AJKD
Original Investigation

Distribution of Biopsy-Proven Presumed Primary Glomerulonephropathies in 2000-2011 Among a Racially and Ethnically Diverse US Population

John J. Sim, MD,[1] Michael Batech, DrPH,[2] Aviv Hever, MD,[3] Teresa N. Harrison, SM,[2] Taurino Avelar, MD,[1] Michael H. Kanter, MD,[4] and Steven J. Jacobsen, MD, PhD[2]

Background: The incidence and distribution of primary glomerulonephropathies vary throughout the world and by race and ethnicity. We sought to evaluate the distribution of primary glomerulonephropathies among a large racially and ethnically diverse population of the United States.

Study Design: Case series from January 1, 2000, through December 31, 2011.

Setting & Participants: Adults (aged ≥ 18 years) of an integrated health system who underwent native kidney biopsy and had kidney biopsy findings demonstrating focal segmental glomerulosclerosis (FSGS), membranous glomerulonephritis (MGN), minimal change disease (MCD), immunoglobulin A nephropathy (IgAN), and other.

Outcomes: Rates and characteristics of the most common primary glomerulonephropathies overall and by race and ethnicity.

Results: 2,501 patients with primary glomerulonephropathy were identified, with a mean age 50.6 years, 45.7% women, 36.1% Hispanics, 31.2% non-Hispanic whites, 17.4% blacks, and 12.4% Asians. FSGS was the most common glomerulonephropathy (38.9%) across all race and ethnic groups, followed by MGN (12.7%), MCD (11.0%), IgAN (10.2%), and other (27.3%). The FSGS category had the greatest proportion of blacks, and patients with FSGS had the highest rate of poverty. IgAN was the second most common glomerulonephropathy among Asians (28.6%), whereas it was 1.2% among blacks. Patients with MGN presented with the highest proteinuria (protein excretion, 8.3 g) whereas patients with FSGS had the highest creatinine levels (2.6 mg/dL). Overall glomerulonephropathy rates increased annually in our 12-year observation period, driven by FSGS (2.7 cases/100,000) and IgAN (0.7 cases/100,000). MGN and MCD rates remained flat.

Limitations: Missing data for urine albumin and sediment, indication bias in performing kidney biopsies, and inexact classification of primary versus secondary disease.

Conclusions: Among a racially and ethnically diverse cohort from a single geographical area and similar environment, FSGS was the most common glomerulonephropathy, but there was variability of other glomerulonephropathies based on race and ethnicity.

Am J Kidney Dis. 68(4):533-544.

INDEX WORDS: Primary glomerulonephropathy; glomerulonephritis; nephrotic syndrome; focal segmental glomerulosclerosis (FSGS); membranous glomerulonephritis (MGN); minimal change disease (MCD); IgA nephropathy (IgAN); epidemiology; race/ethnic predilection; kidney biopsy; case series.

Editorial, p. 503

Glomerulonephropathies are major contributors to kidney failure throughout the world.[1,2] They are the most common cause of end-stage renal disease (ESRD) in certain countries. In the United States of America, glomerulonephropathies rank as the third most common cause of ESRD and thus account for a significant proportion of the $31 billion in annual Medicare costs for ESRD care.[3] The incidence of glomerulopathy-related ESRD has increased in the past 30 years, though it has steadied in the past decade.[3] Worldwide, primary glomerulonephropathy occurs at a rate of up to 2 to 3 cases per 100,000 individuals,[4] and glomerulonephropathies account for more than 100,000 patients with ESRD in the United States.[3]

From the [1]Division of Nephrology and Hypertension, Kaiser Permanente Los Angeles Medical Center; Departments of [2]Research & Evaluation and [3]Renal Pathology, Kaiser Permanente Southern California, Los Angeles; and [4]Regional Quality and Clinical Analysis, Southern California Permanente Medical Group, Kaiser Permanente Southern California, Pasadena, CA.

Received December 10, 2015. Accepted in revised form March 9, 2016. Originally published online April 30, 2016.

Address correspondence to John J. Sim, MD, Division of Nephrology and Hypertension, Kaiser Permanente Los Angeles Medical Center, 4700 Sunset Blvd, Los Angeles, CA 90027. E-mail: john.j.sim@kp.org

0272-6386
http://dx.doi.org/10.1053/j.ajkd.2016.03.416

The distribution and incidence of the different primary glomerulonephropathies vary across countries, race and ethnic groups, and time periods. This suggests the possibility that multiple risk factors play a role in glomerulonephropathy, including environment and innate biological properties. Although immunoglobulin A nephropathy (IgAN) has been the most prevalent glomerulonephropathy described throughout most countries,[5-17] membranous glomerulonephritis (MGN) or focal segmental glomerulosclerosis (FSGS) is the most common in other countries, including the United States.[18-23] There have been variations in time periods as well, with a trend toward increased rates of FSGS in many countries.[2,21,24] Certain race and ethnic groups have been strongly linked with specific glomerulonephropathies, such as IgAN among Asians[2,6,8,10,11] and FSGS among blacks.[22] These population-based studies have been drawn from predominantly homogeneous populations reflective of the country or area of practice. Thus, aside from identified genetic causes of certain glomerulonephropathies, the contributions of environment and/or inborn physiognomies on the risk for glomerulonephropathy is not well known, but is the subject of much speculation.

Given the heterogeneous population of the United States, it is not well known what the distributions of glomerulonephropathies are within different race and ethnic groups that reside in similar areas and environments. Specifically, it would be of interest to determine and compare the distribution of glomerulonephropathies among Hispanics and Asians in addition to whites and blacks within the United States. We sought to characterize primary glomerulonephropathies among a large ethnically diverse contemporary adult population in the Southwestern region of the United States. Using the health information for more than 3 million members of an integrated health system, we reviewed all native kidney biopsies performed over a 12-year period. Based on biopsy findings only, we identified diagnoses presumed to be primary glomerulonephropathy to determine the distribution of primary glomerulonephropathies among the general population and by different race and ethnic groups.

METHODS

Study Overview

A retrospective cohort study was performed in January 1, 2000, through December 31, 2011, within the Kaiser Permanente Southern California (KPSC) health system. KPSC is an integrated prepaid health plan with 14 medical centers and more than 200 satellite medical offices that geographically spans from Bakersfield to San Diego, CA. As of July 2015, there were more than 4 million KPSC members. The membership population is racially and ethnically diverse, reflective of the underlying population and Southern California in general.[25-27] Compared to the distribution of the US population, the KPSC membership has twice as many Asians and 3 times as many Hispanics. Members have similar access to health visits, medications, procedures, and medication and supply benefits. As part of routine clinical care, KPSC maintains all member information collected in the electronic health record (EHR). This includes information for demographics, comorbid conditions, vital signs, laboratory and imaging results, pathology reports, and medications. Race and ethnic information are entered into the EHR based on either patient self-report or provider assessment. Nearly all Hispanics within KPSC are Hispanic whites; Hispanic blacks account for $<1\%$ of KPSC members. Thus, the designation of Hispanics within our study refers to Hispanic whites. All laboratory measurements are performed and reported from an American College of Pathology/Clinical Laboratory Improvement Act (CLIA)-certified laboratory. Income information was derived using resident address and the US Census tract information. This study was approved by the local institutional review board (IRB #5815) and exempted from informed consent.

