Racial-Ethnic Differences in Health-Related Quality of Life among Adults and Children with Glomerular Disease

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Keywords
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Abstract
Introduction: Disparities in health-related quality of life (HRQOL) have been inadequately studied in patients with glomerular disease. The aim of this study was to identify relationships among race/ethnicity, socioeconomic status, disease severity, and HRQOL in an ethnically and racially diverse cohort of patients with glomerular disease. Methods: Cure Glomerulonephropathy (CureGN) is a multinational cohort study of patients with biopsy-proven glomerular disease. Associations between race/ethnicity and HRQOL were determined by the following: (1) missed school or work due to kidney disease and (2) responses to Patient-Reported Outcomes Measurement Information System (PROMIS) ques-
amination. We adjusted for demographics, socioeconomic status, and disease characteristics using multivariable logistic and linear regression. **Results:** Black and Hispanic participants had worse socioeconomic status and more severe glomerular disease than white or Asian participants. Black adults missed work or school most frequently due to kidney disease (30 vs. 16–23% in the other 3 groups, \( p = 0.04 \)), and had the worst self-reported global physical health (median score 44.1 vs. 48.0–48.2, \( p < 0.001 \)) and fatigue (53.8 vs. 48.5–51.1, \( p = 0.002 \)), compared to other racial/ethnic groups. However, these findings were not statistically significant with adjustment for socioeconomic status and disease severity, both of which were strongly associated with HRQOL in adults. Among children, disease severity but not race/ethnicity or socioeconomic status was associated with HRQOL. **Conclusions:** Among patients with glomerular disease enrolled in CureGN, the worse HRQOL reported by black adults was attributable to lower socioeconomic status and more severe glomerular disease. No racial/ethnic differences in HRQOL were observed in children.

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**Introduction**

Black race, unemployment, and lack of college education are associated with worse health-related quality of life (HRQOL) in patients with chronic kidney disease [1, 2]. Much less is known about racial/ethnic and socioeconomic disparities in HRQOL among patients with glomerular disease, in whom nephrotic syndrome and exposure to immunosuppressive therapies might uniquely impact social functioning and well-being.

Small studies in racially homogenous populations report worse physical and mental health, pain, and social functioning among those with glomerular disease compared to healthy populations [3–6]. Within the racially diverse Cure Glomerulonephropathy (CureGN) cohort of children and adults with glomerular disease, HRQOL was poorer among females and those with edema, obesity, or reduced kidney function [7]. However, race/ethnicity was not the focus of this earlier work and neither the impact of kidney disease on social functioning (e.g., missed work or school due to kidney disease) nor socioeconomic factors were considered. Poor understanding of racial/ethnic disparities in HRQOL in patients with glomerular disease and any underlying socioeconomic factors that contribute to these disparities represent a missed opportunity to identify patients who might benefit from greater clinical attention, socioeconomic support, targeted interventions, or healthcare policy reforms.

The aim of this study was to identify relationships among race/ethnicity, socioeconomic status, disease severity, and HRQOL in a racially and ethnically diverse cohort of adults and children with glomerular disease enrolled in CureGN. We hypothesized that Black and/or Hispanic patients would have a poorer HRQOL but that poorer socioeconomic status and more severe glomerular disease among these groups could explain any observed differences.

**Materials and Methods**

**Patient Population**

CureGN is a 70-center, National Institute of Diabetes and Digestive and Kidney Diseases-funded cohort study of almost 2,400 adults and children with glomerular disease recruited from the USA, Canada, Italy, and Poland. Participants must have had an initial biopsy within 5 years of enrollment demonstrating minimal change disease (MCD), focal segmental glomerulosclerosis (FSGS), membranous nephropathy (MN), or immunoglobulin A nephropathy/vasculitis (IgAN/IgAV) [8]. The inclusion criteria and visit schedule have been previously reported [8]. This study was approved by the Institutional Review Board of Stanford University. All participants provided written informed consent (or assent, if a minor) to be included in the study. Pertinent to this study, visits included completion of laboratory investigations and case report forms assessing symptoms, medications, and HRQOL. Participants who had at least partly completed a Patient-Reported Outcomes Measurement Information System (PROMIS) questionnaire at enrollment and who self-reported as white, black, or Asian, with or without Hispanic ethnicity, were included.

**Exposures, Outcomes, and Covariates**

**Exposures**

Patient-reported race/ethnicity was our exposure of interest and was categorized as follows: white included non-Hispanic Whites; Black included patients of Black race and any ethnicity; Asian included patients of Asian race and any ethnicity; and Hispanic included Hispanic Whites. Patients of any other race or with missing race and/or ethnicity were excluded due to small sample sizes.

**Outcomes**

HRQOL at study enrollment was determined using 2 measures. First, the self- or parent-reported frequency of missing work or school in the past 4 months due to kidney disease was assessed and is reported as median number of days missed and frequency of missed days. Second, PROMIS questionnaire responses were queried. PROMIS domains incorporated in the CureGN study protocol include 5 measures for adults (general physical health, general mental health, anxiety, fatigue, and sleep disturbance) and 4 measures for children (global health, anxiety (in those >8 years), fatigue, and mobility). The PROMIS instrument was previously validated in children with nephrotic syndrome [9–11].
questionnaires were completed by participants aged ≥8 years and by a parent proxy if <8 years. Scores were compared to the general population median value of 50 [12]. Higher scores indicate more of the measured trait (e.g., more fatigue or greater mobility) and, accordingly, can represent either better or worse HRQOL depending on the trait. A 3-point “minimally important difference” is considered clinically meaningful [7, 13]. Median scores and frequency of scores that deviated from the median by the minimally important difference are reported.

