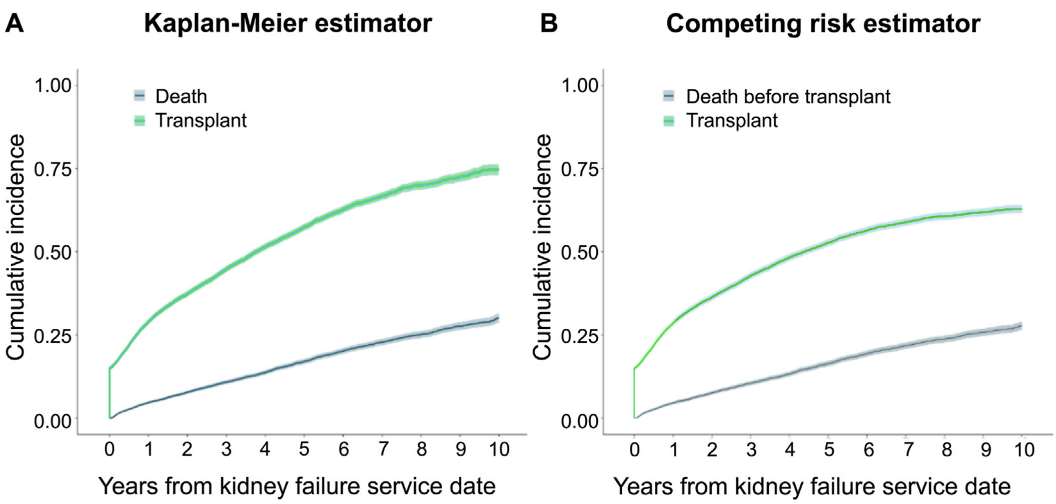


Figure 3. Initial and follow-up period treatment modalities among patients with IgAN-attributed kidney failure (N=10,101). During the follow-up period, patients may have received more than 1 treatment modality. The initial and follow-up treatment modalities were not mutually exclusive, and the treatments summarized for the follow-up period include the initial treatment. The percent for uncertain dialysis as initial treatment modality is not shown as this included fewer than 11 patients. Abbreviation: IgAN, immunoglobulin A nephropathy.



Years from kidney failure service date	Transplant Incidence (95% CI)		Death incidence (95% CI)	
	Kaplan-Meier	Competing Risk	Kaplan-Meier	Competing Risk
1 year	0.290 (0.281, 0.299)	0.286 (0.277, 0.295)	0.047 (0.043, 0.051)	0.046 (0.042, 0.050)
3 years	0.448 (0.437, 0.458)	0.427 (0.417, 0.437)	0.108 (0.102, 0.114)	0.105 (0.098, 0.111)
5 years	0.574 (0.563, 0.586)	0.528 (0.517, 0.538)	0.170 (0.162, 0.178)	0.163 (0.156, 0.171)
10 years	0.747 (0.729, 0.764)	0.628 (0.616, 0.640)	0.301 (0.287, 0.315)	0.277 (0.265, 0.289)

Figure 4. Cumulative incidence curves of death and kidney transplant in the IgAN-attributed kidney failure cohort using Kaplan-Meier and competing risk estimators. In the Kaplan-Meier analysis, patients were censored at the earliest of date of death (for the time to transplant analysis only), loss to follow-up, or end of data availability. In the competing risk analysis of time to transplant, patients were censored at the earliest of loss to follow-up or end of data availability; death was considered a competing risk. In the competing risk analysis of time to death before transplant, patients were censored at the earliest of loss to follow-up or end of data availability; transplant was considered a competing risk. Abbreviations: CI, confidence interval; IgAN, immunoglobulin A nephropathy.

until 2015, from 30.5 (in 2008) to 44.3 persons per million. Incidence decreased more than 2-fold between 2014 and 2016 from 3.8 to 1.5 per million before beginning to increase again, causing the prevalence to taper at approximately 44.3 per million in 2015 and remain relatively steady until 2018. However, the reduction in incidence and prevalence may be associated with a change in the MER forms used at USRDS patient registration. Specifically, the forms used from 1995 until mid-2015 provided disease names and ICD-9-CM codes to choose from, while the forms used from mid-2015 until 2018 did not. This may have led to uncertainty regarding which codes to use to identify IgAN as the cause of kidney failure and potentially an undercounting of IgAN-attributed kidney failure starting in mid-2015.

