Nephrol Dial Transplant (2018) 33: 661–669
doi: 10.1093/ndt/gfx189
Advance Access publication 2 July 2017

# Glomerular disease frequencies by race, sex and region: results from the International Kidney Biopsy Survey

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## ABSTRACT

**Background.** Large-scale studies comparing glomerular disease frequencies across continents are lacking.

**Methods.** We surveyed 29 nephropathology laboratories in four continents using a standardized data collection form. We obtained recent consecutive kidney biopsy diagnosis frequencies at each center and summary demographics for each diagnosis. This report focuses on glomerular disease frequencies by region and race/ethnicity.

**Results.** Among 42 603 glomerular disease diagnoses reported (median age 47 years, 52% male, 57% white), from a total of 60 340 diagnoses, glomerular disease subtype frequencies differed considerably by continent. Diabetic glomerulosclerosis (GS; 19.1%) and focal segmental glomerulosclerosis (FSGS; 19.1%) predominated in North America; lupus nephritis (38.1%) and FSGS (15.8%) predominated in Latin America; IgA nephropathy (IgAN; 22.1%) and FSGS (14.9%) predominated in Europe; and IgAN (39.5%) and lupus nephritis (16.8%) predominated in Asia. After stratifying by race, diabetic GS (17.4% versus 4.3%, $P < 0.001$) and FSGS (17.3% versus 11.8%, $P < 0.001$) were more, and lupus nephritis less (15.8% versus 45.6%, $P < 0.001$), frequent among Latinos in North versus Latin America; FSGS was more (13.1% versus 7.1%, $P < 0.001$), and IgAN less (27.4% versus 40.5%, $P < 0.001$), frequent among Asians in North America versus Asia; and FSGS (18.9% versus 13.5%, $P < 0.001$) and diabetic GS (18.7% versus 6.5%, $P < 0.001$) were more, and IgAN less (14.4% versus 25.4%, $P < 0.001$), frequent among whites in North America versus Europe.

**Conclusions.** We determined that glomerular disease frequencies differed by continent, even among patients of similar race/ethnicity. Regional environmental and lifestyle factors, and local biopsy policies, might influence glomerular disease epidemiology independently of race/ethnicity.

**Keywords:** epidemiology, glomerular disease, glomerulonephritis, histopathology, kidney biopsy

## INTRODUCTION

Glomerular disease development involves a complex interplay of genetic, epigenetic and environmental factors [1–3], although the relative contributions from individual exposures to observed demographic and geographic disease distributions remain poorly understood and probably differ by glomerular disease subtype. Prior efforts to systematically compare kidney biopsy data from several countries and regions have been complicated by non-standardized approaches to disease definitions and groupings [4, 5]. Whether glomerular disease frequency distributions shift in response to environmental or behavioral changes when individuals move away from their country of ancestral origin to a new region has also not adequately been explored, yet may offer clues to disease pathogenesis.

Determining contemporary glomerular disease diagnosis frequencies among patients who undergo renal biopsy, stratified by race and geographic region, while applying standardized disease nomenclature systems, might greatly assist the planning of future glomerular disease research, by providing realistic estimates of the number of biopsies requiring performance or review in order to detect a threshold number of cases. Additionally, exploring the distributions of specific glomerular disease subtypes across racial groups and geographic regions might uncover new insights into the relative importance of genetic and environmental influences on glomerular disease epidemiology.

Accordingly, we conducted a survey of 29 nephropathology laboratories (including two kidney biopsy registries) throughout the USA, Canada, Europe, Asia and Latin America. We collected the total number of diagnoses and summary patient demographics for all consecutive and recent (range 1–6 years) kidney biopsy diagnoses identified at each center. In this report, we specifically focus on glomerular disease diagnoses, comparing disease distributions across geographic regions and patient demographic groups.

## MATERIALS AND METHODS

### Patient population and data source

The International Kidney Biopsy Survey (IKBS) was designed by J.C.J. and A.B.F., with support from the American Society of Nephrology Glomerular Diseases Advisory Group (ASN GDAG), the Renal Pathology Society (RPS), and the European Renal Association–European Dialysis and Transplantation Association (ERA–EDTA) Immunonephrology Working Group. Centers were invited to participate in the survey between 2012 and 2013. According to survey instructions (Supplementary data, Appendix A), all consecutive native kidney biopsy diagnoses reported by the participating center over a self-selected recent time period of at least 1 year were required to be reported. Diagnoses were determined based on light, immunofluorescence and electron microscopic findings, as available, interpreted in the context of provided clinical data. These data could be gathered prospectively or retrospectively. If two or more diagnoses were identified from a single-biopsy specimen, each diagnosis was regarded as a separate observation. Centers were instructed to report demographic data, if available, as summary values for each diagnosis, including: mean age, minimum age, maximum age, number of males, number of females and number of patients with each of four mutually exclusive race/ethnicity categories (white, black, Asian or Latino), for each diagnosis. If sex or race subtotals summed to less than the total number of cases for that diagnosis, or if demographic (sex, race or age) data were missing, the deficit was designated as 'missing or unknown' when collating and analyzing data.

