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Area-level Predictors of Medication Nonadherence among U.S. Medicaid Beneficiaries with Lupus: A Multilevel Study

Candace H. Feldman, MD, ScD¹, Karen H. Costenbader, MD, MPH¹, Daniel H. Solomon, MD, MPH¹, SV Subramanian, PhD², and Ichiro Kawachi, MB.ChB., PhD²

¹Division of Rheumatology, Immunology and Allergy, Department of Medicine, Brigham and Women's Hospital, Boston, MA

²Department of Social and Behavioral Sciences, Harvard T. H. Chan School of Public Health, Boston MA

Abstract

Background: Adherence to hydroxychloroquine (HCQ) among patients with systemic lupus erythematosus (SLE) is suboptimal. Individual-level factors, including younger age and non-white race/ethnicity, have been implicated; contextual factors have not been explored.

Methods: We identified SLE patients with new use of HCQ (no use in 6 months) in Medicaid (2000–2010) from 28 U.S. states. We required 12 months of continuous enrollment with complete drug dispensing data and measured adherence using the proportion of days covered (PDC). We identified individual-level variables from Medicaid, zip code, county and state-level sociodemographic variables from the American Community Survey and health resources from Area Health Resources Files. We used 4-level hierarchical multivariable logistic regression models to examine odds (OR (95% Credible Interval)) of adherence (PDC ≥ 80%) vs. nonadherence.

Results: Among 10,268 HCQ initiators with SLE, 15% were adherent. After adjusting for individual-level characteristics, we observed lower odds of adherence in zip codes with higher percentages of black individuals (highest tertile OR 0.81 (0.69–0.96) vs. lowest). This association persisted after controlling for zip code educational attainment, percent below federal poverty level (FPL), urbanicity and healthcare resources. We did not find statistically significant associations with zip code-level percent Hispanic, percent White, education or percent below FPL. Odds of adherence were higher in counties with more hospitals (OR 1.30 (1.07–1.58)).

Conclusions: Among Medicaid beneficiaries with SLE, we observed significant effects of racial composition and hospital concentration on HCQ adherence. Interventions that acknowledge and address contextual factors should be considered to reduce high rates of nonadherence in vulnerable populations.

Background

SLE is a multisystem autoimmune disease that disproportionately affects racial/ethnic minorities and individuals from lower socioeconomic status (SES) areas.(1, 2) Medication nonadherence is common among patients with SLE, and more pronounced among racial/ethnic minorities and poorer individuals who also suffer from the highest burden of adverse outcomes.(3–5) One study demonstrated an effect of neighborhood poverty on accumulation of SLE-specific damage however the role of medication adherence was not investigated.(6) The majority of adherence-related studies focus on the isolated contribution of patient and disease-related characteristics. Despite the increased awareness of the importance of social determinants on health behaviors and outcomes, few studies have examined their relationship with adherence.(7–9)

We therefore aimed to investigate the effect of contextual factors including racial composition, SES, and healthcare resource concentration, on adherence among SLE patients in Medicaid, the largest federal-state public health insurance program for low income Americans. We focused on adherence to hydroxychloroquine (HCQ) as it is the standard of care therapy both for active treatment and for prevention of complications for nearly all patients with SLE.(10)

We utilized the social ecological model (SEM) that emphasizes the importance of multiple, reciprocal levels of influence on behavior, to consider potential individual and area-level contributors to adherence. (Figure 1).(11) The theoretical framework proposed by August and Billimek linking neighborhood deprivation to increased likelihood of medication nonadherence, provided potential mechanisms to explain the interplay between SEM levels and adherence.(12) August and Billimek hypothesized that living in a disadvantaged neighborhood results in increased exposure to environmental and social stressors and reduces self-regulatory resources to engage in healthy behaviors. Individuals often place disproportionate weight on present relative to future costs and benefits and in high stress environments, this is more pronounced.(13, 14) Adherence to chronic disease medications for potential future benefit may therefore be outweighed by more immediate concerns. Social factors may also contribute to norms that devalue adherence.(15, 16) These aspects together may result in unfavorable beliefs about adherence leading to nonadherence.(12) Based on this theoretical framework and the SEM, we hypothesized that living in poorer, racially segregated areas with fewer health-related resources would be associated with HCQ nonadherence.