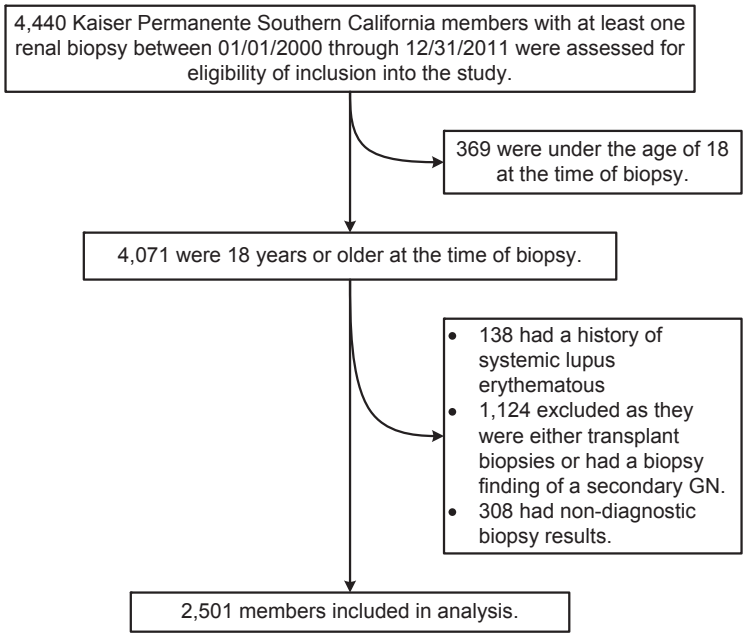

Figure 1. Study population flow diagram. In January 1, 2000, through December 31, 2011, a total of 4,440 Kaiser Permanente Southern California members had a kidney biopsy. Among this cohort, 369 were younger than 18 years and 308 had inconclusive biopsy results. Another 138 had a history of systemic lupus erythematous, and 1,124 were either transplant biopsies or findings revealing secondary glomerulonephropathy (GN). Thus, 2,501 individuals with primary glomerulonephropathy were included in the study cohort.

Table 1. Study Population Characteristics by Most Common Primary Glomerulonephropathy Disease States, 2000-2011

	FSGS (n = 973 [38.9%])	MGN (n = 317 [12.7%])	MCD (n = 274 [11.0%])	IgAN (n = 255 [10.2%])	Other[a] (n = 682 [27.3%])	Total (N = 2,501)	P
Age at index date, y							<0.001
Mean ± SD	51.1 ± 16.21	52.0 ± 15.35	49.9 ± 17.45	42.8 ± 13.23	52.5 ± 17.93	50.6 ± 16.67	
Median	52	52	50	42	54	51	
Range	18.0-91.0	18.0-83.0	18.0-87.0	18.0-84.0	18.0-91.0	18.0-91.0	
Patient sex							0.004
Female	419 (43.1)	130 (41)	136 (49.6)	110 (43.1)	347 (50.9)	1142 (45.7)	
Male	554 (56.9)	187 (59)	138 (50.4)	145 (56.9)	335 (49.1)	1359 (54.3)	
Race/ethnicity							<0.001
Asian, non-Hispanic	129 (13.3)	28 (8.8)	26 (9.5)	73 (28.6)	55 (8.1)	311 (12.4)	
Black, non-Hispanic	217 (22.3)	59 (18.6)	50 (18.2)	3 (1.2)	107 (15.7)	436 (17.4)	
Hispanic	325 (33.4)	113 (35.6)	89 (32.5)	105 (41.2)	271 (39.7)	903 (36.1)	
Other, non-Hispanic	22 (2.3)	4 (1.3)	16 (5.8)	9 (3.5)	19 (2.8)	70 (2.8)	
White, non-Hispanic	280 (28.8)	113 (35.6)	93 (33.9)	65 (25.5)	230 (33.7)	781 (31.2)	
Neighborhood household income[b]							0.03
Mean ± SD, in 1,000's USD	61.1 ± 26.8	62.7 ± 27.0	65.1 ± 28.0	65.8 ± 25.6	64.0 ± 28.2	63.0 ± 27.3	
<$25,000	66 (6.8)	13 (4.1)	17 (6.2)	11 (4.3)	30 (4.4)	137 (5.5)	
$25,000-$49,999	341 (35)	111 (35)	70 (25.5)	72 (28.2)	223 (32.7)	817 (32.7)	
$50,000-$99,999	487 (50.1)	157 (49.5)	160 (58.4)	147 (57.6)	365 (53.5)	1,316 (52.6)	
≥$100,000	79 (8.1)	36 (11.4)	27 (9.9)	25 (9.8)	64 (9.4)	231 (9.2)	
History of hypertension	734 (75.4)	195 (61.5)	153 (55.8)	156 (61.2)	431 (63.2)	1,669 (66.7)	<0.001
History of diabetes	274 (28.2)	51 (16.1)	38 (13.9)	30 (11.8)	141 (20.7)	534 (21.4)	<0.001
Body mass index							<0.001
No. with data	681	203	112	219	379	1,594	
Mean ± SD, kg/m^2	30.9 ± 7.34	30.2 ± 6.16	31.9 ± 7.93	29.0 ± 6.21	28.7 ± 6.47	30.1 ± 6.97	
≤25 kg/m^2	150 (22)	38 (18.7)	20 (17.9)	57 (26)	117 (30.9)	382 (24)	
25-<30 kg/m^2	200 (29.4)	76 (37.4)	32 (28.6)	84 (38.4)	120 (31.7)	512 (32.1)	
30-≤35 kg/m^2	158 (23.2)	49 (24.1)	27 (24.1)	48 (21.9)	88 (23.2)	370 (23.2)	
>35 kg/m^2	173 (25.4)	40 (19.7)	33 (29.5)	30 (13.7)	54 (14.2)	330 (20.7)	

Note: Unless otherwise indicated, values are given as number (percentage). Percentages are totaled across the individual columns.

Abbreviations: FSGS, focal segmental glomerulosclerosis; IgAN, immunoglobulin A nephropathy; MCD, minimal change disease; MGN, membranous glomerulonephritis; SD, standard deviation; USD, US dollar.

[a]Included immune complex glomerulonephropathy not otherwise specified (n = 206), pauci immune/antineutrophil cytoplasmic antibody–associated glomerulonephropathy (n = 178), thin basement membrane disease (n = 121), membranoproliferative glomerulonephritis (n = 50), crescentic glomerulonephropathy not otherwise specified (n = 48), postinfectious glomerulonephritis, anti–glomerular basement membrane disease, fibrillary glomerulonephropathy, dense deposit disease, and others.

[b]Neighborhood income is not reported income but is estimated on the basis of members' addresses using neighborhood income from US Census tract information.

Study Population

All members 18 years and older who underwent a native kidney biopsy were identified for potential inclusion in the study cohort. Individual paper and electronic chart reviews were performed to identify and categorize biopsy findings and diagnoses. Biopsies that had a main diagnosis of primary glomerulonephropathy were included in the study. For individuals who had multiple biopsies, the first biopsy result was used in our study and analyses. Primary glomerulonephropathies to be identified on chart review included FSGS, IgAN, minimal change disease (MCD), MGN, membranoproliferative glomerulonephritis (MPGN) including dense deposit disease, pauci-immune glomerulonephritis/antineutrophil cytoplasmic antibody (ANCA)-associated glomerulonephritis, immune complex nephropathy, crescentic glomerulonephritis not otherwise specified, postinfectious glomerulonephritis, anti–glomerular basement membrane glomerulonephritis, fibrillary glomerulonephritis, and others. Exclusion criteria were members younger than 18 years at the time of biopsy, transplant biopsies, history of systemic lupus erythematous (SLE), and biopsies that demonstrated inconclusive findings or a secondary glomerulonephropathy. Secondary glomerulonephropathies that were excluded were diabetic glomerulosclerosis, SLE-associated nephritis, amyloidosis, nephrocalcinosis, Bence-Jones/cast nephropathy, myelodysplastic disorder–associated glomerulonephropathy, human immunodeficiency virus (HIV)-associated nephropathy, urate nephropathy, sarcoidosis, Alport disease, light or heavy chain deposition disease, and oxalate nephropathy.