### Exposures and outcomes

Geographic region [North America (USA or Canada), Latin America, Asia, Europe] was our primary exposure. Race, sex and mean age were our secondary exposures. Glomerular disease frequency distributions were our primary outcome.

### Statistical analysis

Categorical data (region, race, sex) were summarized as frequencies and percentages and compared across groups using cross-tabulation. The median and range for reported mean, minimum and maximum age values for each diagnosis, weighted by diagnosis frequencies at the individual centers, are reported for each region. Chi-square or Fisher's exact testing, as appropriate, were used to compare the frequencies of each glomerular disease diagnosis across groups. A Bonferroni-corrected two-sided $P < 0.004$ (0.05/12, to account for multiple comparisons) was considered statistically significant. All data were analyzed using SAS Enterprise Guide version 6.1 (Cary, NC, USA). A waiver from Institutional Review Board (IRB) approval was obtained for this study at the coordinating center (University of North Carolina, Chapel Hill, NC, USA), and individual participating centers obtained local IRB approval on an as-needed basis. All submitted data were de-identified and are presented in an aggregate manner.

## RESULTS

### Patient population

Twenty-nine centers participated, including 13 in Europe [Austria, Czech Republic, France, Greece, Italy ($n = 2$), the Netherlands, Norway, Poland ($n = 2$), Russia, UK ($n = 2$)]; 10 in North America (7 in the USA, 3 in Canada); 3 in Latin America (Brazil, Colombia, Mexico); 2 in Asia (Japan, Thailand); and 1 in Saudi Arabia. For the purposes of this analysis, the center from Saudi Arabia was included with the 13 European centers. After excluding inadequate specimens and nonspecific diagnoses, a total of 60 340 specific native kidney biopsy diagnoses—including 42 603 glomerular disease diagnoses—were reported, over a median of 4 (range 1–8) years, and with a median of 428 (range 81–5400) diagnoses annually/center.

The median of the reported mean ages of patients with a glomerular disease diagnosis was 47.3 (IQR 39.7–56.9) years. Among those where a specific sex was indicated, ($n = 39\,841$, 94%), 53% were male. Among those with known race ($n = 21\,829$, 51%), 57% were white, 19% were black, 14% were Latino and 10% were Asian. Population demographics by geographic region are summarized in Table 1, and complete demographic data for all diagnoses (including non-glomerular disease diagnoses) are provided by geographic region in Supplementary data, Appendix B. Patients were youngest at the time of biopsy in Latin America (median of mean ages 30 years versus 43–49 years in the other regions), and the proportion of females was also highest in this region (64% versus 51–58%). All patients with known race in Asia were Asian, whereas 98% in Europe were white and 97% in Latin America were Latino. Racial composition was more heterogeneous in the USA (54% white, 31% black, 11% Latino and 4% Asian).

### Glomerular disease subtype frequency distributions by region

Glomerular disease subtype frequencies are summarized by geographic region in Table 2 and Figure 1. Focal segmental glomerulosclerosis (FSGS) and diabetic glomerulosclerosis (GS) predominated in the USA (each comprising 19% of all glomerular diagnoses), followed by IgA nephropathy (IgAN; 12%), membranous nephropathy (12%) and lupus nephritis (10%). FSGS was also common in Latin America (16%), although lupus nephritis strongly predominated in this region (38%), while diabetic GS (4%) and IgAN (6%) were comparatively rare. In contrast, IgAN predominated in Europe (22%), where the second most frequent diagnosis was FSGS (15%), and

**Table 1. Demographic characteristics among 29 international centers surveyed, by geographic region ($n = 42\,603$ glomerular disease diagnoses)**

| Characteristic | USA/Canada (10 centers) $n = 23\,391$ | Europe (14 centers) $n = 15\,042$ | Asia (2 centers) $n = 1609$ | Latin America (3 centers) $n = 2561$ |
|---|---|---|---|---|
| Age variables, median (range)[a] | | | | |
| Minimum | 1 (0.1–37) | 2 (0.3–34) | 15 (13–78) | 8 (1–64) |
| Mean | 49 (27–66) | 48 (25–63) | 43 (29–82) | 30 (17–71) |
| Maximum | 90 (71–100) | 89 (57–101) | 88 (29–94) | 81 (17–84) |
| Male sex, *n* (% of non-missing)* | 12 004 (52.3) | 7169 (56.4) | 797 (49.5) | 930 (36.4) |
| Missing sex, *n* (% of total) | 439 (1.9) | 2320 (15.4) | 0 | 3 (0.1) |
| Race, *n* (% of non-missing)* | | | | |
| White | 7231 (54.2) | 5118 (98.2) | 0 | 14 (0.8) |
| Black | 4179 (31.4) | 44 (0.8) | 0 | 36 (2.1) |
| Asian | 482 (3.6) | 40 (0.8) | 1569 (100) | 0 |
| Latino | 1440 (10.8) | 8 (0.2) | 0 | 1668 (97.1) |
| Missing race, *n* (% of total) | 10 059 (43.0) | 9832 (65.4) | 40 (2.5) | 843 (32.9) |

[a]Individual patient-level age data not available. Instead, values represent the weighted median and range, by region, for each diagnosis-level age variable (mean, minimum and maximum age).
*Chi-square $P < 0.05$.