Covariates
Demographic (age and sex), socioeconomic, and disease-related characteristics at enrollment were compared across racial/ethnic groups. Adjustment was made for these covariates when determining the associations between race/ethnicity and HRQOL. Candidate socioeconomic variables included the country of residence (USA = reference, Canada, Italy, or Poland), insurance category (private = reference, public, other, or none), patient or parental education (at least a college degree = reference, less than a college degree), and, for adults, student/employment status (employed not a student = reference, employed and student, unemployed and student, unemployed and not a student, medical leave or disability, other). Disease indicators included the glomerular disease subtype (IgAN/IgAV = reference, MCD, FSGS, and MN), family history of kidney disease including kidney failure (no = reference, yes), glomerular disease duration (time from kidney biopsy to enrollment), hypertension status (normal = reference, prehypertension, or hypertension) [14, 15], and weight status (underweight or normal = reference, overweight, and obese). Disease severity included the presence of self-reported edema (less than moderate = reference, moderate or greater), urine protein/creatinine ratio (uPCR), estimated glomerular filtration rate (eGFR), serum albumin, use of glucocorticoids (no = reference, yes), and use of other immunosuppression (no = reference, yes). Additional details of data collection and definitions are provided in online suppl. Table 1; see www.karger.com/doi/10.1159/000516832 for all online suppl. material.

Statistical Analysis
Analyses were stratified by adult or pediatric status. Participant characteristics are reported as median and interquartile range for continuous variables and as number and percent for categorical variables. Between-group comparisons were made using χ² tests for categorical variables and Kruskal-Wallis tests for continuous variables. Logistic regression models were used to examine associations between race/ethnicity and the outcome of missing at least 1 day of work/school in the past 4 months due to kidney disease. Linear regression models were used to examine associations between race/ethnicity and PROMIS scores. Five sequential models for each outcome were assessed: the first examined unadjusted associations between race/ethnicity and the outcome; the second additionally adjusted for demographics; the third additionally adjusted for socioeconomic factors; the fourth additionally adjusted for chronic disease indicators; and the fifth additionally adjusted for disease severity and activity markers. While all the covariates were included in the multivariable models, only those with statistically significant associations at α < 0.05 level are presented in the results tables. Those that remained significant at α < 0.05 level after adjustment for multiple comparisons using the false discovery rate correction [16] are highlighted in bold. Adjusted analyses were restricted to the study population with complete data for all variables. Missing data were not imputed, but sensitivity analyses were performed to assess any potential impact of missing data on study findings, including performing adjusted analyses on the full cohort and comparing baseline characteristics between those with versus without missing data. Additional sensitivity analyses included (1) restricting to participants recruited from the US sites, (2) testing for interactions between race/ethnicity and socioeconomic variables, and (3) stratifying analyses of children according to whether HRQOL questionnaires were self-reported by the child (≥8 years) or by their parent proxy (<8 years). Analyses were performed using SAS 9.4 (SAS Institute, Cary, NC, USA).

Results

Racial/Ethnic Differences in Socioeconomic and Disease Characteristics: Adults
Among the 1,379 adults studied, 884 (64%) were White, 226 (16%) were Black (14 Hispanic), 146 (11%) were Asian, and 123 (9%) were Hispanic (Fig. 1; Table 1, and online suppl. Figure 1). Black (28%) or Hispanic (30%) adults were less likely than White (48%) or Asian (66%) adults to be college-educated. Black adults were most likely to have public health insurance, and Hispanic adults were most likely to be uninsured. Black or Hispanic adults were most likely to be on medical leave or disability, or to be unemployed. Black adults had the highest frequency of FSGS (48%), Hispanic or Asian adults had the highest frequency of IgAN/IgAV (41 and 38%, respectively), and White adults had the highest frequency of MN (34%). Obesity and hypertension were most frequent in Black and least frequent in Asian adults. Black adults had the greatest disease severity, including the highest uPCR, lowest serum albumin, and highest frequency of moderate or greater edema. Hispanic adults had the lowest eGFR. No significant racial/ethnic differences in medication use at enrollment were identified. Findings were overall similar for the 708 adults who had complete data, online suppl. Table 2.

Ethnic Differences in Socioeconomic and Disease Characteristics: Children
Among the 785 children studied, 517 (66%) were White, 146 (18.5%) were Black (3 Hispanic), 45 (5.5%) were Asian (1 Hispanic), and 77 (10%) were Hispanic (Fig. 1, Table 2, and online suppl. Figure 1). Parents of Black or Hispanic children were least likely to be college-educated (22 and 18%, respectively, vs. 43% for White and 65% for Asian children). Private insurance was also less frequent in Black (35%) or Hispanic (35%) than white (58%) or Asian (53%) children. Overall, MCD was the
most common glomerular disease in children, but FSGS occurred almost as frequently as MCD (41 and 47%, respectively) in Black children. Black or Hispanic children were more likely to be obese or hypertensive. Mean eGFR at enrollment was lowest in Black children. No significant racial/ethnic differences in medication use at enrollment were identified in children. Findings were overall similar for the 386 children who had complete data, online suppl. Table 3.

Measures of HRQOL: Adults

Of adults who were employed or studying full- or part-time (n = 974), Black adults were most likely to have missed work or school in the preceding 4 months due to kidney disease (30, 23, 17, and 16% of Black, White, Asian, and Hispanic adults, respectively, p = 0.04), online suppl. Table 4. However, after adjusting for demographics, socioeconomic measures, and disease characteristics, the odds of missing work or school due to kidney disease were no longer higher in Black adults (odds ratio [OR] 1.20, 95% confidence interval [CI] 0.58–2.47) and were numerically lower in Hispanic adults (OR 0.31, 95% CI 0.10–0.92, p = 0.03 not significant after accounting for false discovery), Figure 2 and Table 3. Factors associated with missing work or school in adults were younger age and markers of disease severity (current use of glucocorticoids, and moderate or greater edema), Table 3.