Methods

Patient Population

We used the Medicaid Analytic eXtract (MAX) for the 29 most populous U.S. states (approximately 86% of all Medicaid beneficiaries) from 2000–2010 with drug dispensing data, billing claims and healthcare utilization data. While Ohio was part of our data set, it was excluded from analyses due to incomplete dispensing data (N=388). We identified patients aged 18–65 years with prevalent SLE, defined as 2 ICD-9 codes for SLE (710.0) from hospital discharge diagnoses or physician visit claims 30 days apart, and HCQ

dispensing within 365 days of a SLE ICD-9 code. We restricted our cohort to new users of HCQ, defined as 183 days of continuous enrollment prior to the first dispensing of HCQ (index date) with no use of HCQ during this time. Since >90% of Medicaid beneficiaries received one-month supplies of HCQ, 6 months was determined to be sufficient to define initiation. We were unable to validate our algorithm due to federal restrictions on the use of identifiable Medicaid claims data for research purposes. However, similar claims-based algorithms performed well (sensitivity of 98.2%, specificity of 72.5%) and adding HCQ use likely increased our specificity.(17) We required 365 days of continuous enrollment following the index date to assess adherence. We excluded patients if their dispensing data were missing (N=333), if they were hospitalized for the entire follow-up period (N=18), or if their zip codes were not reported (N=253) or were discordant with their state of residence (N=46).

Outcome: Adherence

Adherence was determined using drug dispensing data: the claims processed by Medicaid when a prescription is filled at a pharmacy and either picked up by or mailed to a patient, including medication name/NDC code, dose, quantity, amount prescribed and number of refills. We defined adherence using the proportion of days covered (PDC) for the 365-day period beginning at the index date. The PDC was defined as the number of days covered by dispensed HCQ prescriptions divided by 365 days, times 100. We subtracted hospitalized days from the numerator and denominator. The PDC is a widely used, validated measure to assess adherence in claims data, including Medicaid.(18, 19) We used a PDC threshold of 80% to define adherence in keeping with the literature on adherence to other chronic disease medications (20). In sensitivity analyses, we examined adherence thresholds of 90% and 70%.

Individual-Level Covariates

We used MAX data to identify individual-level covariates in the 183-day period prior to and including the index date. Our choice of variables was informed by prior adherence literature and our hypothesis that they may be related both to initial HCQ prescribing and to adherence. We included age, sex, and race/ethnicity. Medicaid uses the phrase “Black or African American” and we will use the term “black” to represent this group.(21) We used the SLE risk adjustment index, shown to be a better predictor of mortality among SLE patients than the Charlson comorbidity index, as a marker of disease severity.(22) We separately assessed lupus nephritis using 2 ICD-9 discharge diagnosis codes or physician billing claims for nephritis, proteinuria and/or renal failure occurring on or after one SLE diagnosis code (23) to capture additional cases of lupus nephritis beyond those included in the adjustment index algorithm as we hypothesized that this would be an important confounder. As proxies for SLE disease activity, we assessed number of SLE-related laboratory tests. We measured healthcare utilization (emergency department, inpatient and outpatient visits) as markers of care fragmentation and disease activity/severity. We included number of medications to assess for polypharmacy, and corticosteroids and other immunosuppressive medications to represent disease activity/severity. We included diabetes mellitus (by ICD-9 code or related medication prescription) (24) and antidepressant medication use as a marker of depression given the low PPV of depression-related claims.

(25) To account for health status and healthy/unhealthy behaviors potentially associated with adherence, we included CPT codes for vaccinations, medication (NDC) codes for pneumocystis prophylaxis, obesity (1 ICD-9 code) and smoking (1 ICD-9 code, CPT code for smoking cessation counseling, or dispensing of related medications).(26)

Contextual Covariates

From de-identified Medicaid data, we obtained zip code (the smallest geographic area available), county and state of residence. Using American Community Survey (ACS) data (2006–2010), we extracted zip code percent of the population in each area with incomes below the federal poverty level (FPL), educational attainment (high school or less, some college, and college graduate and beyond) as well as the percent black, white and Hispanic. (27–29) We examined a composite score of percent black and percent below FPL, divided in tertiles as well as a variable that included zip codes with the lowest tertile of percent black and of percent FPL in group 1 (N=760), and with the highest tertile of both in group 3 (N=934), with others in group 2 (N=3236). We used the ACS to determine the state-level Gini coefficient, a marker of income inequality (0–1, where 1 represents greatest inequality). (29) We used the mean of U.S. Census data from 2000 and 2010 to determine percent urban for each county.

To determine county-level concentrations of health services and health professionals, we used the Area Health Resources Files (ARHF) from 2000 and 2010.(30, 31) We obtained the mean numbers of physicians, medicine subspecialists, pharmacists and hospitals from 2000 and 2010 (2009 for pharmacists) and divided these by each county's population size, per 1,000 individuals. There were 52 counties (4%) without reported pharmacist data. We also determined the county Health Professional Shortage Area (HPSA) designation (none, partial, whole). HPSAs are characterized by shortages of primary care providers that may be geographic, for a population group, or of facilities that lack providers. We obtained number of rheumatologists per state from the American College of Rheumatology (2000), and divided this by population size from the U.S. Census (2000), per 10,000 individuals. We examined our contextual variables in tertiles (reference=lowest), to facilitate interpretability and to be consistent across levels.