**Table 2. Glomerular disease diagnosis frequencies among 29 international centers surveyed, by geographic region ($n = 41\,527$ glomerular disease diagnoses)**

| Glomerular disease subtype | USA/Canada (10 centers) $n = 23\,391$ | | Europe (14 centers) $n = 15\,042$ | | Asia (2 centers) $n = 1609$ | | Latin America (3 centers) $n = 2561$ | |
|---|---|---|---|---|---|---|---|---|
| | *n* | % | *n* | % | *n* | % | *n* | % |
| FSGS* | 4462 | 19.1 | 2238 | 14.9 | 111 | 6.9 | 404 | 15.8 |
| IgAN/HSP* | 2762 | 11.8 | 3318 | 22.1 | 636 | 39.5 | 156 | 6.1 |
| Diabetic GS* | 4460 | 19.1 | 1049 | 7.0 | 172 | 10.7 | 110 | 4.3 |
| Membranous nephropathy** | 2710 | 11.6 | 1885 | 12.5 | 162 | 10.1 | 284 | 11.1 |
| Lupus GN* | 2297 | 9.8 | 1524 | 10.1 | 270 | 16.8 | 976 | 38.1 |
| Pauci-immune GN* | 1220 | 5.2 | 1198 | 8.0 | 41 | 2.6 | 121 | 4.7 |
| Minimal change disease* | 967 | 4.1 | 964 | 6.4 | 55 | 3.4 | 175 | 6.8 |
| MPGN/C3GP combined* | 609 | 2.6 | 557 | 3.7 | 17 | 1.1 | 71 | 2.8 |
| Renal amyloid* | 509 | 2.2 | 661 | 4.4 | 14 | 0.9 | 37 | 1.4 |
| TMA* | 652 | 2.8 | 336 | 2.2 | 13 | 0.8 | 30 | 1.2 |
| TBMN* | 520 | 2.2 | 218 | 1.5 | 50 | 3.1 | 19 | 0.7 |
| MesProlif/Prolif GN NOS* | 452 | 1.9 | 263 | 1.8 | 4 | 0.3 | 62 | 2.4 |
| Chronic sclerosing GN NOS* | 245 | 1.1 | 123 | 0.8 | 1 | 0.1 | 6 | 0.2 |
| Acute PIGN* | 182 | 0.8 | 115 | 0.8 | 26 | 1.6 | 43 | 1.7 |
| MIDD* | 249 | 1.1 | 81 | 0.5 | 6 | 0.4 | 4 | 0.2 |
| Fibrillary GN* | 291 | 1.2 | 39 | 0.3 | 2 | 0.1 | 2 | 0.1 |
| [a]Other glomerular disease* | 101 | 0.4 | 175 | 1.2 | 3 | 0.2 | 33 | 1.3 |
| Cryoglobulinemic GN | 155 | 0.7 | 112 | 0.7 | 13 | 0.8 | 5 | 0.2 |
| Alport's syndrome* | 182 | 0.8 | 61 | 0.4 | 9 | 0.6 | 8 | 0.3 |
| Anti-GBM GN (+/−ANCA) | 123 | 0.5 | 80 | 0.5 | 1 | 0.1 | 5 | 0.2 |
| C1q nephropathy* | 137 | 0.6 | 14 | 0.1 | 1 | 0.1 | 3 | 0.1 |
| Idiopathic nodular GS* | 106 | 0.5 | 31 | 0.2 | 2 | 0.1 | 7 | 0.3 |

[a]Includes glomerular disease diagnoses with <100 cases overall (diffuse mesangial sclerosis, Finnish type congenital nephrotic syndrome, immunotactoid glomerulopathy, collagenofibrotic glomerulopathy, fibronectin glomerulopathy, IgM nephropathy, polyarteritis nodosa, preeclampsia/eclampsia, Fabry disease, lipoprotein glomerulopathy, sickle cell glomerulopathy). HSP, Henoch Schonlein purpura; G3GP, C3 glomerulopathy; TMA, thrombotic microangiopathy; NOS, not otherwise specified; MIDD, monoclonal immune deposition disease; GBM, glomerular basement membrane; ANCA, anti-neutrophil cytoplasmic antibody.
*Chi-square $P < 0.002$.
**Chi-square $P = 0.0022$.

especially in Asia (40%), where the second most frequent diagnosis was lupus nephritis (17%).

## Glomerular disease subtype frequency distributions by race and region

Comparing the frequencies of the more common glomerular disease subtypes across regions among patients with a similar reported race revealed some significant shifts in relative disease frequencies when comparing patients living in North America (USA or Canada) with those living in their region of ancestral origin, Figure 2. Comparing Asians in North America to those in Asia, the frequencies of IgAN (27% versus 40%, $P < 0.001$) and lupus nephritis (13% versus 17%, $P = 0.03$) were significantly lower, whereas those of FSGS (13% versus 7%,