Approximately a third and a half of adults reported their HRQOL as being substantially poorer than those reported in the general population (i.e., >3 points lower or higher than the general population median of 50) for each of the PROMIS domains, online suppl. Table 4. Black adults had significantly poorer global physical health scores (44.1 vs. 48.0–48.2 in other 3 groups, p < 0.001) and more fatigue (53.8 vs. 48.5–51.1 in the other 3 groups, p = 0.002) than other adults, online suppl. Table 4. After multivariable adjustment, the only significant association between race/ethnicity and any PROMIS measure was less fatigue among Hispanic adults (beta −3.57, 95% CI −6.02 to −1.11), Table 3 and Figure 2. Socioeconomic factors and disease severity were instead the major drivers of HRQOL among adults. Specifically, medical leave or disability, unemployment, and edema were associated with worse scores in most PROMIS domains, while lack of college education, worse laboratory parameters, and obesity were associated with worse physical health, Table 3.

Measures of HRQOL: Children

There were no significant associations between the race/ethnicity and likelihood to miss school for children or their parents (Fig. 3; online suppl. Table 5). Parents...
missing school or work was associated with a more recent glomerular disease diagnosis (Table 4).

The PROMIS domain of global health was the most severely impacted in children with glomerular disease, with approximately half of children reporting a score at least 3 points lower than the general population median. The median scores for anxiety, fatigue, and mobility reflected better HRQOL among pediatric CureGN partici-

Table 1. Demographic, socioeconomic, and clinical characteristics at enrollment: adults (n = 1,379)

| Characteristic                          | White (n = 884) | Black (n = 226) | Asian (n = 146) | Hispanic (n = 123) | p value |
|----------------------------------------|-----------------|-----------------|-----------------|-------------------|---------|
| Age, years                             | 49 (34–62)      | 46 (32–57)      | 43 (32–55)      | 39 (31–51)        | <0.001  |
| Male                                   | 541 (61)        | 92 (41)         | 78 (53)         | 65 (53)           | <0.001  |
| Country of residence                   |                 |                 |                 |                   |         |
| The USA                                | 744 (84)        | 216 (96)        | 107 (73)        | 113 (92)          |         |
| Canada                                 | 97 (11)         | 10 (4)          | 39 (27)         | 10 (8)            | <0.001  |
| Italy                                  | 8 (1)           | 0 (0)           | 0 (0)           | 0 (0)             |         |
| Poland                                 | 35 (4)          | 0 (0)           | 0 (0)           | 0 (0)             |         |
| Insurance status at enrollment[^a]    |                 |                 |                 |                   |         |
| Private                                | 660 (76)        | 142 (64)        | 105 (73)        | 57 (49)           |         |
| Public                                 | 179 (21)        | 62 (28)         | 25 (17)         | 19 (16)           | <0.001  |
| Other                                  | 25 (3)          | 12 (5)          | 13 (9)          | 25 (21)           |         |
| None                                   | 6 (1)           | 6 (3)           | 0 (0)           | 16 (14)           |         |
| College education                      | 423 (48)        | 63 (28)         | 96 (66)         | 37 (30)           | <0.001  |
| Current student/employment status      |                 |                 |                 |                   |         |
| Employed, not a student                | 509 (58)        | 123 (54)        | 99 (68)         | 67 (54)           |         |
| Employed and a student                 | 59 (7)          | 17 (8)          | 9 (6)           | 7 (6)             |         |
| Student, not employed                  | 53 (6)          | 14 (6)          | 8 (6)           | 9 (7)             |         |
| Medical leave or disabled              | 44 (5)          | 20 (9)          | 0 (0)           | 14 (11)           | <0.001  |
| Unemployed                             | 40 (5)          | 25 (11)         | 3 (2)           | 9 (7)             |         |
| Other                                  | 177 (20)        | 27 (12)         | 26 (18)         | 17 (14)           |         |
| Disease type                           |                 |                 |                 |                   |         |
| MCD                                    | 140 (16)        | 29 (13)         | 26 (18)         | 9 (7)             |         |
| FSGS                                   | 199 (23)        | 109 (48)        | 24 (16)         | 39 (32)           | <0.001  |
| MN                                     | 298 (34)        | 68 (30)         | 40 (27)         | 25 (20)           |         |
| IgAN/IgAV                              | 247 (28)        | 20 (9)          | 56 (38)         | 50 (41)           |         |
| Family history of kidney disease[^a]   | 260 (30)        | 98 (44)         | 44 (31)         | 33 (28)           | <0.001  |
| Disease duration, months               | 14.2 (5.0–36.5) | 17.0 (5.7–41.2) | 22.1 (6.1–41.7) | 12.8 (4.2–45.0) | 0.1     |
| Hypertension status at enrollment[^b]  |                 |                 |                 |                   |         |
| Normal                                 | 275 (33)        | 62 (29)         | 72 (50)         | 47 (39)           |         |
| Prehypertensive                        | 355 (43)        | 81 (38)         | 45 (31)         | 49 (41)           | <0.001  |
| Hypertensive                           | 205 (25)        | 70 (33)         | 26 (18)         | 24 (20)           |         |
| Weight status at enrollment[^a]        |                 |                 |                 |                   |         |
| Normal/underweight                     | 253 (29)        | 42 (19)         | 71 (51)         | 35 (29)           |         |
| Overweight                             | 280 (33)        | 55 (25)         | 55 (39)         | 40 (33)           | <0.001  |
| Obese                                  | 327 (38)        | 123 (56)        | 14 (10)         | 46 (38)           |         |
| Moderate or greater edema at enrollment[^b] | 230 (27)  | 86 (42)         | 33 (24)         | 38 (33)           | <0.001  |
| uPCR, g/g[^c]                          | 1.50 (0.37–4.11) | 2.60 (0.77–5.90) | 1.35 (0.40–4.09) | 1.61 (0.52–3.61) | 0.003   |
| eGFR, mL/min/1.73 m[^2][^b]             | 69 (44–93)      | 62 (34–89)      | 78 (44–97)      | 57 (37–96)        | 0.02    |
| Serum albumin, g/dL[^c]                | 3.8 (3.1–4.2)   | 3.5 (2.7–3.9)   | 3.8 (3.2–4.3)   | 3.8 (3.1–4.1)     | <0.001  |
| Current glucocorticoids                | 256 (29)        | 67 (30)         | 31 (21)         | 32 (26)           | 0.2     |
| Current other immunosuppression        | 250 (28)        | 63 (28)         | 40 (27)         | 34 (28)           | 0.9     |