Kidney Biopsies at KPSC

All kidney biopsy information in the study period was obtained from routine clinical practice, whereby all biopsies were determined as clinically indicated by the practitioners. Kidney biopsies are performed in both the inpatient and outpatient settings, with nearly all member biopsies occurring at a KPSC medical center.[28] Approximately 3% are performed at non-KPSC facilities, but all specimens are transported to the KPSC renal pathology department for processing and reading. All samples are received at the

Table 2. Clinical Laboratory Markers by Most Common Biopsy-Proven Primary Glomerulonephropathy Disease States, 2000-2011

	FSGS (n = 973 [38.9%])	MGN (n = 317 [12.7%])	MCD (n = 274 [11.0%])	IgAN (n = 255 [10.2%])	Other (n = 682 [27.3%])	Total (N = 2,501)	*P*
Serum creatinine							<0.001
No. with data	954	310	262	253	654	2,433	
Mean ± SD, mg/dL	2.6 ± 1.9	1.4 ± 1.0	1.7 ± 1.4	1.9 ± 1.5	3.1 ± 2.5	2.4 ± 2.0	
Median [IQR], mg/dL	2.1 [1.4-3.2]	1.1 [0.8-1.5]	1.3 [0.8-2.1]	1.5 [1.1-2.1]	2.2 [1.3-3.9]	1.7 [1.1-2.9]	
Range, mg/dL	0.4-15.4	0.4-8.3	0.4-10.6	0.5-15.0	0.5-15.2	0.4-15.4	
eGFR[a]							<0.001
No. with data	954	310	262	253	654	2,433	
Mean ± SD, mL/min/1.73 m^2	40.6 ± 28.2	74.5 ± 34.3	64.3 ± 37.9	56.2 ± 31.3	40.6 ± 34.1	49.1 ± 34.5	
Median [IQR], mL/min/1.73 m^2	32.5 [19.8-54.4]	76.1 [47.8-101.4]	60.7 [31.3-94.8]	49.4 [33.1-79.5]	30.3 [13.2-57.4]	39.9 [21.3-71.4]	
Range, mL/min/1.73 m^2	3.8-143.5	6.1-153.8	4.3-157.1	3.4-137.4	3.0-136.8	3.0-157.1	
SUN, mg/dL							<0.001
No. with data	943	310	261	249	649	2412	
Mean ± SD	35.1 ± 21.6	20.9 ± 14.9	27.9 ± 22.0	27.1 ± 17.7	40.0 ± 25.5	33.0 ± 22.6	
Median [IQR]	30 [19.0-44.0]	17 [12.0-24.0]	21 [13.0-35.0]	21 [16.0-34.0]	33 [20.0-55.0]	26 [17.0-43.0]	
Range	6.0-130.0	6.0-115.0	6.0-133.0	7.0-101.0	6.0-138.0	6.0-138.0	
Serum albumin							<0.001
No. with data	854	299	242	217	595	2,207	
Mean ± SD, g/dL	3.3 ± 0.8	2.4 ± 0.8	2.8 ± 1.1	3.6 ± 0.6	3.0 ± 0.8	3.1 ± 0.9	
Median [IQR], g/dL	3.5 [2.9-3.9]	2.3 [1.8-3.1]	3 [1.8-3.7]	3.7 [3.3-4.0]	3.1 [2.4-3.6]	3.3 [2.4-3.8]	
Range, g/dL	1.0-4.8	0.9-4.6	0.9-4.7	1.4-4.7	0.9-4.8	0.9-4.8	
Urine protein quantification	710 (73.0)	220 (69.4)	148 (54.0)	214 (83.9)	393 (57.6)	1,685 (67.4)	<0.001
24-h urinary total protein							<0.001
No. with data	227	103	34	92	82	538	
Mean ± SD, g	4.9 ± 5.2	8.3 ± 6.4	6.7 ± 4.8	2.3 ± 1.9	3.4 ± 3.3	5.0 ± 5.2	
Median [IQR], g	3.3 [1.5-6.2]	6.5 [3.5-11.0]	4.8 [3.5-8.9]	1.6 [0.8-3.5]	2.1 [0.7-5.1]	3.4 [1.5-6.5]	
Range, g	0.1-30.9	0.7-31.8	0.2-17.1	0.0-7.7	0.1-13.2	0.0-31.8	
Urine PCR							<0.001
No. with data	452	131	68	145	218	1,014	
Mean ± SD, g/g	4.6 ± 4.4	8.3 ± 5.4	5.3 ± 4.6	2.3 ± 2.1	3.5 ± 4.4	4.6 ± 4.6	
Median [IQR], g/g	3.4 [1.5-6.5]	7.2 [4.3-11.6]	3.8 [1.6-8.4]	1.7 [0.8-3.2]	1.9 [0.9, -4.2]	3 [1.3-6.3]	
Range, g/g	0.1-24.9	0.4-28.7	0.1-19.3	0.1-15.4	0.1-24.1	0.1-28.7	

(Continued)

Table 2 (Cont'd). Clinical Laboratory Markers by Most Common Biopsy-Proven Primary Glomerulonephropathy Disease States, 2000-2011

	FSGS (n = 973 [38.9%])	MGN (n = 317 [12.7%])	MCD (n = 274 [11.0%])	IgAN (n = 255 [10.2%])	Other (n = 682 [27.3%])	Total (N = 2,501)	P
Urine ACR							<0.001
No. with data	583	175	115	159	294	1,326	
Mean ± SD, g/g	2.7 ± 2.6	5.2 ± 3.4	3.2 ± 3.6	1.5 ± 1.5	2.0 ± 2.6	2.8 ± 2.9	
Median [IQR], g/g	2 [0.9-3.7]	4.6 [2.5-7.4]	1.8 [0.5-4.1]	1.1 [0.4-2.2]	1.0 [0.3-2.7]	1.8 [0.7-3.8]	
Range, g/g	0.0-14.6	0.0-16.7	0.0-15.8	0.0-8.6	0.0-18.3	0.0-18.3	
Hematuria[b]	254/691 (36.8)	106/220 (48.2)	53/139 (38.1)	141/216 (65.3)	306/430 (71.2)	860/1,696 (50.7)	<0.001

Note: Unless otherwise indicated, categorical values are given as number (percentage). Comparisons between each laboratory measure and the glomerulonephropathy categories were made using χ^2 or Fisher exact test for categorical variables and Kruskal-Wallis or analysis of variance for continuous variables, as appropriate. Patients with MGN had the highest degree of proteinuria and lowest serum albumin levels at the time of biopsy. Other and FSGS had the highest creatinine values at biopsy.

Abbreviations: ACR, albumin-creatinine ratio; eGFR, estimated glomerular filtration rate; FSGS, focal segmental glomerulosclerosis; IgAN, immunoglobulin A nephropathy; IQR, interquartile range; MCD, minimal change disease; MGN, membranous glomerulonephritis; PCR, protein-creatinine ratio; SD, standard deviation; SUN, serum urea nitrogen.

[a]Estimated with the Chronic Kidney Disease Epidemiology Collaboration creatinine equation.