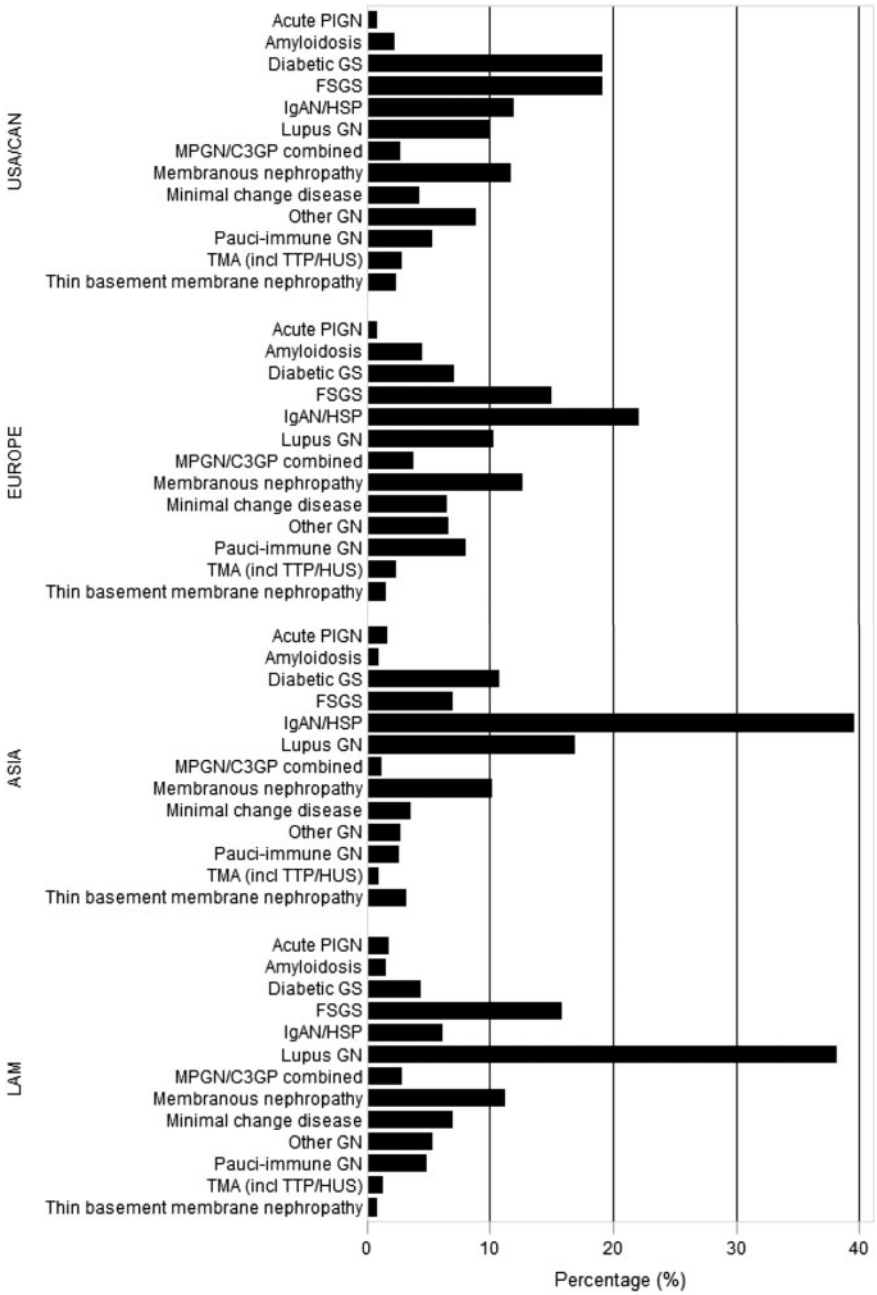


**FIGURE 1:** Glomerular disease subtype kidney biopsy frequencies, by geographic region, showing the 13 most common glomerular disease diagnoses only. CAN, Canada; LAM, Latin America; HSP, Henoch Schonlein purpura; C3GP, C3 glomerulopathy; TMA, thrombotic microangiopathy; TTP, thrombotic thrombocytopenic purpura; HUS, hemolytic uremic syndrome.

$P < 0.001$), minimal change disease (6% versus 3%, $P = 0.0028$) and membranoproliferative glomerulonephritis (MPGN) (2% versus 1%, $P = 0.01$) were significantly higher. Comparing Latinos in North America with those in Latin America, the frequency of lupus nephritis (15% versus 45%, $P < 0.001$) was significantly lower, whereas those of FSGS (17% versus 11%, $P < 0.001$), membranous nephropathy (12% versus 8%, $P = 0.0008$), IgAN (13% versus 6%, $P < 0.001$) and especially diabetic GS (17% versus 4%, $P < 0.001$) were significantly higher. Finally, comparing whites in North America with those in Europe, significant differences were identified in the frequencies of all common glomerular disease subtypes, except lupus nephritis, with the most notable differences being lower frequencies of IgAN (14% versus 25%, $P < 0.001$), pauci-immune glomerulonephritis (GN) (6% versus 9%, $P < 0.001$) or renal amyloid (2% versus 5%, $P < 0.001$) and higher frequencies of FSGS (18% versus 13%, $P < 0.001$), diabetic GS (18% versus 6%, $P < 0.001$) and thin basement membrane nephropathy (TBMN) (3% versus 1%, $P < 0.001$).