Statistical Analyses for Multilevel Models

Given the hierarchical nature of our data and our goal to examine associations across contextual variables with individual-level adherence and to understand the potential heterogeneities underlying these associations, we constructed hierarchical four-level multivariable random intercepts logistic regression models with individuals (level 1) nested in zip codes (level 2), in counties (level 3), in states (level 4).(32) All analyses used Markov Chain Monte Carlo (MCMC) procedures using a Metropolis-Hasting algorithm.(33) This is a Bayesian approach, which relies on sequential learning, whereby prior information is accounted for in the estimates and the distributional assumptions of maximum likelihood methods are not required.(33, 34) For our fixed effect estimates, we present the MCMC estimates with 95% credible intervals (CIs). Unlike confidence intervals, credible intervals do not have to be normally distributed and provide the potential range of values following the MCMC simulation of many model runs. For random effects parameters, we present

level-specific residual variance estimates, and the percent of variance partitioned at each level.

We examined fixed effects of individual-level and contextual variables, and accounted for random effects at each geographic level. We conducted sensitivity analyses adjusting for fewer individual-level covariates. We examined variance partitioning at each level to understand the level at which most between-area variability was occurring and the degree to which our fixed effects could account for this. For models examining health resources, we began with the model with the smallest deviance information criteria (DIC) statistic, which is used to compare hierarchical models obtained by MCMC procedures. We used SAS 9.4 (Cary, NC) to organize variables and MLwiN 2.36 (Center for Multilevel Modeling, Bristol University, London, UK) to conduct multilevel analyses. MAX data were obtained through a Data Use Agreement from CMS and findings are reported in accordance with their specifications. This work used only de-identified, aggregated data and was approved by the Partners Healthcare IRB.

Results

Individual and Area-Level Characteristics

We identified 10,268 Medicaid beneficiaries residing within 4,930 zip codes, in 1,414 counties, in 28 states, with prevalent SLE who were HCQ initiators. On average, there were 2.1 ± 2.8 (range 1–29) individuals/zip code, 7.3 ± 28.7 (range 1–739) individuals/county, and 366.7 ± 416.9 (range 84–1960) individuals/state. There were, on average, 3.5 ± 7.5 (range 1–190) zip codes/county and 50.5 ± 24.9 (range 13–120) counties/state. The mean age was 37.7 ± 11.8 years and 94% were female (Table 1). The mean PDC was $42.3\% \pm 28.7$ and 1,567 individuals (15.3%) were adherent (PDC $\geq 80\%$) to HCQ. Area-level sociodemographic and health resource characteristics are presented in Table 2.

Individual-Level Fixed Effects

In our four-level random intercepts logistic regression model, we found lower odds of adherence (vs. nonadherence) associated with younger age (vs. older age), with black race and Hispanic ethnicity (vs. white), with diabetes, antidepressant medication use, and with more emergency department visits (Table 3). We found higher odds of adherence associated with Asian race, higher SLE risk adjustment index, and more laboratory tests and medications.

Area-Level Fixed Effects: Sociodemographics

After accounting for individual-level fixed effects, and random effects at each level, we found lower odds of adherence vs. nonadherence in zip codes with higher percent black. Comparing tertile 2 to 1 (lowest percent black), the OR was 0.85 (95% CI 0.74–0.98) and comparing tertile 3 to 1, the OR was 0.81 (95% CI 0.69–0.96) (Table 4). We did not find statistically significant associations with percent white or Hispanic, or with percent below FPL or educational attainment. When we adjusted our model by percent below FPL and education, the effect of percent black remained significant (OR 0.80, 95% CI 0.67–0.96 (tertile 3 vs. 1) and OR 0.86, 95% CI 0.74–0.99 (tertile 2 vs. 1)). We did not find statistically

significant associations between our combined percent black/percent below FPL measures and adherence or with the Gini coefficient.

We examined cross-level interactions between race (categorized as black, white, Hispanic, other) and percent black and with percent below PFL to determine whether the relationship between race and adherence differs by the racial composition or poverty status of the zip code in which a person lives. The interaction term was significant for black race*percent black tertile 3 (ref=white and tertile 1). The OR for adherence vs. nonadherence for black vs. white race among individuals living in tertile 3 vs. 1, was 0.49 (compared to OR of 0.56 in the model without the interaction term). The interaction terms were not significant when black race was used as the reference, or for race*percent below FPL.

Area-Level Fixed Effects: Health Resources

We built our subsequent models including individual-level factors (Table 3) as well as zip code-level percent black both because we aimed to test whether health resource concentration and urbanicity accounted for the effect of zip code percent black on adherence and because it had a lower DIC compared to the individual variable-only model. We found higher odds of adherence vs. nonadherence comparing the county-level highest number of hospitals per capita compared to the lowest (OR 1.30, 95% CI 1.07–1.58) (Table 5). We found borderline significant lower odds of adherence vs. nonadherence associated with residing in a whole health professional shortage area (OR 0.88, 95% CI 0.77–1.01). We did not find statistically significant associations with number of physicians, medicine subspecialists, pharmacists per capita, or rheumatologists. We also explored urbanicity and found a borderline significant relationship with higher percent urban and reduced odds of adherence (OR 0.82, 95% CI 0.66–1.02, tertile 3 vs. 1). The magnitude of the effect of zip code percent black and adherence remained consistent and either significant or nearly significant in all models (Table 5).