Table 2. The 10 Most Common Causes of Death Among Patients With IgAN-Attributed Kidney Failure

	IgAN-Attributed Kidney Failure N=10,101
Cause of death, n (%)	
Patients who died (any cause)	2,133 (21.1%)
Cardiac arrest, cause unknown	475 (4.7%)
Withdrawal from dialysis/uremia	273 (2.7%)
Septicemia, other	111 (1.1%)
Other identified cause of death, not specified	101 (1.0%)
Myocardial infarction, acute	56 (0.6%)
Malignant disease	52 (0.5%)
Cerebrovascular accident (including intracranial hemorrhage)	41 (0.4%)
Cachexia	38 (0.4%)
Cardiac arrhythmia	31 (0.3%)
Unknown	317 (3.1%)

Abbreviations: IgAN, immunoglobulin A nephropathy.

The clinical burden observed for this study's cohort was high. Patients in the USRDS with IgAN-attributed kidney failure relied more on kidney transplantation than the general kidney failure population, with 53% receiving a transplant over the entire study period compared to approximately 30% in the general prevalent kidney failure population with a functioning transplant.[16] In particular, the rate of preemptive kidney transplant (ie, the initial mode of kidney failure treatment) was higher among the IgAN-attributed kidney failure population in our study (15%) compared to the general kidney failure population in the USRDS (3% in 2020).[16] This may in part be attributed to the population with IgAN being younger and having fewer comorbid conditions than the general kidney failure population, resulting in a higher proportion being good candidates for kidney transplantation.

Table 3. HRU for the Medicare Coverage and 1-Year Medicare Coverage Subgroups During the 1-Year Period Following the Index Date

HRU	Proportion with ≥1 Visit n (%)	Number of Visits PPPM[a] Mean (SD) [median]
Medicare Coverage subgroup	N=1,696	N=1,696
Inpatient admissions	1,261 (74.4%)	0.2 (0.3) [0.1]
Inpatient length of stay,[b] (days)	—	3.6 (5.3) [1.6]
Outpatient visits	1,656 (97.6%)	2.5 (1.5) [2.3]
Emergency room visits	1,142 (67.3%)	0.3 (0.6) [0.1]
Home health agency visits	916 (54.0%)	0.4 (0.7) [0.1]
Skilled nursing facility visits	223 (13.1%)	0.7 (3.0) [0.0]
Hospice	33 (1.9%)	0.1 (1.2) [0.0]
1-y Medicare Coverage subgroup	N=1,510	N=1,510
Inpatient admissions	1,091 (72.3%)	0.2 (0.2) [0.1]
Inpatient length of stay,[b] (days)	—	2.4 (3.2) [1.2]
Outpatient visits	1,482 (98.2%)	2.5 (1.5) [2.3]
Emergency room visits	972 (64.4%)	0.2 (0.3) [0.1]
Home health agency visits	816 (54.0%)	0.4 (0.6) [0.1]
Skilled nursing facility visits	144 (9.5%)	0.4 (2.4) [0.0]
Hospice[c]	<11	0.0 (0.8) [0.0]

Notes: [a]The number of visits was calculated among all patients in the Medicare Coverage subgroup. [b]Inpatient length of stay was calculated among patients in the Medicare Coverage subgroup with at least 1 inpatient admission. [c]The number and percent of patients with a hospice visit is not shown as this included fewer than 11 patients.
Abbreviations: HRU, health care resource utilization; PPPM, per-patient-per-month; SD, standard deviation.

HRU and health care costs were also high among the subset of patients with Medicare-linked data, with >70% requiring hospitalization and >60% visiting the ER in the year after USRDS registration. Of those with inpatient admissions, patients required an average 2-3 days PPPM in the hospital. Hospitalization and emergency care were not the only large contributors to HRU and costs—the mean number of outpatient visits was approximately 2.5 PPPM. The total annual health care costs across the entire Medicare Coverage subgroup totaled over $100 million. It should be noted that the true cost is assumed to be much higher because the cost of organ acquisition during kidney transplant could not be assessed. Given the high rate of kidney transplant observed in this patient population, these costs are likely to be substantial. For example, the average kidney transplant cost in the US was $442,500 in 2020.[20]

This study also provides evidence of the high costs associated with mortality in this population. For example, while the PPPM total health care costs were $5,284 when excluding patients who died, including these patients increased the PPPM total health care costs to $6,293. The largest increase was observed in inpatient costs, rising from $1,666 to $2,592 PPPM when patients who died were included in the sample.

The prevalence of kidney failure overall has risen steadily over the past 30 years, along with increasing expenditure for related services, adjusted for inflation. In 2018, total Medicare-related expenditures for beneficiaries with kidney failure were $49.2 billion, increasing to $51 billion in 2019.[16] These costs are driven by the chronic and progressive nature of the disease and costly treatment modalities such as dialysis and kidney transplant. Moreover, these treatments not only impose an economic burden on payors and health care providers, but a high clinical burden on patients due to potential complications of surgery and the substantial time devoted to dialysis sessions. Novel therapies which target the source of kidney failure, to delay or entirely prevent the need for transplant or dialysis, may be an effective approach for addressing this large health care burden and improving patients' clinical outcomes.