### Glomerular disease subtype distributions by sex

A marked female preponderance was noted for lupus nephritis and TBMN, whereas a modest male predominance was noted for acute post-infectious GN (PIGN), idiopathic nodular

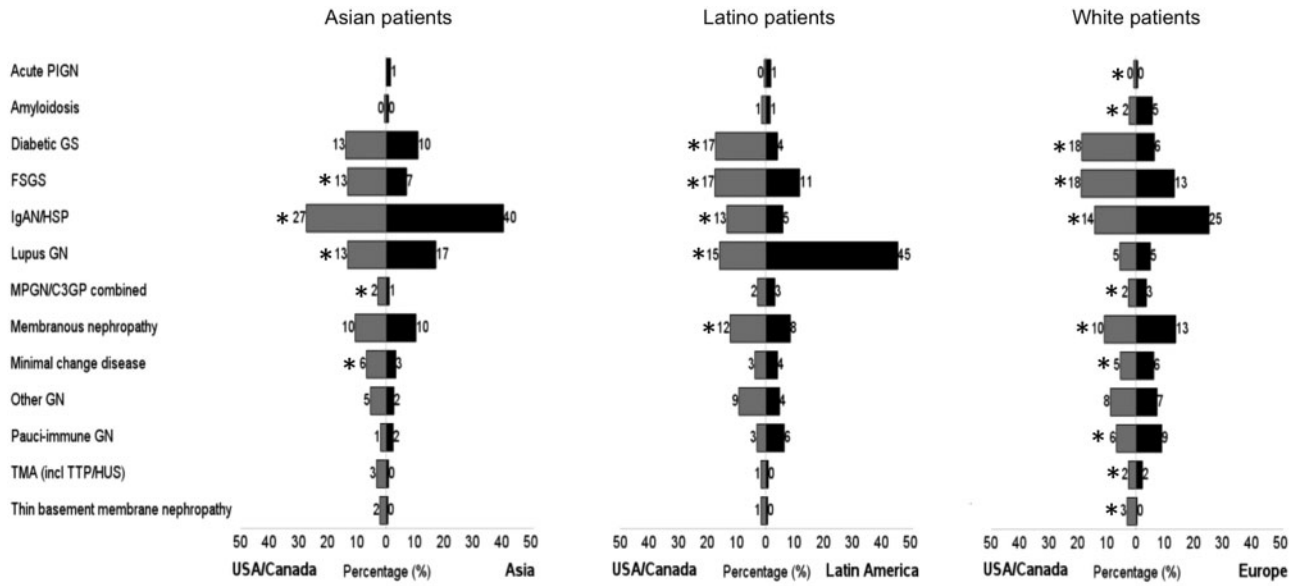


**FIGURE 2:** Glomerular disease subtype kidney biopsy frequencies, by race, comparing regions of ancestral origin to USA/Canada. Showing the 13 most common glomerular disease diagnoses only. *P < 0.004. HSP, Henoch Schonlein purpura; C3GP, C3 glomerulopathy; TMA, thrombotic microangiopathy; TTP, thrombotic thrombocytopenic purpura; HUS, hemolytic uremic syndrome.

GS and IgAN (Figure 3). Comparing glomerular disease subtype frequency distributions across sexes (Supplementary data, Figure S1) identified a high frequency of FSGS (19% in males and 15% in females) and diabetic GS (16% in males and 12% in females) in either sex; however, IgAN was the most frequent diagnosis in males (20%) and lupus nephritis the most frequent in females (20%), overall.

## DISCUSSION

This report highlights important findings from an international collaborative effort across 29 major nephropathology centers to develop a standardized approach to kidney biopsy disease classification and reporting. In this study focusing on 42 603 glomerular disease diagnoses, among a total of 60 340 specific diagnoses within 58 disease categories, we identified substantial variation in the relative frequencies of glomerular disease diagnoses across the four geographic regions examined. Whereas FSGS predominated in North America (USA and Canada), it was the second-most common diagnosis in Europe or Latin America and the fifth-most common in Asia. Conversely, while IgAN predominated in Europe and Asia, and lupus nephritis in Latin America, these were notably less frequent (third- and fifth-most common, respectively) in North America. In an effort to distinguish the influence of race/ethnicity (i.e. genetic factors) from that of region (i.e. environmental or lifestyle factors, including biopsy policies), we also compared frequency distributions across regions stratified by race/ethnicity. Using this approach, we identified a significantly higher frequency of FSGS, and a numerically higher frequency of diabetic GS, along with significantly lower frequencies of IgAN and lupus nephritis, among Asians in North America compared with those in Asia. Similarly, the frequency of diabetic GS was dramatically higher, whereas that of lupus nephritis was substantially lower, among Latinos in North America compared with those in Latin America. Finally, FSGS and diabetic GS were significantly more frequent, and IgAN significantly less frequent, among whites in North America compared with those in Europe.