Random Effects

We observed modest between state, county and zip code-level variation in adherence. Most variance detected was attributable to between states (1.4% in our null model) with <1% attributable to between counties or zip codes. We observed minor differences in random effects in our adjusted models (between state variances of 1–1.5%, between county variances of 0.1–0.3%, and between zip code variances of 0.03–0.2%) (Supplemental Table1).

Sensitivity Analyses

We examined the relationship between zip code percent black and adherence at two different adherence thresholds. For PDC 70%, 22.2% of our cohort were now categorized as adherent. At this threshold, we found similar associations as our primary analyses both for tertile 2 vs. 1 (OR 0.83, 95% CI 0.72–0.94) and for tertile 3 vs. 1 (OR 0.81, 95% CI 0.69–0.94), as well as for all individual-level variables. For PDC 90%, 7.7% of our cohort were considered adherent and while the magnitude and direction of associations were similar, the 95% CIs were wider (tertile 2 vs. 1, OR 0.83, 95% CI 0.69–1.01; tertile 3 vs. 1 0.89, 95% CI 0.71–1.11). In addition, we examined more parsimonious models that included only sex, age, race/ethnicity, SLE risk adjustment index, number of medications and calendar year at

the individual level, and found estimates similar in magnitude and significance for fixed and random effects at all levels (Supplemental tables 2a, 2b, and 3).

Discussion

In this vulnerable population of individuals with SLE where only 15% were adherent to HCQ over the first year of use, we observed significant relationships between individual and contextual factors and adherence. While it is challenging to compare across studies given differences in populations (e.g. academic-based cohorts vs. public insurance beneficiaries), and in adherence measures (e.g. self-reported surveys vs. claims-based refill data), our findings were similar to estimates of adherence to other SLE-related medications in the Medicaid population.(35) In line with prior studies, younger age, black race, Hispanic ethnicity and antidepressant use were associated with poorer adherence(5, 24, 36–38) Nonadherence particularly among black lupus patients is associated with poorer outcomes overall.(3, 5, 36, 37) As HCQ is the backbone of SLE care and has been associated with fewer flares and improved outcomes, it is plausible that differences in adherence by race/ethnicity may contribute to disparities in outcomes.(3, 39–41)

There are few studies that explore the contribution of contextual factors to these disparities. (6) We found a significant dose-response relationship between zip code-level percent black and poorer adherence to HCQ, which remained after adjusting for individual race, area poverty and education. We did not however observe associations with percent white or percent Hispanic. We also found more pronounced reduced odds of adherence among black individuals residing in the highest tertile of percent black zip codes. While zip code is an imperfect proxy for neighborhood (42), these observations suggest a potential effect of racial residential segregation on HCQ nonadherence. Our lack of addresses did not allow us to geocode our data to examine the differential distribution by race across smaller residential units (e.g. census blocks) within larger geographic areas, or to look at spatial relationships. (43) We hypothesize that in these areas, there may be reduced access to high quality hospitals, outpatient providers, and pharmacy services and to transportation.(43, 44) There may be increased stress and depression from racial discrimination and crime which may contribute to nonadherence.(44, 45) There may also be reverse causation as individuals who are less likely to engage in healthy behaviors may also be less equipped to move out of racially segregated areas. This may be related to the known differences in the opportunities afforded to individuals who live in segregated neighborhoods.(44)

It is also possible that social and cultural norms within neighborhoods influence adherence behavior. Racial bias experienced in healthcare is one plausible mechanism.(44) Prior studies suggest differences between black and white patients in their willingness to accept certain SLE-related medications, in beliefs about medication effectiveness, and in health provider trust.(46) In one study, >50 percent of black SLE patients experienced racial discrimination in healthcare and this was linked to increased depression.(45) Similar patterns have been described among black patients with hypertension where racial discrimination has been associated with medication nonadherence.(47) Living near individuals with negative healthcare experiences from racism may contribute to nonadherence norms.

We did not observe effects from area percent below FPL or income inequality. There was a moderate correlation between zip code percent below FPL and percent black ($r^2=0.46$, $p<0.0001$). While our composite measures of individual race and area poverty were in the expected direction, the estimates were not statistically significant. The effect of zip code percent black on adherence persisted after adjusting for percent below FPL, suggesting that other mechanisms beyond socioeconomic deprivation contribute. We hypothesize that we may not see an independent area-level effect of poverty because of the dominant individual-level effect in this low-income population.