[b]Defined as any urine dipstick result ≥ 1+ for blood or urine microscopy reporting 5 or more red blood cells/high-power field. Numbers are reported as number of patients with hematuria over total number with available laboratory measurement (percentage).

KPSC regional laboratory in North Hollywood, CA, for processing and preparation. All samples are separately prepared in hematoxylin-eosin, Masson trichrome, periodic acid–Schiff, and Jones methenamine silver stains for light microscopy viewing. Immunofluorescence studies and electron microscopy viewing are performed on all specimens. When prepared, samples are sent to Los Angeles Medical Center for review and interpretation by 2 renal pathologists. After each renal pathologist views the specimens separately, the final diagnoses are determined after a consensus is reached by the 2 renal pathologists.

Kidney biopsy results were extracted by chart review performed by 4 research associates (see Acknowledgements). Results were categorized based on the primary diagnoses as reported on the pathology report. Any discrepancies in results were adjudicated by both a nephrologist (J.J.S.) and a renal pathologist (A.H.). If there were 2 primary diagnoses, a prioritization algorithm was used to consistently and reliably prioritize based on which primary glomerulonephropathy would be more likely (Fig S1, available as online supplementary material). For example, FSGS is often a descriptive finding and also a primary glomerulonephropathy. When another concrete glomerulonephropathy such as IgAN or MPGN was reported concurrently as the primary diagnosis, those primary glomerulonephropathies would take precedence over FSGS as the primary biopsy diagnosis.

Analysis Plan

The objective of the study was to identify all KPSC members who had biopsy-proven primary glomerulonephropathy and determine the distribution and characteristics of the common glomerulonephropathies among race and ethnic groups. Demographic and laboratory characteristics were compared across the 4 most prevalent glomerulonephropathies using χ^2 or Fisher exact test for categorical variables and Kruskal-Wallis or analysis of variance for continuous variables, as appropriate. Shapiro-Wilks test of normality assessed the normality assumption of parametric tests. In addition, we reported age- and sex-adjusted (standardized) rates among patients overall and for the 4 most prevalent glomerulonephropathies (FSGS, MCD, IgAN, and MGN) by year to determine average annual rates of the different glomerulonephropathies in our observation window. Using KPSC's electronic enrollment records for each patient, we first combined all enrollment periods with less than a 30-day gap in enrollment coverage. The person-time denominator for each rate is the number of patients who were members at any stage in the year by age, sex, and year weighed by the time each person was a member in that year. For example, a man in 2002 who was a member for 6 calendar months would contribute 0.5 male-year to the 2002 denominator. The numerator is the sum of the number of patients who had each reported event in that year. Age- and sex-adjusted rates were subsequently directly standardized to the 2000 age and sex distribution of the United States.[29] Use of the US Standard Population in 2000 for age and sex adjustment ensures valid comparison of the rates computed for each of the study years. Standard errors for the rates are estimated assuming a Poisson distribution. All rates are reported per 100,000 person-years, all tests were 2 sided, and all analyses were performed using SAS, version 9.3 (SAS Institute Inc).

RESULTS

Biopsy Numbers and Study Population

A total of 4,440 kidney biopsies were performed at KPSC in January 1, 2000, through December 31, 2011. There were 369 biopsies performed on members younger than 18 years, 1,124 biopsies were either transplant biopsies or had a diagnosis of secondary

Table 3. Age- and Sex-Adjusted Incidence of the Most Common Biopsy-Proven Primary Glomerulonephropathy Disease States by Year and All Years Combined Among Members, 2000-2011

	2000 (n = 145)	2001 (n = 144)	2002 (n = 139)	2003 (n = 169)	2004 (n = 174)	2005 (n = 172)	2006 (n = 216)	2007 (n = 206)	2008 (n = 222)	2009 (n = 258)	2010 (n = 303)	2011 (n = 353)	All Years Combined
Overall													
New cases	145	144	139	169	174	172	216	206	222	258	303	353	2,501
Person-y at risk	2,084,875	2,151,545	2,231,244	2,226,002	2,190,386	2,236,411	2,313,282	2,368,610	2,391,020	2,402,749	2,439,293	2,567,451	27,602,867
Rate	5.3	5.3	4.7	5.7	6.3	5.8	7.4	7.3	7.3	8.9	9.7	10.7	7.1
SE	0.5	0.5	0.4	0.5	0.6	0.5	0.6	0.6	0.6	0.7	0.7	0.6	0.2
FSGS													
New cases	49	55	42	54	40	64	71	82	84	113	133	186	973
Person-y at risk	2,084,875	2,151,545	2,231,244	2,226,002	2,190,386	2,236,411	2,313,282	2,368,610	2,391,020	2,402,749	2,439,293	2,567,451	27,602,867
Rate	1.6	2	1.3	1.7	1.4	2.1	2.5	2.9	3	3.8	4.1	5.3	2.7
SE	0.2	0.3	0.2	0.2	0.3	0.3	0.4	0.4	0.4	0.4	0.4	0.4	0.1
MGN													
New cases	16	14	15	24	31	20	29	34	34	23	33	44	317
Person-y at risk	2,084,875	2,151,545	2,231,244	2,226,002	2,190,386	2,236,411	2,313,282	2,368,610	2,391,020	2,402,749	2,439,293	2,567,451	27,602,867
Rate	0.7	0.6	0.5	0.8	1	0.6	0.9	1	1	0.7	1	1.4	0.9
SE	0.2	0.2	0.1	0.2	0.2	0.1	0.2	0.2	0.2	0.1	0.2	0.2	0.1
MCD													
New cases	34	29	32	21	28	24	34	14	15	17	11	15	274
Person-y at risk	2,084,875	2,151,545	2,231,244	2,226,002	2,190,386	2,236,411	2,313,282	2,368,610	2,391,020	2,402,749	2,439,293	2,567,451	27,602,867
Rate	1.2	1.2	1.2	0.7	0.9	0.8	1.1	0.8	0.4	0.6	0.5	0.4	0.8
SE	0.2	0.3	0.3	0.1	0.2	0.2	0.2	0.3	0.1	0.2	0.2	0.1	0.1
IgAN													
New cases	4	9	6	7	7	6	13	37	37	34	52	43	255
Person-y at risk	2,084,875	2,151,545	2,231,244	2,226,002	2,190,386	2,236,411	2,313,282	2,368,610	2,391,020	2,402,749	2,439,293	2,567,451	27,602,867
Rate	0.1	0.3	0.2	0.2	0.2	0.2	0.4	1.4	1.1	1.2	1.6	1.6	0.7
SE	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.3	0.2	0.2	0.2	0.3	0.1

(Continued)

Table 3 (Cont'd). Age- and Sex-Adjusted Incidence of the Most Common Biopsy-Proven Primary Glomerulonephropathy Disease States by Year and All Years Combined Among Members, 2000-2011

	2000 (n = 145)	2001 (n = 144)	2002 (n = 139)	2003 (n = 169)	2004 (n = 174)	2005 (n = 172)	2006 (n = 216)	2007 (n = 206)	2008 (n = 222)	2009 (n = 258)	2010 (n = 303)	2011 (n = 353)	All Years Combined
Other													
New cases	42	37	44	63	68	58	69	39	52	71	74	65	682
Person-y at risk	2,084,875	2,151,545	2,231,244	2,226,002	2,190,386	2,236,411	2,313,282	2,368,610	2,391,020	2,402,749	2,439,293	2,567,451	27,602,867
Rate	1.6	1.2	1.5	2.4	2.7	2	2.5	1.2	1.8	2.6	2.6	1.9	2
SE	0.3	0.2	0.2	0.4	0.4	0.3	0.4	0.2	0.3	0.4	0.4	0.2	0.1

Note: The total rate of primary glomerulonephropathy in the observation window was 7.1 cases/100,000 person-years. FSGS and IgAN rates increased throughout the observation period, whereas MCD and MGN rates remained stable. All rates are reported as per 100,000 person-years and standardized to the US Census 2000 population. Population at risk is the overall Kaiser Permanente Southern California population, 18 years or older, in that year.