All values represent n (%) or median (IQR) unless otherwise indicated. MCD, minimal change disease; FSGS, focal segmental glomerulosclerosis; MN, membranous nephropathy; IgAN, IgA nephropathy; IgAV, IgA vasculitis; eGFR, estimated glomerular filtration rate; uPCR, urine protein-to-creatinine ratio. Missing data (all data missing at <1% unless otherwise indicated):[^a] 1–5% missing,[^b] 6–10% missing,[^c] 20–25% missing. There were no significant differences across racial/ethnic groups in the percent missing for any of the variables in Table 1. Bold p values indicate significance at α < 0.05 after False Discovery Rate (FDR) correction.
pants than in the general population (online suppl. Table 5). There were no significant associations between race/ethnicity and PROMIS scores in children, both prior to and after multivariate adjustment (Fig. 3; online suppl. Table 5). PROMIS scores in children were strongly associated with obesity and edema. No significant associations between socioeconomic variables and PROMIS scores were observed (Table 4).

### Missing Data

With the exception of edema, uPCR, and serum albumin, percent missing was <10% for all covariates and outcomes, Tables 1 and 2. Overall, 49% of our cohort (48% adults and 51% children) had missing data for at least 1 variable, resulting in 1,094 participants in our complete cohort (708 adults and 386 children). Missingness did not differ by racial/ethnic groups (Tables 1, 2; online suppl. Table 2).

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### Table 2. Demographic, socioeconomic, and clinical characteristics at enrollment: children (n = 785)

|                          | White (n = 517) | Black (n = 146) | Asian (n = 45) | Hispanic (n = 77) | p value |
|--------------------------|----------------|----------------|--------------|-----------------|---------|
| Age, years               | 11 (7–15)      | 13 (8–16)      | 11 (7–13)    | 11 (7–15)       | 0.1     |
| Male                     | 312 (60)       | 75 (51)        | 28 (62)      | 41 (53)         | 0.12    |
| Country of residence     |                |                |              |                 |         |
| The USA                  | 441 (85)       | 143 (98)       | 35 (78)      | 73 (95)         |         |
| Canada                   | 10 (2)         | 3 (2)          | 9 (20)       | 1 (1)           |         |
| Italy                    | 66 (13)        | 0 (0)          | 1 (2)        | 3 (4)           |         |
| Insurance status at enrollment\(^b\) |                |                |              |                 |         |
| Private                  | 283 (58)       | 47 (35)        | 23 (53)      | 26 (35)         |         |
| Public                   | 186 (38)       | 81 (60)        | 18 (42)      | 44 (59)         |         |
| Other                    | 10 (2)         | 5 (4)          | 1 (2)        | 5 (7)           |         |
| None                     | 5 (1)          | 2 (1)          | 1 (2)        | 0 (0)           |         |
| College education\(^b\) |                |                |              |                 |         |
| Mother                   | 182 (38)       | 20 (15)        | 22 (55)      | 9 (13)          |         |
| Father                   | 151 (33)       | 17 (15)        | 23 (58)      | 9 (14)          | <0.001  |
| Either parent            | 207 (43)       | 30 (22)        | 26 (65)      | 13 (18)         | <0.001  |
| Disease type             |                |                |              |                 |         |
| MCD                      | 189 (37)       | 68 (47)        | 22 (49)      | 30 (39)         |         |
| FSGS                     | 98 (19)        | 60 (41)        | 8 (18)       | 14 (18)         | <0.001  |
| MN                       | 22 (4)         | 11 (8)         | 1 (2)        | 6 (8)           |         |
| IgAN/IgAV                | 208 (40)       | 7 (5)          | 14 (31)      | 27 (35)         |         |
| Family history of kidney disease\(^a\) | 132 (26)   | 52 (37)        | 12 (30)      | 26 (35)         | 0.05    |
| Disease duration, months | 14.5 (4.9–35.8)| 15.6 (5.1–44.7)| 22.7 (6.5–44.4)| 15 (5.3–37.6) | 0.7     |
| Hypertension status at enrollment\(^a\) |                |                |              |                 |         |
| Normal                   | 328 (67)       | 72 (53)        | 30 (70)      | 41 (55)         |         |
| Prehypertensive          | 63 (13)        | 23 (17)        | 3 (7)        | 10 (14)         | 0.04    |
| Hypertensive             | 101 (21)       | 41 (30)        | 10 (23)      | 23 (31)         |         |
| Weight status at enrollment\(^a\) |                |                |              |                 |         |
| Normal/underweight       | 262 (51)       | 58 (41)        | 26 (58)      | 31 (41)         |         |
| Overweight               | 109 (21)       | 25 (18)        | 5 (11)       | 14 (18)         | 0.01    |
| Obese                    | 138 (27)       | 59 (42)        | 14 (31)      | 31 (41)         |         |
| Moderate or greater edema at enrollment\(^c\) | 57 (13)     | 25 (21)        | 5 (12)       | 9 (13)          | 0.1     |
| uPCR, g/g\(^c\)          | 0.33 (0.11–1.93)| 1.08 (0.15–3.29)| 0.40 (0.13–2.54)| 0.63 (0.12–3.37)| 0.2     |
| eGFR, mL/min/1.73 m\(^2\),\(^b\) | 101 (86–121) | 95 (72–114) | 110 (97–131) | 107 (90–131) | <0.001  |
| Serum albumin, g/dL\(^c\) | 3.8 (3.0–4.2) | 3.5 (2.9–4.0) | 4.0 (3.6–4.3) | 3.9 (3.1–4.3) | 0.01    |
| Current glucocorticoids  | 207 (40)       | 52 (36)        | 20 (44)      | 28 (36)         | 0.7     |
| Current other immunosuppression | 251 (49) | 68 (47)        | 24 (53)      | 36 (47)         | 0.9     |