We also found that adjusting for health resource concentration did not significantly attenuate the relationship between zip code percent black and adherence. However, we could not assess the quality of services provided. While we did find an association with greater numbers of hospitals and increased odds of adherence, we did not find a parallel association with more health providers. Hospital-based clinics provide care to complex patients, whereas private practice physicians may not accept Medicaid, or sicker patients. Adherence may be more related to the quality of care received, and patient-provider interactions rather than to the concentration of services available. Alternatively, there might be more physicians that come to practice in areas with high concentrations of complex patients and therefore adherence may be poorer overall in these areas to begin with.

Notably, we found only small between-area variation in adherence despite our expectation that this would be greater due to variation in Medicaid eligibility criteria by state. However, variations in poverty-level eligibility among overall poor individuals may not be that significant. It is also possible that we did not see significant differences because HCQ copayments and days supplied requirements between the states were similar. At the zip code and county level, it is possible that the lack of between-area variation observed was a result of a significant proportion of areas with few SLE patients, and the high prevalence of overall nonadherence in this population.

This study had a number of strengths. We used multilevel models to examine the relationship across contextual characteristics with adherence while accounting for individual-level factors, as well as for potential clustering and heterogeneity by geographic area. To our knowledge, this is the first study to examine the role of contextual factors on adherence in a high-risk SLE population. Among patients with SLE, researchers highlight the need for a better understanding of the contribution of social determinants to disparities in health outcomes however few studies examine this.(48) We propose that our findings are hypothesis-generating and provide impetus to explore the mechanisms behind the associations uncovered.

Our study also has limitations. We excluded individuals over age 65 because of possible dual eligibility in Medicare. We did not exclude younger dual-eligible individuals because we did not have complete data available. While we likely captured most prescription claims for this population, adherence may be underestimated for those who changed their drug coverage after the index date. While low income is part of the criteria for Medicaid eligibility, we did not have other individual-level measures of SES (e.g. occupation, education). In addition, we lacked more granular geographic area data and therefore were unable to assess direct

neighborhood effects or geocode our data. Our use of claims data did not enable us to directly measure SLE disease activity, however SLE-related laboratory tests and the SLE risk adjustment index were used to approximate this. Our study may also have excluded patients with more severe SLE and lupus nephritis since we required new use of HCQ but not a new diagnosis of SLE. While this is not an incident SLE cohort, we suspect that many of the patients included are early in their disease course which is reflected by the low mean SLE risk adjustment index, and the low prevalence of lupus nephritis and immunosuppressive medication use despite the vulnerable nature of this population. Due to the nature of claims, there may also be misclassification of individuals with SLE and of comorbidities. Certain variables such as obesity, vaccinations and smoking are also underestimated due to underreporting. It is also possible that antidepressant use may capture both SLE patients with chronic pain and those with depression as some antidepressants are used to treat both, although these are often co-morbid conditions. We measured adherence using the PDC which reflects drug dispensing and refills, however filling a medication may not always translate to taking the medication in the way in which it was prescribed. In addition, the PDC is an aggregate measure over the course of a year and may not capture the dynamic nature of adherence behavior.

In this study of Medicaid beneficiaries with SLE, adherence to HCQ was poor. In addition to reaffirming the role of certain individual-level sociodemographic and disease-related factors on adherence, we propose that contextual influences contribute as well. Our findings should pave the way for further work examining the importance of social determinants, including racial residential segregation and racial discrimination, as well as neighborhood-specific healthcare quality, on health behaviors and outcomes in vulnerable populations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Significance and Innovation

- Despite the increasingly recognized importance of social determinants on health and health behaviors, the influence of contextual factors including area-level sociodemographics and healthcare resource concentration on medication adherence has not been well studied.
- The study demonstrates nearly 20% reduced odds of hydroxychloroquine (HCQ) adherence among SLE patients living in zip codes with higher percentages of black individuals, after adjusting for individual demographics and health-related factors, as well as zip code poverty. This suggests a possible effect of racial residential segregation on HCQ adherence.
- While higher concentration of hospitals was associated with increased odds of adherence, other healthcare resources including numbers of physicians and pharmacists per capita, were not associated with improved adherence suggesting that other factors, such as the quality of healthcare resources in underserved areas may play a stronger role.
- The study findings suggest that contextual factors play a role in adherence behavior among SLE patients and should be considered in the design of interventions that aim to reduce the racial/ethnic disparities observed.

Figure 1.
Social ecological model adapted to demonstrate potential multilevel contributors to adherence behavior among patients with SLE

Table 1.