Abbreviations: FSGS, focal segmental glomerulosclerosis; IgAN, immunoglobulin A nephropathy; MCD, minimal change disease; MGN, membranous glomerulonephritis; SE, standard error.

glomerulonephropathy, and 308 kidney biopsies had an inconclusive result; 138 members were excluded for having a history of SLE. Thus, a total of 2,501 native kidney biopsies that had a diagnosis of primary glomerulonephropathy were included in our study (Fig 1). Mean age of the study population was 50.6 ± 16.7 (standard deviation) years, with 45.7% being women. Hispanics accounted for 36.1% of the study population, followed by non-Hispanic whites (31.2%), blacks (17.4%), Asians (12.4%), and others (2.8%; Table 1). In terms of comorbid conditions, hypertension (66.7%) and diabetes mellitus (21.4%) were prevalent among the study population. Ninety-five percent of the cohort had household income in the $25,000 to $99,999 range.

Distribution and Characteristics of Glomerulonephropathies

Among the 4 most prevalent primary glomerulonephropathies, FSGS was most common (n = 973 [38.9%]), followed by MGN (n = 317 [12.7%]), MCD (n = 274 [11.0%]), and IgAN (n = 255 [10.2%]; Table 1). A total of 682 (27.3%) biopsies were categorized as other, which included immune complex glomerulonephropathy not otherwise specified, pauci-immune/ANCA-associated glomerulonephropathy, thin basement membrane disease, membranoproliferative glomerulonephropathy, crescentic glomerulonephropathy not otherwise specified, postinfectious glomerulonephritis, anti–glomerular basement membrane disease, fibrillary glomerulonephropathy, dense deposit disease, and others. Of those, the descriptive category of immune complex nephropathy not otherwise specified (n = 206) and pauci-immune/ANCA-associated glomerulonephritis (n = 178) accounted for the largest proportion. There were 50 diagnoses of MPGN, which accounted for 2.0% of study population (Table S1).

Laboratory findings with mean and median values are reported in Table 2. Mean and median serum creatinine values at the time of kidney biopsy were 2.4 mg/dL (estimated glomerular filtration rate, 49 mL/min/1.73 m^2) and 1.7 mg/dL (estimated glomerular filtration rate, 40 mL/min/1.73 m^2), respectively (Table 2). The highest creatinine level at biopsy was in the "other" glomerulonephropathy group (3.1 mg/dL), followed by FSGS (2.6 mg/dL) and IgAN (1.9 mg/dL). Mean serum albumin level was 3.1 g/dL for the cohort; MGN had the lowest mean serum albumin level (2.4 g/dL). Urine protein quantification as reported by spot ratios was available in up to 67.4% of the study cohort. Mean urine protein-creatinine ratio was 4.6 g/g, and mean urine albumin-creatinine ratio was 2.8 g/g. Whereas MGN had the highest levels of proteinuria (protein-creatinine ratio, 8.3 g/g; albumin-creatinine ratio,

5.2 g/g), IgAN had the lowest degree of proteinuria (protein-creatinine ratio, 2.3 g/g; albumin-creatinine ratio, 1.5 g/g). Hematuria was present among 65% of patients with IgAN and 71% of biopsies categorized as other (Table 2).

Distribution of Glomerulonephropathies by Race and Ethnicity

Among all race and ethnic groups, FSGS was the most common glomerulonephropathy (Table 1). In the black population, FSGS accounted for 49.8%, followed by MGN (13.5%) and MCD (11.5%). There were only 3 cases of IgAN diagnosed among blacks within our study period. The distribution of glomerulonephropathies in non-Hispanic whites was similar to blacks, with FSGS (35.9%) being most prevalent, followed by MGN (14.5%), MCD (11.9%), and IgAN (7.8%). Among Asians, FSGS was most prevalent (41.5%), followed by IgAN (23.5%), MGN (9.0%), and MCD (8.4%). Among Hispanics, FSGS accounted for 36.0%, followed by MGN (12.5%), IgAN (11.6%), and MCD (9.9%).

Rates of Primary Glomerulonephropathies During the Observation Period

Age- and sex-adjusted rates of primary glomerulonephropathies by year are shown in Table 3 and Fig 2. In the 12-year observation period, annual rates of glomerulonephropathies had steadily increased from 5.3 cases in 2000 to 10.7 cases (per 100,000 person-years) in 2011. Among the common glomerulonephropathies, rates were highest for FSGS (2.7 cases/100,000 person-years), followed by MGN, IgAN, and MCD (Table 4). FSGS also had the greatest increase in rate from 1.6 cases in 2000 to 5.3 cases (per 100,000 person-years) in 2011. This increase was observed in all race and ethnic groups (Table 4; Fig 3). IgAN increased in rate from 0.1 to 1.6 cases (per 100,000 person-years). The increased rate of IgAN was driven by Hispanics and non-Hispanic Asians. The overall rate of MGN appeared to remain stable, although it increased among blacks. The rate of MCD declined to 0.4 case (per 100,000 person-years) by 2011 (Table 3).

Sensitivity Analyses

In order to exclude potential bias against performing kidney biopsies in certain populations, we performed sensitivity analyses evaluating rates of primary glomerulonephropathies among individuals who were younger than 80 years and who did not have diabetes mellitus. Within this subpopulation (n = 1,838), FSGS was also the most common primary glomerulonephropathy (n = 651), followed by MGN (n = 252), MCD (n = 224), and IgAN (n = 218; Tables S2 and S3).