The reasons for the generally higher frequencies of diabetic GS and FSGS among biopsied patients in North America, even when compared with patients of a similar racial/ethnic background residing in their country of ancestral origin, cannot directly be determined from this study. Without knowing the size of the referral population (denominator), we could not distinguish whether this finding represents a higher absolute frequency of FSGS or diabetic GS, a lower absolute frequency of comparator diagnoses (e.g. IgAN or lupus nephritis), a lower threshold to biopsy patients with morbidities such as diabetes or obesity, or a combination of these factors, within North America as compared with in other regions. Given that diabetic GS and obesity-related secondary forms of FSGS are heavily influenced by lifestyle factors, and that the incidences of diabetes and obesity are steadily rising in the USA [6, 7], we suspect that an absolute increase in the biopsy frequencies of diabetic GS and FSGS (as opposed to a major reduction in the incidences of other subtypes) when patients migrate to North America is the most important contributor to this finding. Of additional note, the biopsy term 'FSGS' could also include secondary types of FSGS lesions in this category in this survey. Based on the limitations of our data, the question remains as to whether this represents a truly higher disease incidence or a differing biopsy practice. It is possible, for example, that physicians in North America have the lowest threshold to biopsy diabetic or obese patients with modest proteinuria, thus increasing the detection rate for diabetic GS or secondary forms of FSGS, respectively. At the same time, physicians in Asia might be most likely to biopsy patients with isolated hematuria (on account of national urinary screening programs), contributing to the high frequencies of IgAN and thin basement membrane lesions observed in this region.

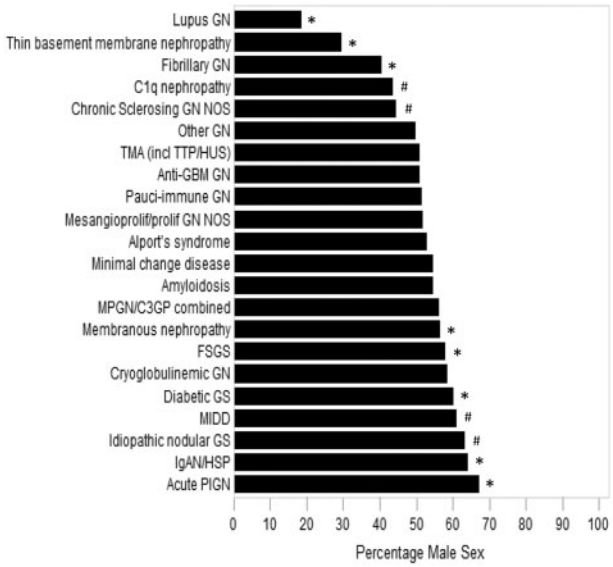


**FIGURE 3:** Male sex frequencies among glomerular disease subtypes. Remaining patients female (missing sex excluded). *$P < 0.002$. #$0.002 < P < 0.05$. NOS, not otherwise specified; TMA, thrombotic microangiopathic anemia; TTP, thrombotic thrombocytopenic purpura; HUS, hemolytic uremic syndrome; GBM, glomerular basement membrane; C3GP, C3 glomerulopathy; MIDD, monoclonal immune deposition diseases; HSP, Henoch Schonlein purpura. 'Other GN' includes diagnoses with <100 cases overall (diffuse mesangial sclerosis, Finnish type congenital nephrotic syndrome, immunotactoid glomerulopathy, collagenofibrotic glomerulopathy, fibronectin glomerulopathy, IgM nephropathy, polyarteritis nodosa, preeclampsia/eclampsia, Fabry disease, lipoprotein glomerulopathy, sickle cell glomerulopathy).

Ultimately, additional studies are required to address these hypotheses; however, if FSGS and diabetic GS truly are more frequent in North America, and become more frequent after moving to North America among those immigrating from other regions (representing a waning of the 'healthy immigrant effect' [8, 9]), then this finding is of major public health relevance. Diabetic nephropathy is the leading cause of end-stage kidney disease in the USA, and FSGS is the leading cause among primary glomerular diseases [10]. While cardiovascular risks are generally increased among all patients with chronic kidney disease, they may be particularly so among patients with either of these glomerular disease subtypes [11, 12]. Finally, diabetic GS and secondary forms of FSGS are potentially preventable, through promoting healthy lifestyle choices and reducing obesity, issues that are at the forefront of public health campaigns.

Our findings of differing frequencies of certain autoimmune glomerular diseases across regions, particularly a high frequency of lupus nephritis in Latin America and high frequencies of IgAN in Europe or Asia, also deserve further mention. While these differences may relate to ancestrally determined genetic factors, as have previously been described [13, 14], our findings support an additional role for environmental factors in disease etiology, i.e. disease predispositions appear to wane when individuals move from their region of ancestral origin to the USA or Canada. Again, whether this finding is explained by differences in lifestyle or environmental exposure factors, by differences in biopsy practices (e.g. approach to investigating isolated hematuria, or approach to repeat biopsies in patients with lupus), and/or by a relative increase in FSGS or diabetic GS risk that outweighs the risk for autoimmune disease development, should be the subject of future studies.

In addition to examining differences in glomerular disease frequency distributions by race and region of residence, we also explored differences in glomerular disease frequencies by patients' sex. Although many of our findings have previously been reported (e.g. a predominance of lupus nephritis among females, and of IgAN among males), by reporting frequency distributions of glomerular disease within males and females separately, we provide a useful summary of the overall disease burden within these patient groups. Also, while we confirmed that lupus nephritis was the most common glomerular disease among females, and IgAN the most common among males, neither sex was spared from the high prevalence of FSGS and diabetic GS that we identified in the cohort overall.