Individual-Level Baseline Characteristics of New Users of HCQ with Lupus enrolled in U.S. Medicaid 2000–2010[#]

Baseline characteristics*	N=10,268
Age- mean $\pm$ SD	37.7 $\pm$ 11.8
Age group (years)- N (%)	
18–34	4542 (44.2)
35–50	3902 (38.0)
50–65	1824 (17.8)
Sex- N (%)	
Female	9669 (94.2)
Male	599 (5.8)
Race/ethnicity-N (%)	
Black	4289 (41.8)
White	3194 (31.1)
Hispanic	2036 (19.8)
Asian	397 (3.9)
American Indian/Alaska Native	121 (1.2)
Other	231 (2.3)
SLE risk adjustment index – mean $\pm$ SD	1.0 $\pm$ 1.9
Lupus nephritis- N (%)	1049 (10.2)
Diabetes mellitus- N (%)	964 (9.4)
Smoking – N (%)	616 (6.0)
Obesity – N (%)	240 (2.3)
Antidepressant use – N (%)	2976 (29)
Preventive care – N (%)	
Influenza vaccine	178 (1.7)
Pneumococcal vaccine	58 (0.6)
Pneumocystis prophylaxis	903 (8.8)
Immunosuppressive medication use** - N (%)	1127 (11)
Number of laboratory tests⁺ - mean $\pm$ SD	1.6 $\pm$ 2.8
Corticosteroids	
Ever use – N (%)	6112 (59.5)
Mean number of medications – mean $\pm$ SD	4.2 $\pm$ 3.4
Healthcare utilization	
ED Visits – median (25, 75)	0 (0, 1)
Hospitalizations – median (25, 75)	0 (0, 1)
Outpatient visits – median (25, 75)	2 (0, 6)
Hospitalized days – mean $\pm$ SD	3.9 $\pm$ 10.6; Median 0 (25 th 0, 75 th 4)

[#]Data from the following 28 U.S. states were included: Alabama, Arkansas, California, Colorado, Florida, Georgia, Illinois, Indiana, Kentucky, Louisiana, Maryland, Massachusetts, Michigan, Minnesota, Mississippi, Missouri, Montana, New Jersey, New Mexico, New York, North Carolina, Oklahoma, Oregon, Pennsylvania, South Carolina, Texas, Washington and Wisconsin

^{*}Baseline characteristics determined from the 183 days prior to and including the index date of first dispensing of HCQ

^{**}Includes use of azathioprine, cyclophosphamide, leflunomide, methotrexate, mycophenolate mofetil, sulfasalazine, tacrolimus

⁺Includes BUN, creatinine, urinalysis, complement (C3, C4), ESR, CRP, anti-dsDNA

Table 2.

Zip Code, County and State-level Demographic and Health Services Characteristics of New Users of HCQ with Lupus Enrolled in in U.S. Medicaid 2000–2010

Area-level Characteristics	ZIP Code (N= 4,930)	County (N= 1,414)	State (N=28)
Percent with income below the federal poverty level⁺ - mean $\pm$ SD	14 $\pm$ 9		
Tertile 1- mean $\pm$ SD, range	5.4 $\pm$ 2.2 (0–8.9)		
Tertile 2- mean $\pm$ SD, range	12.4 $\pm$ 2.1 (8.9–16.3)		
Tertile 3- mean $\pm$ SD, range	34.5 $\pm$ 7.3 (16.3–70.7)		
Percent black⁺ - mean $\pm$ SD	18 $\pm$ 23		
Tertile 1- mean $\pm$ SD, range	1.1 $\pm$ 1.0 (0–3.2)		
Tertile 2- mean $\pm$ SD, range	8.9 $\pm$ 4.2 (3.2–17.8)		
Tertile 3- mean $\pm$ SD, range	45.1 $\pm$ 22.1 (17.8–100)		
Percent white - mean $\pm$ SD	67 $\pm$ 25		
Tertile 1- mean $\pm$ SD, range	37.1 $\pm$ 16 (0–58.4)		
Tertile 2- mean $\pm$ SD, range	71.4 $\pm$ 6.9 (58.4–82.5)		
Tertile 3- mean $\pm$ SD, range	91.5 $\pm$ 4.9 (82.5–100)		
Percent Hispanic - mean $\pm$ SD	18 $\pm$ 22		
Tertile 1- mean $\pm$ SD, range	2 $\pm$ 1 (0–3.9)		
Tertile 2- mean $\pm$ SD, range	8.3 $\pm$ 3.3 (3.9–15.9)		
Tertile 3- mean $\pm$ SD, range	42.8 $\pm$ 22.6 (15.9–99.1)		
Educational attainment⁺ - N (%)			
High school or less	3904 (79.2)		--
Some college	288 (5.8)		--
College graduate and beyond	738 (15)		--
Total number of Total MDs^{**} - mean $\pm$ SD	--	1.53 $\pm$ 1.75	--
Tertile 1- mean $\pm$ SD, range	--	0.43 $\pm$ 0.18 (0–0.72)	--
Tertile 2- mean $\pm$ SD, range	--	1.09 $\pm$ 0.25 (0.72–1.56)	--
Tertile 3- mean $\pm$ SD, range	--	3.06 $\pm$ 2.3 (1.56–25.3)	--
Total number of hospitals^{**} - mean $\pm$ SD	--	0.03 $\pm$ 0.03	--