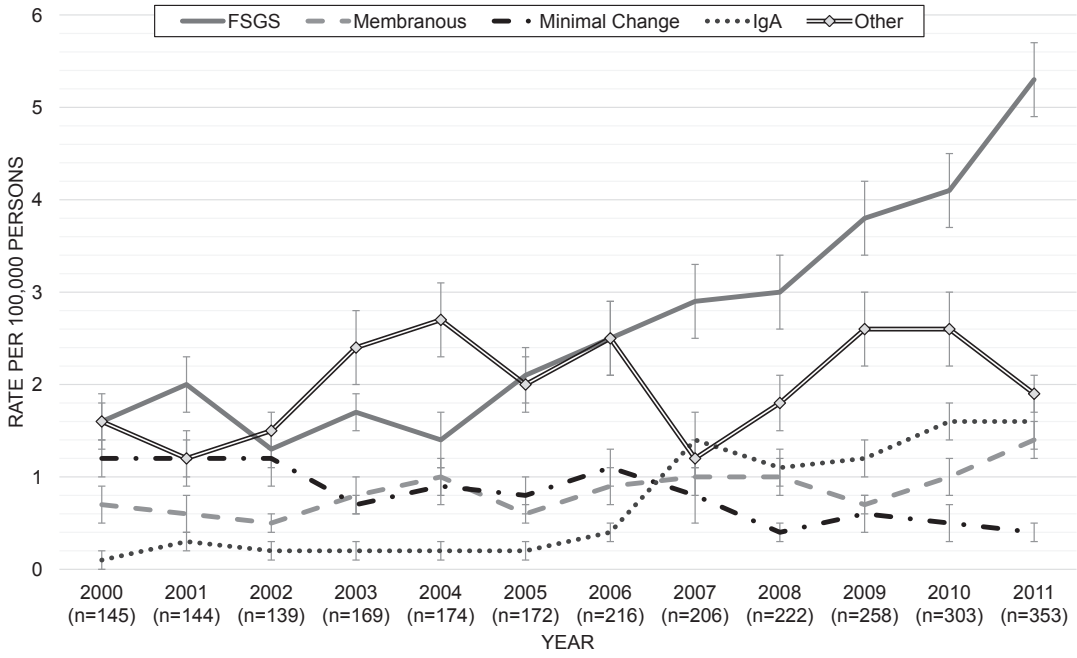

Figure 2. The distribution of primary glomerulonephropathy in the 12-year observation window. Focal segmental glomerulosclerosis (FSGS) rates, and to a lesser degree immunoglobulin A (IgA) nephropathy rates, increased throughout the period. Minimal change disease and membranous glomerulonephritis rates remained flat throughout our observation period. The "other" category included immune complex glomerulonephritis not otherwise specified, pauci-immune/antineutrophil cytoplasmic antibody–associated glomerulonephritis, thin basement membrane disease, membranoproliferative glomerulonephritis, crescentic glomerulonephritis not otherwise specified, postinfectious glomerulonephritis, anti–glomerular basement membrane disease, fibrillary glomerulonephritis, dense deposit disease, and others.

Table 4. Members' Age- and Sex-Adjusted Rates of Glomerulonephropathy Types by Race and Ethnicity and Combined, 2000-2011

	White, Non-Hispanic	Black, Non-Hispanic	Hispanic	Asian, Non-Hispanic	Other, Non-Hispanic	All Groups Combined
Overall						
New cases	781	436	903	311	70	2,501
Person-y at risk	9,857,160	2,546,554	8,051,203	2,237,143	4,910,807	27,602,867
Rate	5.9	13.62	9.74	10.61	1.37	7.15
SE	0.29	0.77	0.38	0.7	0.2	0.16
FSGS						
New cases	280	217	325	129	22	973
Person-y at risk	9,857,160	2,546,554	8,051,203	2,237,143	4,910,807	27,602,867
Rate	1.89	6.81	3.72	4.26	0.41	2.73
SE	0.13	0.55	0.25	0.4	0.1	0.1
MGN						
New cases	113	59	113	28	4	317
Person-y at risk	9,857,160	2,546,554	8,051,203	2,237,143	4,910,807	27,602,867
Rate	0.78	1.62	1.09	0.82	0.06	0.85
SE	0.09	0.22	0.12	0.16	0.03	0.05
MCD						
New cases	93	50	89	26	16	274
Person-y at risk	9,857,160	2,546,554	8,051,203	2,237,143	4,910,807	27,602,867
Rate	0.67	1.61	0.96	0.93	0.31	0.8
SE	0.1	0.28	0.12	0.19	0.09	0.06
IgAN						
New cases	65	3	105	73	9	255
Person-y at risk	9,857,160	2,546,554	8,051,203	2,237,143	4,910,807	27,602,867
Rate	0.72	0.1	0.96	2.75	0.13	0.75
SE	0.12	0.06	0.1	0.44	0.04	0.05
Other						
New cases	230	107	271	55	19	682
Person-y at risk	9,857,160	2,546,554	8,051,203	2,237,143	4,910,807	27,602,867
Rate	1.84	3.48	3.01	1.85	0.46	2.02
SE	0.18	0.41	0.22	0.27	0.13	0.09

Note: Age- and sex-adjusted rates of primary glomerulonephropathy by race and ethnic groups. Rates paralleled the overall distribution of primary glomerulonephropathy. All rates are reported as per 100,000 person-years and standardized to the US Census 2000 population. Population at risk is the overall Kaiser Permanente Southern California population, 18 years or older, in that race and ethnic category in the study period.

Abbreviations: FSGS, focal segmental glomerulosclerosis; IgAN, immunoglobulin A nephropathy; MCD, minimal change disease; MGN, membranous glomerulonephritis; SE, standard error.

DISCUSSION

Historically, the distribution and prevalence of glomerulonephropathies has been described by pooling separate studies of relatively homogeneous populations in specific countries or areas throughout the world. In our study, we had an opportunity to describe the distribution of glomerulonephropathies within a single yet heterogeneous population living in a similar environment of Southern California, but differing in race and ethnic roots. A total of 2,501 individuals with biopsy-proven primary glomerulonephropathy were identified from a large racially and ethnically diverse contemporary population in Southern California. We found that FSGS was the most prevalent primary glomerulonephropathy, with racial and ethnic variations occurring in the distribution of the different glomerulonephropathies. FSGS accounted for 38.9% of the biopsy findings, followed by MGN, MCD, and IgAN. Patients with MGN presented with the greatest degree of proteinuria, whereas those with FSGS presented with the lowest kidney function among the 4 common glomerulonephropathies. Overall, glomerulonephropathy rates increased in our 12-year observation period, driven by increasing rates of FSGS and IgAN.

Glomerulonephropathy is an important cause of chronic kidney disease in the United States and worldwide. Overall, glomerulonephropathies are generally considered treatable, and if diagnosed and managed early, kidney damage and progression to failure can be potentially avoided. Nevertheless, tens of thousands of patients initiate dialysis therapy or receive kidney transplants annually in the United States as a consequence of glomerulonephropathies.[3]

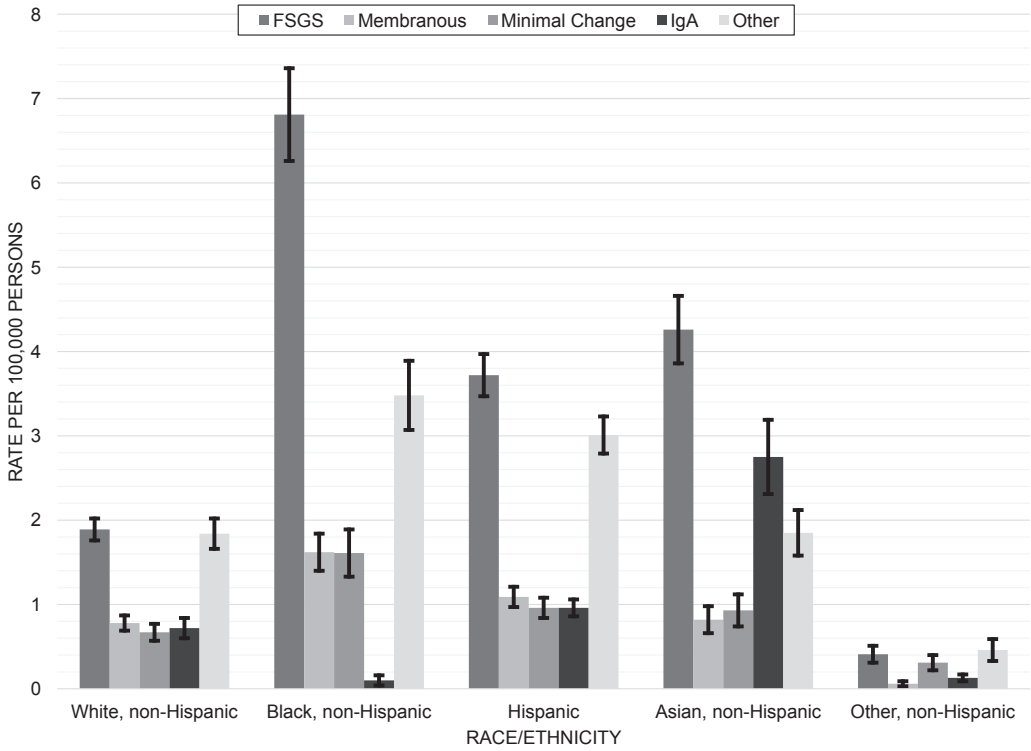

Figure 3. Average annual age- and sex-adjusted rates for the most common primary glomerulonephropathy disease states by race and ethnicity, 2000 to 2011. Rates for the primary glomerulonephropathy and by different race and ethnic groups were similar to the distribution for the entire period. Abbreviations: FSGS, focal segmental glomerulosclerosis; IgA, immunoglobulin A.