All values represent n (%) or median (IQR) unless otherwise indicated. MCD, minimal change disease; FSGS, focal segmental glomerulosclerosis; MN, membranous nephropathy; IgAN, IgA nephropathy; IgAV, IgA vasculitis; eGFR, estimated glomerular filtration rate; uPCR, urine protein-to-creatinine ratio. Missing data (all data missing at <1% unless otherwise indicated):\(^a\) 1–5% missing,\(^b\) 6–10% missing,\(^c\) 10–20% missing. There were no significant differences across racial/ethnic groups in the percent missing for any of the variables in Table 2. Bold p values indicate significance at α < 0.05 after False Discovery Rate (FDR) correction.
Table 3. Variables significantly associated with health-related quality of life in the final, fully adjusted models: adults ($n = 708^a$)

| Variable                                      | Any missed work or school/college ($95\%$ CI) | $p$ value | PROMIS physical health Beta ($95\%$ CI) Higher = better | $p$ value | PROMIS mental health Beta ($95\%$ CI) Higher = better | $p$ value | PROMIS anxiety Beta ($95\%$ CI) Lower = better | $p$ value | PROMIS fatigue Beta ($95\%$ CI) Lower = better | $p$ value | PROMIS sleep disturbance Beta ($95\%$ CI) Lower = better | $p$ value |
|-----------------------------------------------|---------------------------------------------|-----------|----------------------------------------------------------|-----------|----------------------------------------------------------|-----------|-------------------------------------------------|-----------|-------------------------------------------------|-----------|-------------------------------------------------|-----------|
| Race (ref = white)                            |                                             | 0.1       | 0.7                                                      | 0.9       | 0.7                                                      | 0.04      | 0.8                                             | 0.0003    | 0.5                                             | 0.01      | 10                                              | 0.01      |
| Black                                         | 1.20 (0.58, 2.47)                           | 0.06      | 0.25                                                     | 0.8       | 0.36                                                     | 0.7       | 0.13                                            | 0.9       | 0.68                                            | 0.05      | 0.91                                            | 0.01      |
| Asian                                         | 0.62 (0.24, 1.63)                           | 0.3       | 0.72                                                     | 0.5       | 0.11                                                     | 0.9       | 1.09                                            | 0.3       | 0.24                                            | 0.8       | 0.60                                            | 0.06      |
| Hispanic                                      | 0.31 (0.10, 0.92)                           | 0.03      | 1.06                                                     | 0.4       | 0.80                                                     | 0.5       | 0.60                                            | 0.6       | 3.57                                            | 0.004     | 0.82                                            | 0.05      |
| Age (per 10 year increase)                    | 0.68 (0.55, 0.84)                           | 0.0003    | –1.70 (–2.98, –0.43)                                     | 0.009     | 1.99 (0.82, 3.15)                                        | 0.0009    | 2.45 (1.09, 3.8)                                | 0.0004    | 0.52 (–0.72, 1.76)                              | 0.4       |
| Country (ref = USA)                           |                                             |           |                                                          |           |                                                          |           |        |                                                |           |        |                                                |           |        |
| Canada                                        |                                             |           |                                                          |           |                                                          |           |        |                                                |           |        |                                                |           |        |
| Italy                                         |                                             |           |                                                          |           |                                                          |           |        |                                                |           |        |                                                |           |        |
| Poland                                       |                                             |           |                                                          |           |                                                          |           |        |                                                |           |        |                                                |           |        |
| College education                             | 2.14 (0.82, 1.45)                           | 0.001     |                                                          |           |                                                          |           |        |                                                |           |        |                                                |           |        |
| Student/employment status                     |                                             |           | <0.0001                                                   | <0.0001   | 0.02                                                      |           | 0.02                                           |           | 0.002                                          |           |
| Employed and student                          | –4.11 (–8.98, 0.76)                         | 0.01      | –5.39 (–10.41, –0.36)                                    | 0.04      | 0.28 (–4.86, 5.46)                                       | 0.09      | 0.68 (–4.04, 5.39)                             | 0.08      |
| Student, no employment                        | –4.15 (–8.98, 0.76)                         | 0.05      | –2.02 (–4.96, 0.97)                                      | 0.1       | –0.42 (–3.21, 2.38)                                      | 0.08      | –0.52 (–3.08, 2.05)                           | 0.07      |
| Medical leave or disability                   | –6.88 (–10.38, –3.37)                       | 0.0001    | –7.14 (–10.76, –3.53)                                    | 0.0001    | 4.13 (0.39, 7.86)                                        | 0.03      | 4.38 (0.95, 7.82)                              | 0.01      |
| Unemployed                                    | –6.36 (–10.06, –2.73)                       | 0.0006    | –7.12 (–10.87, –3.36)                                    | 0.0002    | 2.65 (–2.21, 6.51)                                       | 0.2       | 2.62 (–0.94, 6.17)                             | 0.1       |
| Other                                         | –3.49 (–6.82, –0.16)                        | 0.04      | –3.60 (–7.03, –0.17)                                     | 0.04      | 0.05 (–3.48, 3.58)                                       | 1.0       | –0.51 (–3.75, 2.73)                           | 0.08      |
| Weight status                                 |                                             |           | <0.0001                                                   |           |                                                          |           |        |                                                |           |        |                                                |           |        |
| Overweight                                    | –1.62 (–3.21, –0.04)                        | 0.05      |                                                          |           |                                                          |           |        |                                                |           |        |                                                |           |        |
| Obese                                         | –3.60 (–5.37, –2.03)                        |           | <0.0001                                                   |           |                                                          |           |        |                                                |           |        |                                                |           |        |
| Moderate or greater edema                     | 3.87 (2.22, 6.75)                           | <0.0001   | –7.07 (–9.67, –4.48)                                     | <0.0001   | –5.04 (–6.88, –3.20)                                     | <0.0001   | 3.78 (2.5, 5.06)                               | <0.0001   | 6.72 (5.24, 8.2)                               | <0.0001   | 3.52 (2.37, 4.88)                              | <0.0001   |
| uPCR (per unit increase)                      | 1.10 (1.02, 1.19)                           | 0.01      | –0.30 (–0.64, –0.05)                                     | 0.008     | 0.09 (–0.24, 0.06)                                       | 0.2       | 0.23 (0.07, 0.38)                              | 0.004     |
| eGFR (per unit increase)                      | 0.99 (0.98, 1)                              | 0.03      | 0.02 (0.00, 0.05)                                         | 0.04      |                                                          |           |        |                                                |           |        |                                                |           |        |
| On glucocorticoid                             | 2.83 (1.65, 4.87)                           | 0.0002    |                                                          |           |                                                          |           |        |                                                |           |        |                                                |           |        |