Area-level Characteristics	ZIP Code (N= 4,930)	County (N= 1,414)	State (N=28)
Tertile 1- mean $\pm$ SD, range	--	0.01 $\pm$ 0.01 (0–0.02)	--
Tertile 2- mean $\pm$ SD, range	--	0.03 $\pm$ 0.01 (0.02–0.04)	--
Tertile 3- mean $\pm$ SD, range	--	0.07 $\pm$ 0.04 (0.04–0.59)	--
Total number of medicine subspecialists ^{**} - mean $\pm$ SD	--	0.46 $\pm$ 0.64	--
Tertile 1- mean $\pm$ SD, range	--	0.08 $\pm$ 0.05 (0–0.16)	--
Tertile 2- mean $\pm$ SD, range	--	0.30 $\pm$ 0.09 (0.16–0.47)	--
Tertile 3- mean $\pm$ SD, range	--	1 $\pm$ 0.87 (0.47–10.5)	--
Total number of pharmacists ^{**} - mean $\pm$ SD	--	0.54 $\pm$ 0.33	--
Tertile 1- mean $\pm$ SD, range	--	0.23 $\pm$ 0.07 (0–0.34)	--
Tertile 2- mean $\pm$ SD, range	--	0.45 $\pm$ 0.07 (0.34–0.60)	--
Tertile 3- mean $\pm$ SD, range	--	0.90 $\pm$ 0.30 (0.60–2.73)	--
Health Professional Shortage Area [#] - N (%)			
None	--	236 (16.7)	--
Partial	--	615 (43.5)	--
Whole	--	563 (39.8)	--
Percent Urban ⁺⁺ - mean $\pm$ SD		51.2 $\pm$ 29.8	
Tertile 1- mean $\pm$ SD, range		17.0 $\pm$ 12.8 (0–36.8)	
Tertile 2- mean $\pm$ SD, range		51.5 $\pm$ 8.6 (36.8–67.3)	
Tertile 3- mean $\pm$ SD, range		85.2 $\pm$ 10.2 (67.3–100)	
Number of rheumatologists [*] - mean $\pm$ SD	--	--	0.13 $\pm$ 0.04
Tertile 1- mean $\pm$ SD, range	--	--	0.09 $\pm$ 0.01 (0.07–0.11)
Tertile 2- mean $\pm$ SD, range	--	--	0.12 $\pm$ 0.01 (0.11–0.14)
Tertile 3- mean $\pm$ SD, range	--	--	0.17 $\pm$ 0.04 (0.14–0.26)
Gini Coefficient - mean $\pm$ SD ⁺	--	--	0.46 $\pm$ 0.02
Tertile 1- mean $\pm$ SD, range	--	--	0.44 $\pm$ 0.01 (0.43–0.45)
Tertile 2- mean $\pm$ SD, range	--	--	0.46 $\pm$ 0.003 (0.45–0.47)
Tertile 3- mean $\pm$ SD, range	--	--	0.47 $\pm$ 0.01 (0.47–0.50)

⁺From the American Community Survey (2000–2006)

* From the American College of Rheumatology (2000), per 10,000 state population in 2000 (US Census)

** Per capita, per 1,000 individuals in the county, mean from the Area Health Resources Files 2000 and 2010; MD data from the American Medical Association, hospital data from HRSA; For pharmacists, N=1362, 52 counties (4%) do not report pharmacist data

Defined and reported by HRSA, 2010

++ From the Area Health Resources Files 2000 and 2010 (mean)

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Table 3.

Individual-level Model^{*} Examining the Odds of HCQ Adherence (PDC ≥ 80%) vs. Nonadherence (PDC <80%) with 95% Credible Intervals (CI) among HCQ New Users with Lupus Enrolled in U.S. Medicaid, 2000–2010

Individual-level fixed effects	Odds ratio (OR)	95% Credible Interval
Male (ref=female)	1.21	0.97–1.50
Age (ref = 51–65 years)		
18–34 years	0.60	0.51–0.71
35–50 years	0.71	0.61–0.82
Race/ethnicity (ref=White)		
Black	0.61	0.54–0.71
Hispanic	0.71	0.60–0.83
Asian	1.49	1.15–1.92
AI/AN	0.78	0.45–1.92
Other	0.85	0.59–1.22
SLE risk adjustment index	1.04	1.01–1.07
Lupus nephritis	1.13	0.92–1.38
Diabetes mellitus	0.82	0.68–1.00
Antidepressant use	0.86	0.76–0.98
Corticosteroid use	1.04	0.92–1.16
Number of lab tests	1.03	1.00–1.05
Number of medications	1.10	1.08–1.12
Immunosuppressives use	0.91	0.77–1.07
Healthcare Utilization		
# ED visits	0.96	0.93–1.00
# outpatient visits	1.00	0.99–1.01
# hospitalizations	0.95	0.90–1.00 [†]

^{*} Four-level random intercepts multivariable regression model additionally adjusted for calendar year of index date, and healthy adherer effect variables (obesity, smoking, and preventive care (influenza or pneumonia vaccines, PCP prophylaxis)) as well as random effects at each level

[†] Bayesian p-value <0.05 with 95% credible interval that just crosses 1; Bolded 95% credible intervals do not cross 1 and Bayesian p-value <0.05.