Patient predilections for glomerulonephropathy are variable, affecting all age groups and sexes and those with comorbid conditions.

We think that our findings lend insight into the nature-versus-nurture aspects of glomerulonephropathy. Aside from the familial/genetic glomerulonephropathies, the contributions of innate biology and environmental exposure on glomerulonephropathy risk are difficult to quantitate or study. Certain glomerulonephropathies occur more frequently in different parts of the world and certain glomerulonephropathies are more common in specific populations or race and ethnic groups.[2,30] Woo et al[2] have suggested that infections, sanitation/hygiene, and overstimulated immune function may be the underlying mechanisms for these differences. Whereas FSGS may be a byproduct or consequence of the increasing trend of worldwide obesity, within the United States, there have been varying observations suggesting a race predilection (FSGS in blacks and MGN in whites) and perhaps by time periods (in the past, there has been more MGN described, whereas more recently, FSGS is more frequently described).[21,22,24,31]

Our study cohort included a racially and ethnically diverse population all living in a Westernized environment of Southern California. We originally hypothesized that blacks would have more FSGS and Asians would have more IgAN. We observed that FSGS was the most predominant primary glomerulonephropathy among all race groups including Asians. Individuals with FSGS had the highest rate of poverty (6.8%) and appeared to present in more advanced stages of chronic kidney disease, which may suggest a socioeconomic predilection and an association with access to care. The high rate of FSGS is consistent with previous observations within the United States that evaluated less diverse populations in the Midwestern and Eastern United States, where FSGS accounted for 12% to 25% of biopsies.[20,21] However, other observations within the United States have reported IgAN as the most common finding, seen in up to 22% of all biopsies.[31,32] Annual rates of glomerulonephropathies increased in our observation period, which was driven by higher rates of FSGS and to a lesser degree by IgAN. MGN and MCD rates remained flat, which was also consistent with trends observed in previous US studies.[21,24] We think that the high FSGS rates in our study reflect the Westernization of the different race and ethnic groups in terms of lifestyles and environmental exposures, including diet. However, we did not have information about body mass index available for the entire study cohort, which would provide additional insights into obesity trends paralleling FSGS theories.

There are several potential limitations that may confound the interpretation of our study findings. Our study population was drawn from insured members of an integrated health system and thus may not necessarily reflect the US general population. Our study cohort had similar socioeconomic status relative to the underlying KPSC membership population from which they were drawn[25] and thus may not be representative of those in the extremes of wealth, including those with no insurance and those who preferred to self-pay for health care. The kidney biopsy population also may have been a reflection of those seeking health care more frequently and those willing to undergo invasive diagnostic testing. Individuals with more indolent glomerulonephropathies such as IgAN may have been underdiagnosed compared with other studies in which there was active screening for kidney disease.[33] We did not have reasons or indications for biopsy for the entire study population. In addition, a significant proportion of our biopsy findings were categorized descriptively as immune-complex nephropathy, which likely included early or inconclusive IgAN or MPGN that were not diagnosed. Each glomerulonephropathy was given one primary diagnosis using a hierarchical schema and thus we may have under-reported when patients had 2 legitimate primary glomerulonephropathy diagnoses. In a similar regard, primary glomerulonephropathy was determined somewhat arbitrarily because certain glomerulonephropathies (eg, ANCA-associated glomerulonephropathy) can be categorized as a secondary glomerulonephropathy similar to SLE. We excluded patients who had a diagnosis of SLE in order to rule out systemic diseases that resulted in glomerulonephropathy and attempted to include conditions that solely had renal involvement as primary glomerulonephropathy. Thus our primary glomerulonephropathies are "presumed" given the lack of complete history for each biopsy patient. We also could not account for recent immigrants who may have constituted the different race and ethnic groups and may be less representative of the Southern California population.

Despite these potential limitations, our study is one of the largest racially and ethnically diverse kidney biopsy cohorts described to date. Our EHR-based study included comprehensive information for patient demographics, including socioeconomics, comorbid conditions, laboratory information, and medications. We believe that the comprehensive and longitudinal information for medication use and overall utilization through the EHR within our integrated health system may pave the way to providing valuable insights into the natural history of glomerulonephropathies and also assess comparative management strategies. When we can assess comparative management strategies, it may be possible to use the database generated in this study as a prospective glomerulonephropathy registry that can track patients over time, drive decision support and case management, and serve as a tool to ensure that all patients are followed up appropriately, as we have done for many other chronic diseases.[34]

Our kidney biopsy cohort drawn from a large racially and ethnically diverse population of the United States demonstrated an increase in rates of primary glomerulonephropathies within the 12-year observation period. The most prevalent glomerulonephropathy among all race and ethnic groups, including Asians and Hispanics, was FSGS. Our study cohort derived using an EHR-based approach with comprehensive longitudinal information has the potential to provide valuable insights into characterizing primary glomerulonephropathies and studying their outcomes.

ACKNOWLEDGEMENTS

The authors thank Sean S. Anand, Joy S. Gelfond, Nidia Y. Golla, and Radha M. Bathala for their tireless work on the information extraction; Randi Burke, MD, from the KPSC Division of Renal Pathology for valuable contributions to viewing and interpretation of the kidney biopsy specimens; Sejal Vora for support and assistance with this study; and Stephen S. Cho, MPA, for research and literature support for this manuscript.

Support: This study was funded by an investigator-initiated research grant (Dr Sim, Principal Investigator) from the Autoimmune and Rare Diseases division of Mallinckrodt Pharmaceuticals. The study sponsor had no role in study design; collection, analysis, and interpretation of data; writing the report; or the decision to submit the report for publication.

Financial Disclosure: The authors declare that they have no other relevant financial interests.

Contributions: Research area and study design: JJS, AH; data acquisition: MB, JJS, TNH, TA; data analysis/interpretation: MB, JJS, AH, TNH, SJJ, MHK; study supervision: JJS, SJJ, MHK; statistical analysis: MB; administrative, technical, or material support: SJJ, MHK. Each author contributed important intellectual content during the manuscript drafting or revision and accepts accountability of the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved. JJS takes responsibility that this study has been reported honestly, accurately, and transparently; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

Peer Review: Evaluated by 3 external peer reviewers, a Statistical Editor, a Co-Editor, and the Editor-in-Chief.

SUPPLEMENTARY MATERIAL

Table S1: Disease states among the "other" category.

Table S2: Age- and sex-adjusted incidence rates of glomerulonephropathy types, by year, in patients <80 y without DM.

Table S3: Age- and sex-adjusted incidence rates of glomerulonephropathy types, by race/ethnicity, in patients <80 y without DM.

Figure S1: Prioritization algorithm.