Shown are variables significantly associated with health-related quality of life for adults in the final fully adjusted models. Note that associations with race/ethnicity are reported even when not statistically significant. uPCR, urine protein-to-creatinine ratio (g/g); eGFR, estimated glomerular filtration rate (mL/min/1.73 m²); CI, confidence interval; OR, odds ratio; PROMIS, Patient-Reported Outcomes Measurement Information System. Bold p values indicate significance at $α < 0.05$ after False Discovery Rate (FDR) correction.

$^a$ Only patients with complete data for all variables were included for adjusted analyses. $^b$ Among participants either in school or employed ($n = 974$).
Tables 4 and 5). Characteristics of those with complete data were very similar to those with missing data (online suppl. Tables 6, 7), and comparisons in baseline characteristics across racial/ethnic groups in the complete data cohort (online suppl. Tables 2, 3) produced similar findings to those identified in the full cohort (Tables 1, 2). Finally, adjusted analyses performed on the full cohort, with patient numbers decreasing in sequential models due to increasing missing data, produced very similar results to the analyses performed on the cohort with complete data (data not shown). Accordingly, we consider results obtained from the complete data cohort to be generalizable to the full CureGN cohort.

**Sensitivity Analyses**

Restricting analyses to patients enrolled at US sites did not alter our main study findings (online suppl. Tables 8 and 9). No interactions between race/ethnicity and any of the studied socioeconomic measures were identified (data not shown). Finally, stratifying by whether pediatric HRQOL questionnaires were self-reported or reported by parent proxy did not identify new associations between race/ethnicity and HRQOL in children (data not shown).

**Discussion**

This study determined relationships among race/ethnicity, socioeconomic factors, disease severity, and HRQOL in CureGN, an international multicenter cohort study of children and adults with glomerular disease. We found that these patients frequently miss school or work due to glomerular disease and that many rate their HRQOL as being substantially poorer than the general population. Further, we explored the complex interplay...
among race/ethnicity, socioeconomic status, disease severity, and HRQOL in the CureGN population. We identified poorer HRQOL among Black than white adults, largely explained by worse socioeconomic status (as measured by health insurance, education, and employment) and more severe glomerular disease (as measured by laboratory parameters and self-reported edema). For children, glomerular disease severity was the strongest driver of HRQOL, rather than race/ethnicity or socioeconomic factors.

The present study substantially extends previous findings from 2 small studies that showed associations between glomerular disease severity and HRQOL. In a Brazilian study of glomerulopathy in adults [4] and a Dutch study of steroid-sensitive nephrotic syndrome in children [6], poorer physical health, mental health, and social functioning were associated with heavier proteinuria and greater medication use. In a prior study from the CureGN cohort, edema was the strongest predictor of poorer HRQOL in patients with glomerular disease [7]. However, socioeconomic factors were not previously assessed, and yet in the present study, these are central drivers of HRQOL in adults. Race/ethnicity did not predict worse HRQOL in either adults or children with adjustment for key covariates. In fact, Black race was actually associated with better global health and less fatigue in children, after adjusting for disease severity and other factors. Missed school or work within the last 4 months due to glomerular disease, a marker of the social and societal impact of disease, occurred in 22% of adult participants and in 40% of parents or 35% of child participants. While Black adults were more likely than others to miss work or school, this difference was largely explained by more severe disease.

Important differences between children and adults were identified in this study. Black race was associated with poorer HRQOL (missed work or school and responses to PROMIS questionnaires) in unadjusted analyses only in adults, but these differences were no longer apparent after multivariable adjustment. Markers of glomerular disease severity were associated with HRQOL in both children and adults, but after multivariable adjust-