This study benefits from multiple strengths, including the use of USRDS data, a comprehensive and contemporary longitudinal data source on the kidney failure population in the US. This permitted the construction of a large cohort with IgAN-attributed kidney failure as well as subgroups for specific analyses. In addition, the ability to link USRDS data to Medicare claims data allowed for the analysis of HRU and health care costs for subgroups of the cohort. The results of this study are also subject to several limitations, some of which are inherent to claims database analyses such as the potential for data miscoding or missingness. First, patients are included in the USRDS only if they receive treatment for kidney failure (dialysis or transplant). Accordingly, for this study and all studies using USRDS data, kidney failure should be interpreted as "treated KF." Second, the analyses of HRU are limited to patients with Medicare coverage for the 12-month period following the index date. Patients who progress to kidney failure typically become eligible for Medicare coverage, although the timing of eligibility and enrollment may vary.[21] As patients with Medicare at the index date are more likely to be aged ≥65 years, their HRU may not be representative of the general population with IgAN-attributed kidney failure or those with non-Medicare insurance coverage; in

Table 4. Health Care Costs for the Medicare Coverage and 1-Year Medicare Coverage Subgroups During the 1-Year Period Following the Index Date, Overall and by Treatment Categories

PPPM health care Costs,[a] mean (SD) Median [25th-75th percentile]	Overall	By Treatment Received[b]			
		In-center hemodialysis	Peritoneal	Other/mixed dialysis[c]	Kidney transplant
Medicare Coverage Subgroup, N	1,696	862	331	226	277
Total health care costs	6,293 (6,934) 4,851 [3,564-7,103]	7,779 (8,825) 5,750 [4,205-8,795]	4,033 (2,726) 3,822 [3,101-4,600]	6,047 (4,198) 5,187 [3,791-7,016]	4,569 (3,604) 4,173 [2,192-6,301]
Pharmacy	237 (486) 87 [0-261]	266 (481) 109 [0-300]	188 (619) 69 [0-200]	197 (364) 96 [0-246]	237 (399) 26 [0-275]
Medical	6,056 (6,905) 4,614 [3,402-6,789]	7,513 (8,819) 5,414 [3,968-8,351]	3,845 (2,629) 3,661 [2,998-4,353]	5,850 (4,168) 4,848 [3,670-6,885]	4,332 (3,497) 4,012 [1,937-6,112]
Inpatient	2,592 (6,685) 635 [0-2,917]	3,487 (8,784) 982 [37-3,769]	603 (2,383) 0 [0-286]	1,933 (3,676) 420 [10-2,551]	2,723 (2,879) 2,658 [542-3,674]
Outpatient	2,206 (1,761) 2,084 [540-3,585]	2,463 (1,846) 2,535 [665-3,910]	2,311 (1,505) 2,910 [620-3,481]	2,617 (1,881) 2,966 [695-3,840]	944 (933) 630 [344-1,175]
ER	46 (108) 14 [0-51]	67 (141) 27 [0-75]	17 (30) 0 [0-22]	42 (69) 15 [0-56]	19 (41) 0 [0-25]
HHA	140 (352) 0 [0-129]	117 (316) 0 [0-91]	49 (172) 0 [0-14]	99 (449) 0 [0-65]	355 (439) 213 [1-515]
Hospice	3 (69) 0 [0-0]	5 (97) 0 [0-0]	0 (5) 0 [0-0]	0 (0) 0 [0-0]	0 (0) 0 [0-0]
SNF	71 (440) 0 [0-0]	129 (578) 0 [0-0]	0 (7) 0 [0-0]	38 (389) 0 [0-0]	2 (36) 0 [0-0]
Other[d]	998 (1,191) 357 [97-1,963]	1,245 (1,286) 546 [229-2,521]	864 (1,059) 276 [118-1,764]	1,121 (1,161) 501 [203-2,170]	289 (619) 16 [0-211]
1-y Medicare Coverage subgroup, N	1,510	691	327	215	277
Total health care costs	5,284 (3,455) 4,599 [3,459-6,375]	6,087 (3,555) 5,203 [4,036-7,380]	3,878 (1,800) 3,812 [3,095-4,583]	5,761 (3,968) 5,055 [3,708-6,850]	4,569 (3,604) 4,173 [2,192-6,301]
Pharmacy	244 (498) 99 [0-269]	286 (501) 143 [0-321]	190 (622) 76 [0-200]	198 (361) 96 [0-249]	237 (399) 26 [0-275]
Medical	5,040 (3,348) 4,377 [3,310-6,036]	5,801 (3,438) 4,949 [3,792-7,005]	3,689 (1,637) 3,660 [2,969-4,344]	5,563 (3,935) 4,713 [3,526-6,599]	4,332 (3,497) 4,012 [1,937-6,112]
Inpatient	1,666 (2,774) 422 [0-2,512]	1,801 (2,820) 591 [18-2,343]	443 (1,007) [0-266]	1,734 (3,550) 295 [7-2,094]	2,723 (2,879) 2,658 [542-3,674]
Outpatient	2,215 (1,738) 2,179 [556-3,584]	2,556 (1,805) 2,808 [772-3,946]	2,325 (1,507) 2,934 [640-3,487]	2,593 (1,892) 2,956 [658-3,816]	944 (933) 630 [344-1,175]
ER	32 (62) 12 [0-41]	42 (75) 18 [0-50]	16 (29) 0 [0-21]	40 (67) 14 [0-55]	19 (41) 0 [0-25]
HHA	140 (347) 0 [0-133]	113 (301) 0 [0-88]	43 (127) 0 [0-13]	96 (456) 0 [0-63]	355 (439) 213 [1-515]
Hospice	2 (71) 0 [0-0]	4 (105) 0 [0-0]	0 (0) 0 [0-0]	0 (0) 0 [0-0]	0 (0) 0 [0-0]