Note: The supplementary material accompanying this article (http://dx.doi.org/10.1053/j.ajkd.2016.03.416) is available at www.ajkd.org

REFERENCES

1. Maisonneuve P, Agodoa L, Gellert R, et al. Distribution of primary renal diseases leading to end-stage renal failure in the United

States, Europe, and Australia/New Zealand: results from an international comparative study. *Am J Kidney Dis*. 2000;35(1):157-165.

2. Woo KT, Chan CM, Chin YM, et al. Global evolutionary trend of the prevalence of primary glomerulonephritis over the past three decades. *Nephron Clin Pract*. 2010;116(4):c337-c346.

3. Collins AJ, Foley RN, Chavers B, et al. US Renal Data System 2013 annual data report. *Am J Kidney Dis*. 2014;63(1)(suppl 1):e1-e420.

4. McGrogan A, Franssen CF, de Vries CS. The incidence of primary glomerulonephritis worldwide: a systematic review of the literature. *Nephrol Dial Transplant*. 2011;26(2):414-430.

5. Braun N, Schweisfurth A, Lohofener C, et al. Epidemiology of glomerulonephritis in Northern Germany. *Int Urol Nephrol*. 2011;43(4):1117-1126.

6. Chang JH, Kim DK, Kim HW, et al. Changing prevalence of glomerular diseases in Korean adults: a review of 20 years of experience. *Nephrol Dial Transplant*. 2009;24(8):2406-2410.

7. Heaf J, Lokkegaard H, Larsen S. The epidemiology and prognosis of glomerulonephritis in Denmark 1985-1997. *Nephrol Dial Transplant*. 1999;14(8):1889-1897.

8. Li LS, Liu ZH. Epidemiologic data of renal diseases from a single unit in China: analysis based on 13,519 renal biopsies. *Kidney Int*. 2004;66(3):920-923.

9. Maixnerova D, Jancova E, Skibova J, et al. Nationwide biopsy survey of renal diseases in the Czech Republic during the years 1994-2011. *J Nephrol*. 2015;28(1):39-49.

10. Moriyama T, Suzuki K, Sugiura H, et al. Frequency of renal disease in Japan: an analysis of 2,404 renal biopsies at a single center. *Nephron Clin Pract*. 2010;115(3):c227-c236.

11. Narasimhan B, Chacko B, John GT, Korula A, Kirubakaran MG, Jacob CK. Characterization of kidney lesions in Indian adults: towards a renal biopsy registry. *J Nephrol*. 2006;19(2):205-210.

12. Rychlik I, Jancova E, Tesar V, et al. The Czech registry of renal biopsies. Occurrence of renal diseases in the years 1994-2000. *Nephrol Dial Transplant*. 2004;19(12):3040-3049.

13. Simon P, Ramee MP, Boulahrouz R, et al. Epidemiologic data of primary glomerular diseases in Western France. *Kidney Int*. 2004;66(3):905-908.

14. Stratta P, Segoloni GP, Canavese C, et al. Incidence of biopsy-proven primary glomerulonephritis in an Italian province. *Am J Kidney Dis*. 1996;27(5):631-639.

15. Tiebosch AT, Wolters J, Frederik PF, van der Wiel TW, Zeppenfeldt E, van Breda Vriesman PJ. Epidemiology of idiopathic glomerular disease: a prospective study. *Kidney Int*. 1987;32(1):112-116.

16. Zaza G, Bernich P, Lupo A; Triveneto' Register of Renal Biopsies (TVRRB). Incidence of primary glomerulonephritis in a large North-Eastern Italian area: a 13-year renal biopsy study. *Nephrol Dial Transplant*. 2013;28(2):367-372.

17. Jegatheesan D, Nath K, Reyaldeen R, et al. Epidemiology of biopsy-proven glomerulonephritis in Queensland adults. *Nephrology (Carlton)*. 2016;21(1):28-34.

18. Baez Bonilla R, Parrilla F, Kidd O, Cangiano JL. Registry of kidney biopsy in a single center in Puerto Rico: university district hospital. *Bol Asoc Med P R*. 2011;103(3):10-12.

19. Bahiense-Oliveira M, Saldanha LB, Mota EL, Penna DO, Barros RT, Romao-Junior JE. Primary glomerular diseases in Brazil (1979-1999): is the frequency of focal and segmental glomerulosclerosis increasing? *Clin Nephrol*. 2004;61(2):90-97.

20. Braden GL, Mulhern JG, O'Shea MH, Nash SV, Ucci AA Jr, Germain MJ. Changing incidence of glomerular diseases in adults. *Am J Kidney Dis*. 2000;35(5):878-883.

21. Haas M, Spargo BH, Coventry S. Increasing incidence of focal-segmental glomerulosclerosis among adult nephropathies: a 20-year renal biopsy study. *Am J Kidney Dis*. 1995;26(5):740-750.

22. Korbet SM, Genchi RM, Borok RZ, Schwartz MM. The racial prevalence of glomerular lesions in nephrotic adults. *Am J Kidney Dis*. 1996;27(5):647-651.

23. Mazzarolo Cruz HM, Cruz J, Silva AL Jr, Saldanha LB, de Oliveira Penna D. Prevalence of adult primary glomerular diseases: retrospective analysis of 206 kidney biopsies (1990-1993). *Rev Hosp Clin*. 1996;51(1):3-6.

24. Haas M, Meehan SM, Karrison TG, Spargo BH. Changing etiologies of unexplained adult nephrotic syndrome: a comparison of renal biopsy findings from 1976-1979 and 1995-1997. *Am J Kidney Dis*. 1997;30(5):621-631.

25. Koebnick C, Langer-Gould AM, Gould MK, et al. Sociodemographic characteristics of members of a large, integrated health care system: comparison with US Census Bureau data. *Perm J*. 2012;16(3):37-41.

26. Sim JJ, Handler J, Jacobsen SJ, Kanter MH. Systemic implementation strategies to improve hypertension: the Kaiser Permanente Southern California experience. *Can J Cardiol*. 2014;30(5):544-552.

27. Sim JJ, Shi J, Kovesdy CP, Kalantar-Zadeh K, Jacobsen SJ. Impact of achieved blood pressures on mortality risk and end-stage renal disease among a large, diverse hypertension population. *J Am Coll Cardiol*. 2014;64(6):588-597.

28. Pham TT, Sim JJ, Kujubu DA, Liu IL, Kumar VA. Prevalence of nondiabetic renal disease in diabetic patients. *Am J Nephrol*. 2007;27(3):322-328.

29. Breslow NE, Day NE. Statistical methods in cancer research. Volume II–the design and analysis of cohort studies. *IARC Sci Publ*. 1987;82:1-406.

30. Pesce F, Schena FP. Worldwide distribution of glomerular diseases: the role of renal biopsy registries. *Nephrol Dial Transplant*. 2010;25(2):334-336.

31. Swaminathan S, Leung N, Lager DJ, et al. Changing incidence of glomerular disease in Olmsted County, Minnesota: a 30-year renal biopsy study. *Clin J Am Soc Nephrol*. 2006;1(3):483-487.

32. Nair R, Walker PD. Is IgA nephropathy the commonest primary glomerulopathy among young adults in the USA? *Kidney Int*. 2006;69(8):1455-1458.

33. Briganti EM, Dowling J, Finlay M, et al. The incidence of biopsy-proven glomerulonephritis in Australia. *Nephrol Dial Transplant*. 2001;16(7):1364-1367.

34. Kanter MH, Lindsay G, Bellows J, Chase A. Complete care at Kaiser Permanente: transforming chronic and preventive care. *Jt Comm J Qual Patient Saf*. 2013;39(11):484-494.