Our findings generally support, and supplement, those reported from single centers or regional databases from the continents examined. For example, multiple studies in the USA have reported that FSGS is the most frequent glomerular disease diagnosis among biopsied populations [15–23], although only one recent study has described the escalating frequency of diabetic nephropathy in the USA [23]. In Europe, IgAN is reported to be the most frequent glomerular disease diagnosis in Lithuania [24], Northern Ireland [25], Croatia [26], Poland [27], the Czech Republic [28, 29], Spain [30] and Italy [31, 32]. However, membranous nephropathy was recently reported to be most frequent glomerular disease in biopsies at a center in Turkey [33], non-IgA mesangioproliferative (MesProlif) GN at a center in Serbia [34] and MesProlif GN with or without IgA deposition (in the most recently reported era) at centers in Germany [35] and Romania [36]. In Asia, IgAN is consistently the most frequently observed glomerular disease in studies from Korea [37, 38] and China [39, 40], corroborating our data from Japan and Thailand. Finally, FSGS and lupus nephritis are generally reported to be the most frequent primary and secondary glomerular disease subtypes, respectively, in Latin America, although which of these two is the most frequent overall varies by study [41–44]. These consistencies between our and prior reports validate our study findings, and add credibility to our data regarding the relative frequencies of less common glomerular disease subtypes (for which existing data are less consistent), and our findings regarding discrepant disease frequencies in individuals of a similar race/ethnicity living in different regions (which, to our knowledge, has not previously been examined).

Our study does have several limitations. As data were most commonly obtained retrospectively within each of the centers, misclassification may have arisen when converting diagnoses from non-standardized original diagnoses to the standardized diagnosis categories adopted for the study. Information regarding biopsy management and processing procedures (e.g. number of sections examined, routine use of immunofluorescence and/or electron microscopy techniques) was not

collected, and the potential confounding influence of such factors on study findings could not be evaluated. Data were provided at the diagnosis level and not the patient level to avoid patient identification; thus, diagnoses of additional primary diseases (e.g. primary FSGS in addition to IgAN or diabetic GS) versus secondary lesions (e.g. secondary segmental sclerosis in the setting of IgAN or diabetic GS) could not be distinguished, which may be particularly relevant for FSGS and diabetic GS diagnoses. While we obtained data from 29 centers in 17 countries and across 4 continents, it remains unlikely that the disease burden we report is perfectly representative of the worldwide disease burden. In particular, the number of centers surveyed in Asia and Latin America was relatively small, and patients residing in North America who were reported to be of Asian or Latino race/ethnicity might have originated from countries other than those included (e.g. China, India, Argentina or Chile). Centers in Africa, Australia and parts of Europe (especially Eastern Europe) were not represented. Some of the included centers may have been specialty referral centers for certain glomerular disease subtypes, inflating local disease frequencies at that center, albeit that this effect should be diluted by inclusion of more than one center/ region. Demographic data, especially race/ethnicity, were frequently missing, and differentially so across regions. However, centers generally either provided or did not provide these data, and did so uniformly across all glomerular disease diagnoses; thus, while missing data reduced our sample size (by reducing the numbers of centers included in certain demographic analyses), when examining particular sex or racial/ethnic groups we expect our conclusions regarding glomerular disease frequency distributions across demographic groups to be valid. Without individual patient-level data regarding age, we could not stratify by age group in our analyses; thus, we could not evaluate whether differences in biopsy practices or disease incidences in certain age groups might have contributed to our study findings, and would welcome this as a focus of future studies. Finally, an estimate of referral population size was available only from two of the centers, and thus background biopsy rates for each of the regions could not be calculated.

Despite these limitations, our study has several strengths. In addition to identifying marked differences in glomerular disease epidemiology across geographic regions, and providing data to suggest that environmental/lifestyle factors and biopsy policies might contribute importantly to this finding, this study marks the first step toward creating a collaborative, international, glomerular disease registry. The potential to expand these efforts to additional centers, and to collect patient-level clinical data along with electronic histologic images, is exciting. In the meantime, the data collected for this project can be meaningfully applied to future research, by providing estimates of disease burden within particular regions or demographic groups, thus guiding disease or high-risk patient identification strategies, and informing hypothesis-driven studies aiming to explain these epidemiologic findings.

To conclude, in this first ever IKBS involving participation from 29 centers across 4 continents, we identified marked variations in glomerular disease frequencies across geographic regions, even within specific racial/ethnic groups, with a particularly high frequency of FSGS and diabetic GS identified among patients in the USA. Whether these findings reflect differences in patient behaviors (e.g. dietary intake, weight management), environmental exposures (e.g. infections, pollutants) and/or biopsy practices (e.g. urinary screening programs, threshold to biopsy patients with diabetes) should be the subject of future studies. Additionally, we confirmed that sex predispositions to glomerular disease development previously described in smaller, often single-center, patient populations, are also evident when examining data from over 40 000 diagnoses. This study represents an exciting step toward studying glomerular disease at the global level, and demonstrates the feasibility of engaging multiple stakeholders from diverse geographic, economic and cultural regions in a collaborative research effort.