(Continued)

Table 4 (Cont'd). Health Care Costs for the Medicare Coverage and 1-Year Medicare Coverage Subgroups During the 1-Year Period Following the Index Date, Overall and by Treatment Categories

PPPM health care Costs,[a] mean (SD) Median [25th-75th percentile]		By Treatment Received[b]			
	Overall	In-center hemodialysis	Peritoneal	Other/mixed dialysis[c]	Kidney transplant
SNF	35 (239) 0 [0-0]	72 (343) 0 [0-0]	0 (7) 0 [0-0]	11 (111) 0 [0-0]	2 (36) 0 [0-0]
Other[d]	950 (1,167) 325 [90-1,859]	1,213 (1,282) 479 [227-2,497]	861 (1,059) 276 [118-1,764]	1,090 (1,133) 499 [200-2,151]	289 (619) 16 [0-211]

Notes: [a]Health care costs were evaluated during the 12-month period immediately following the index date, or until death. All health care costs were inflated to 2020 USD and presented on a PPPM basis to account for varying follow-up times. [b]Patients were categorized into mutually exclusive groups based on the treatment modality received during the 12 months following the index date. [c]Other/mixed dialysis includes home hemodialysis, uncertain dialysis, or multiple types of dialysis during the follow-up period. [d]Other medical services include claims where the place of service is not inpatient, outpatient, ER, HHA, hospice, or SNF. This includes but is not limited to kidney failure treatment facilities, assisted living facilities, community mental health centers, inpatient psychiatric facilities, independent care, ambulatory surgical centers, nursing facilities, state/local public health clinics, and urgent care facilities.
Abbreviations: ER, emergency room; HHA, home health agency; PPPM, per-patient-per-month; SD, standard deviation; SNF, skilled nursing facility; USD, United States dollars.

addition, the cost analyses reflect payments by Medicare and may not be representative of costs to other insurers. Third, health care costs associated with kidney transplants did not include organ acquisition costs, which are assumed to be substantial but are not available in the Medicare claims data. Fourth, as Medicare Part D coverage was not required, prescription drug costs may be underestimated in this study. However, a sensitivity analysis was conducted among a sample of patients with Medicare Part D coverage required. Although the sample size was reduced substantially (ie, from 1,510 to 507 patients), pharmacy costs represented approximately 6% of total costs (compared to 4.6% in the current sample), indicating that prescription drugs were not a large driver of total costs for these patients.

In conclusion, IgAN-attributed kidney failure is associated with a substantial burden to patients and health care systems in the US. There is a high unmet medical need for IgAN treatments that delay or prevent the need for dialysis and/or transplantation and reduce the risk of death among this patient population.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Table S1. Prevalence and incidence of IgAN-attributed kidney failure by year and age groups.

Table S2. US prevalence and incidence of IgAN-attributed kidney failure by race/ethnic group.

Table S3. Patients with cardiovascular events during the 1-year period following the index date among the Medicare Coverage and 1-year Medicare Coverage subgroups.

Table S4. Annual costs for the 1-year Medicare Coverage subgroup during the 1-year period following the index date, overall and by treatment category.

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