![Fig. 3. OR for missing work or school and betas for PROMIS scores in sequential regression models for children. OR, odds ratio; PROMIS, Patient-Reported Outcomes Measurement Information System; CI, confidence interval.](image-url)
Table 4. Variables significantly associated with health-related quality of life in the final, fully adjusted models: children (*n* = 386)  

| Race (ref = white) | Any missed school, OR (95% CI) | p value | Parents: any missed work or school, OR (95% CI) | p value | PROMIS global health beta | p value | PROMIS anxiety beta (95% CI) | Lower = better | p value | PROMIS fatigue beta (95% CI) | Lower = better | p value | PROMIS mobility beta (95% CI) | Higher = better |
|-------------------|-------------------------------|---------|------------------------------------------------|---------|--------------------------|---------|---------------------------|--------------|---------|---------------------------|--------------|---------|---------------------------|---------------|
| Black             | 1.30 (0.66, 2.55)             | 0.5     | 0.87 (0.43, 1.79)                               | 0.3     | 2.92 (0.24, 5.61)        | 0.1     | −1.44 (−3.64, 0.75)       | 0.03         | 3.32 (−6.79, 3.06)       | 0.03         | 1.32 (−9.63, 8.61)        | 0.3          | 0.04         | 1.32 (−17.13, 17.13)      | 0.10          |
| Asian             | 0.79 (0.28, 2.17)             | 0.6     | 0.30 (0.09, 1.05)                               | 0.06    | −1.20 (−5.45, 3.06)      | 0.6     | −3.26 (-6.00, 0.16)       | 0.3          | −0.66 (−5.82, 4.51)      | 0.8           | −0.11 (−17.13, 12.92)     | 1.0          | 0.01         | −2.49 (−17.13, 17.13)      | 0.96          |
| Hispanic          | 1.72 (0.74, 3.95)             | 0.2     | 1.18 (0.52, 2.71)                               | 0.7     | 0.8 (−3.95, 2.36)        | 0.6     | −1.12 (−4.06, 1.83)       | 0.5          | 3.10 (−7.86, 6.97)       | 0.1           | 0.18 (−2.49, 2.85)        | 0.01         |
| Female            |                               |         |                                                |         |                          |         | PROMIS anxiety beta (95% CI) | Lower = better | p value | PROMIS fatigue beta (95% CI) | Lower = better | p value | PROMIS mobility beta (95% CI) | Higher = better |
|                   |                               |         | 2.31 (0.79, 3.61)                               |         | 0.003                    |         |                          |              |         |                          |              |         |                          |               |
| Country (ref = USA) |                              |         |                                                |         |                          |         | PROMIS anxiety beta (95% CI) | Lower = better | p value | PROMIS fatigue beta (95% CI) | Lower = better | p value | PROMIS mobility beta (95% CI) | Higher = better |
|                   |                               |         | 0.81 (0.72, 0.92)                               |         | 0.001                    |         | −0.20 (−0.82, −0.10)      | 0.007         | 0.001                    | 0.002         | 0.002                    | 0.002         | 0.004         | 0.003         |
|                   |                               |         | Weight status (ref = normal/underweight)        |         | 0.004                    |         | −0.20 (−0.82, −0.10)      | 0.007         | 0.001                    | 0.002         | 0.002                    | 0.002         | 0.004         | 0.003         |
|                   |                               |         | Overweight                                      |         | 0.004                    |         | −0.20 (−0.82, −0.10)      | 0.007         | 0.001                    | 0.002         | 0.002                    | 0.002         | 0.004         | 0.003         |
|                   |                               |         | Obese                                           |         | 0.004                    |         | −0.20 (−0.82, −0.10)      | 0.007         | 0.001                    | 0.002         | 0.002                    | 0.002         | 0.004         | 0.003         |
|                   |                               |         | Duration of disease (per year)                  |         | 0.001                    |         | −0.20 (−0.82, −0.10)      | 0.007         | 0.001                    | 0.002         | 0.002                    | 0.002         | 0.004         | 0.003         |
|                   |                               |         | Moderate or greater edema                       |         | 0.001                    |         | −0.20 (−0.82, −0.10)      | 0.007         | 0.001                    | 0.002         | 0.002                    | 0.002         | 0.004         | 0.003         |
|                   |                               |         | uPCR (per unit increase)                        |         | 0.001                    |         | −0.20 (−0.82, −0.10)      | 0.007         | 0.001                    | 0.002         | 0.002                    | 0.002         | 0.004         | 0.003         |
|                   |                               |         | eGFR (per unit increase)                        |         | 0.001                    |         | −0.20 (−0.82, −0.10)      | 0.007         | 0.001                    | 0.002         | 0.002                    | 0.002         | 0.004         | 0.003         |

Shown are variables significantly associated with health-related quality of life for children in the final, fully adjusted models. Note that associations with race/ethnicity are reported even when not statistically significant. Bold *p* values indicate significance at α < 0.05 after FDR correction. IgAN, IgA nephropathy; IgAV, IgA vasculitis; MCD, minimal change disease; MN, membranous nephropathy; FSGS, focal segmental glomerulosclerosis; uPCR, urine protein-to-creatinine ratio (g/g); eGFR, estimated glomerular filtration rate (mL/min/1.73 m²); FDR, false discovery rate; PROMIS, Patient-Reported Outcomes Measurement Information System. *Only patients with complete data for all variables included for adjusted analyses. †Administered only to children aged 8 years or older.
ment, measures of socioeconomic status were associated with HRQOL only in adults. There are few previous reports evaluating race/ethnicity, socioeconomic status, and HRQOL in adults with glomerular disease. In children with glomerular disease, such reports have yielded conflicting findings. In the PROMIS I study, aiming to validate PROMIS measures in children with nephrotic syndrome, Hispanic children had worse social-peer relationships, upper extremity functioning, and mobility scores, while Black children overall had higher pain interference scores and those whose guardians were better educated had lower pain interference scores [11]. In contrast, the follow-up longitudinal PROMIS II study, restricted to children with active nephrotic syndrome, reported no association between race/ethnicity and PROMIS scores [17] and no differences by race in changes to PROMIS scores over 1 year [10]. Our findings suggest that disease severity is the primary driver of HRQOL in children with glomerular disease, while race/ethnicity and socioeconomic status contribute minimally.