## ACKNOWLEDGEMENTS

The authors wish to thank the ASN GDAG, the RPS, and the ERA–EDTA Immunonephrology Working Group for facilitating this work. They also wish to thank the following centers and individuals who collected and submitted biopsy data: Cedars Sinai-Medical Center, Los Angeles, CA, USA (Cynthia C. Nast, Mark Haas); Columbia University Medical Center, New York, NY, USA (Barry Stokes); Department of Pathology, University of Vienna, Vienna, Austria (Renate Kain, Dontscho Kerjaschki, Heinz Regele, Nicolas Kozakowski); The Norwegian Kidney Biopsy Registry, Haukeland University Hospital, Bergen, Norway (Sabine Leh); Hammersmith Hospital, London, UK (Terry Cook, Candice Roufosse); Hennepin County Medical Center, Minneapolis, MN, USA (Gretchen S. Crary); Hopital Tenon, service de nephrologie et dialyses, Paris, France (Emmanuelle Plaisier, Alexandre Cez, Isabelle Brocheriou, Patrice Callard, David Buob); Hospital do Rim e Hipertensao, Federal University of Sao Paulo, Sao Paulo, Brazil (Luiz A. Moura, Elizabeth S. Aragao); Institute for Clinical and Experimental Medicine, Department of Pathology, Prague, Czech Republic (Eva Honsova); Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Department of Anatomic Pathology and Department of Nephrology and Mineral Metabolism, Mexico City, Mexico (Norma Ofelia Uribe-Uribe, Juan Manuel Mejia-Vilet); King Saud University Medical City (KSUMC), King Saud University, Riyadh, Saudi Arabia (Hala Kfoury, Sufia Husain); London Health Sciences Center, London, Ontario, Canada (Madeleine Moussa); Maisonneuve-Rosemont Hospital, Montreal, Quebec, Canada (Virginie Royal); Mayo Clinic, Rochester, MN, USA (Lynn D. Cornell); McMaster University, Department of Pathology and Molecular Medicine, Hamilton, Ontario, Canada (Dusan Lukic); Medical University of Białystok, 1st Department of Nephrology and Transplantation, Białystok, Poland (Tomasz Hryszko, Beata Naumnik, Jolanta Kowalewska); Medical University of South Carolina Department of Pathology & Laboratory Medicine, Charleston, SC, USA (Sally Self); Medical University of Warsaw, Dept of Nephrology and Transplantation Medicine, Warsaw, Poland [Agnieszka Perkowska-Ptasinska, Malgorzata Wagrowska-Danilewicz

(University of Lodz)]; Moscow City Nephrology Center, Moscow City Hospital N52, Moscow, Russia (Ekaterina Stolyarevich, Tatiana Zhilinskaya); National and Kapodistrian University of Athens Medical School, Department of Pathology, Athens, Greece (Lydia Nakopoulou); Nephropathology Center, San Gerardo Hospital, Monza, Italy (Ferrario Franco, Fabio Pagni); Nephropathology Working Group, Academic Medical Center, University of Amsterdam, Amsterdam, The Netherlands (Sandrine Florquin, Joris Hoelbeek, Joris Roelofs); Scottish Renal Biopsy Registry, Glasgow Renal and Transplant Unit, Glasgow, UK (Colin Geddes, Graham Stewart, Bruce Mackinnon, Stewart Fleming, David Walbaum, Jamie Traynor, David Kipgen, Nicola Joss); Tohoku University Graduate School of Medicine, Sendai, Japan (Kensuke Joh); Siriraj Hospital, Mahidol University, Bangkok, Thailand (Boonyarit Cheunsuchon); University of Antioquia, Department of Pathology, Medellín, Antioquia, Colombia (Luis F. Arias); University of Bari, Division of Nephrology, Dialysis and Transplantation Unit, Bari, Italy (Loreto Gesualdo, Michele Rossini); University of North Carolina, Division of Nephropathology, Chapel Hill, NC, USA (J.C.J., B.D.T.); Vanderbilt University Medical Center Pathology, Division of Renal/EM, Nashville, TN, USA (Agnes Fogo).

## SUPPLEMENTARY DATA

Supplementary data are available online at http://ndt.oxfordjournals.org.

## AUTHORS' CONTRIBUTIONS

M.M.O'S., S.L.H., B.D.T., R.C., A.B.F. and J.C.J. were responsible for the research idea and study design; M.M.O'S., B.D.T., R.C., A.B.F. and J.C.J. carried out the data acquisition; M.M.O'S., S.L.H. and J.C.J. carried out data analysis/interpretation; M.M.O'S., S.L.H., B.D.T., R.C., A.B.F. and J.C.J. provided intellectual content during manuscript drafting or revision; and M.M.O'S., S.L.H., B.D.T., R.C., A.B.F. and J.C.J. gave final approval of manuscript submission.

## CONFLICT OF INTEREST STATEMENT

None declared. The results presented in this article have not been published previously in whole or part, except in abstract format.

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*Received: 23.2.2017; Editorial decision: 19.4.2017*