Table 4.

Models examining the odds of HCQ adherence (PDC ≥ 80%) vs. nonadherence (PDC <80%) with 95% Credible Intervals by contextual sociodemographic factors

Area-level Sociodemographic Factors	Odds ratio (OR)	95% Credible Intervals
Zip Code-level Percent Black (ref=lowest tertile)		
Tertile 2	0.85	0.74–0.98
Tertile 3	0.81	0.69–0.96
Zip Code-level Percent White (ref=lowest tertile)		
Tertile 2	0.93	0.81–1.08
Tertile 3	1.13	0.94–1.34
Zip Code-level Percent Hispanic (ref=lowest tertile)		
Tertile 2	0.92	0.77–1.07
Tertile 3	0.90	0.74–1.06
Zip Code-level Percent below FPL (ref=lowest tertile)		
Tertile 2	0.98	0.83–1.16
Tertile 3	1.02	0.88–1.19
Zip Code-level Educational attainment (ref=HS or less)		
Some college	1.10	0.83–1.46
College graduate	1.00	0.83–1.19
Zip Code-level Composite Percent Black/Percent below FPL * (ref=lowest tertile)		
Tertile 2	0.97	0.83–1.14
Tertile 3	0.91	0.76–1.08
Zip Code-level Overlapping Percent Black/Percent below FPL (ref=Group 1)		
Group 2	0.88	0.73–1.04
Group 3	0.87	0.70–1.07
State-level Gini Coefficient (ref=least income inequality)		
Tertile 2	1.09	0.84–1.40
Tertile 3	1.12	0.86–1.42

Each variable was examined in a separate model adjusted for individual-level factors (Table 2), calendar year at index date, and random effects at each level. Bolded 95% credible intervals do not cross 1 and Bayesian p-value <0.05.

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* Composite score of % black and % below FPL divided into tertiles
** Group 1=zip codes with the lowest tertiles of % black and % below FPL, Group 3= zip codes with the highest tertiles of % black and % below FPL

Table 5.

Models examining the odds of HCQ adherence (PDC ≥ 80%) vs. nonadherence (PDC <80%) with 95% Credible Intervals by contextual health resources and urbanicity accounting for zip code percent black [†]

Area-level Health Resources	Odds Ratio (OR)	95% Credible Interval	OR for % Black	95% Credible Interval
Total MDs per capita (ref=lowest tertile)				
Tertile 2	0.88	0.70–1.08	0.86	0.73–1.01 *
Tertile 3	0.86	0.71–1.06	0.82	0.70–0.98
Total subspecialists per capita (ref=lowest tertile)				
Tertile 2	0.92	0.71–1.16	0.87	0.75–1.01 *
Tertile 3	0.84	0.67–1.04	0.84	0.71–1.01 *
Number of hospitals per capita (ref=lowest tertile)				
Tertile 2	1.13	0.97–1.31	0.87	0.76–1.00
Tertile 3	1.30	1.07–1.58	0.83	0.70–0.97
Health Professional Shortage Area (Primary Care) (ref=none)				
Partial	1.10	0.86–1.43	0.86	0.74–1.00
Whole	0.88	0.77–1.01 *	0.83	0.70–0.99
Number of pharmacists per capita (ref=lowest tertile)				
Tertile 2	0.91	0.75–1.09	0.85	0.74–0.99
Tertile 3	0.89	0.75–1.05	0.81	0.68–0.95
Number of rheumatologists per capita (ref=lowest tertile)				
Tertile 2	1.22	0.95–1.55	0.85	0.73–0.99
Tertile 3	1.16	0.89–1.47	0.82	0.69–0.96
Percent urban (ref=lowest tertile)				
Tertile 2	0.92	0.74–1.17	0.87	0.75–1.01 *
Tertile 3	0.82	0.66–1.02 *	0.83	0.70–1.00

[†] Each variable was examined in a separate model adjusted for individual-level factors (Table 2), calendar year at index date, zip code level percent black, and random effects at each level. All variables are at the county-level except for number of rheumatologists which is at the state level.

* Bayesian p-value <0.05 with 95% credible interval that just crosses 1; Bolded 95% credible intervals do not cross 1 and Bayesian p-value <0.05.