Due to the cross-sectional nature of this study, causality, directionality, and temporality cannot be assigned when examining associations between disease severity, socioeconomic measures, and HRQOL. It may be that severe disease manifestations in childhood affect ability to attend school or study, impairing future educational success and employment. Later in life, inability to work or study might then impair HRQOL independent of disease severity, as seen in a prior study showing that colorectal cancer survivors who continue to work have better HRQOL [18]. Relationships between socioeconomic status, disease severity, and HRQOL are likely to be complex and reciprocal, and the extent to which experiences in childhood affect HRQOL and socioeconomic status in adulthood warrants further longitudinal study.

Our findings of poorer HRQOL among black adults (in unadjusted analyses only) differ somewhat from prior studies examining race/ethnicity, socioeconomic status, and HRQOL in other disease states. Two prior studies of the US adults with coronary artery disease or cancer determined that Hispanic adults, those without a college education, and those with lower income – but not those of Black race – had worse HRQOL [19, 20]. However, another study of adults with prostate cancer determined that a higher level of medical mistrust was associated with worse HRQOL and that Black men typically experienced a higher level of medical mistrust than white men [21].

Black patients with high-risk APOL1 genotypes are at increased risk for FSGS and certain other kidney diseases, as well as faster kidney function decline [22, 23]. However, genetic factors do not entirely explain the higher risk for kidney disease and its progression among the Black patients, and environmental and socioeconomic factors likely contribute [22]. Among these, patients with inadequate health insurance might have reduced access to specialized nephrology care [24–26], resulting in delayed treatment and worse clinical outcomes. Notably, in this CureGN cohort of participants with glomerular disease – who all had access to medical care – immunosuppressive medication use was not more frequent among the Black patients, despite greater disease severity at enrollment. Whether this finding is explained by biases in prescribing behavior, reduced access to medications, poorer medication adherence, or more frequent therapeutic failures requires further study.

There are important practical implications to our findings. First, clinicians caring for patients with glomerular disease should pay increased attention to the greater symptom burden and more severe socioeconomic consequences of glomerular disease (e.g., missed work) borne by Black adults. Second, clinicians, investigators, and policymakers are well-equipped to identify and advocate for interventions (e.g., education, pharmaceutical coverage, flexible work practices, and policies that mitigate effects of bias and racism) to reduce the socioeconomic contributors to and consequences of glomerular disease. Finally, we suggest careful monitoring of HRQOL in Black children as disparities in HRQOL not yet apparent during childhood might emerge during the disease course.

Limitations to the present analyses and their potential implications are important to consider. First, PROMIS questionnaires were developed to measure patient-reported outcomes across common health conditions and not specifically in glomerular disease, although these tools have been validated in children with nephrotic syndrome [10, 11, 17]. Second, we used employment, education, and health insurance as proxies for socioeconomic status and lacked information on income. Third, the majority of study participants were from the USA, and sub-analyses focusing on other regional groups were limited by sample size; thus, we could not explore the impact of healthcare organization on study findings. Fourth, patients with diabetes or kidney failure are excluded from CureGN, while cardiovascular comorbidities (e.g., heart failure and coronary artery disease) are present in <5% of the participants at enrollment. Accordingly, we could not determine the extent to which these comorbidities might impact HRQOL as patients with glomerular disease accrue them with time. Finally, our study was restricted to
patients with access to health care who have been referred to specialty centers in 4 countries, underwent a kidney biopsy, and participated in a clinical study. The generalizability of these study findings to populations outside of specialty referral centers is unknown.

In conclusion, in this large multinational cohort study of children and adults with glomerular disease, disease severity was associated with worse HRQOL in both adults and children, socioeconomic factors were associated with worse HRQOL only in adults, and race/ethnicity was not a primary driver of HRQOL in either age-group. Longitudinal studies examining dynamic associations between disease severity, socioeconomic status, and HRQOL are urgently needed to further disentangle the complex relationships exposed in this study and, ultimately, to inform the development of targeted interventions to reduce health disparities.

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Statement of Ethics

All procedures performed in this study were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments. This study was approved by the Institutional Review Board of Stanford University, protocol number 49739. All participants provided written informed consent (or assent, if a minor) to be included in the study.

Conflict of Interest Statement

Dr. Greenbaum reports receiving research support from Vertex Pharmaceuticals, Apellis Pharmaceuticals, Reata Pharmaceuticals, Alexion Pharmaceuticals, and an honorarium from Alexion Pharmaceuticals. Dr. Almaani is a consultant for Aurinia Pharmaceuticals Inc. Dr. Reidy is a primary investigator for Complexa and Advicenne studies unrelated to this current manuscript. Dr. Gibson holds advisory roles for Aurinia Inc., Reata Inc., and Retrophin, Inc. Dr. Tuttle has received the research support from Goldfinch Bio and Travere/Retrophin and holds an advisory role for Goldfinch Bio. Dr. Sperati reports receiving research support for clinical trials from Alexion Pharmaceuticals and Alnylam, and honoraria for serving as chair of DSMB. All other authors declare that they have no known competing financial interests personal relationships that could appear to influence the work reported in this manuscript. Results of this manuscript have not been published previously in whole or part, with the exception of abstract format ( ASN Kidney Week 2019).

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Author Contributions

Research idea, study design: J.R.K., M.E.H., and M.M.O. with input from all the listed authors. Data acquisition and statistical analysis: M.E.H. Data interpretation: all authors. Supervision: M.E.H. and M.M.O. Each author contributed to important intellectual content during the manuscript drafting or revisions, accepts personal accountability for the author’s own contributions, and agrees to ensure that the questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved.

Availability of Data and Material

Data are available upon the request through the CureGN Ancillary Studies program. Data access is governed by the CureGN Steering Committee and NIDDK. Additional data sets will be provided to the NIDDK Central Repository after completion of the study recruitment, which is currently ongoing. After data are deposited, the data will be available through the NIDDK Central Repository at https://repository.niddk.nih.gov/home/.

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