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Authors

Feldman, Candace H
Yazdany, Jinoos
Guan, Hongshu
et al.

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Medication Nonadherence is Associated with Increased Subsequent Acute Care Utilization among Medicaid Beneficiaries with Systemic Lupus Erythematosus

Candace H. Feldman[1], **Jinoos Yazdany**[2], **Hongshu Guan**[1], **Daniel H. Solomon**[1,3], and **Karen H. Costenbader**[1]

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

[2]Division of Rheumatology, Department of Medicine, UCSF School of Medicine, San Francisco, CA

[3]Division of Pharmacoepidemiology and Pharmacoeconomics, Department of Medicine, Brigham and Women's Hospital, Boston, MA

Abstract

Objective—We examined whether nonadherence to hydroxychloroquine (HCQ) or immunosuppressive medications (IS) was associated with higher subsequent acute care utilization among Medicaid beneficiaries with systemic lupus erythematosus (SLE).

Methods—We utilized U.S. Medicaid data from 2000–2006 to identify adults 18–64 years with SLE who were new users of HCQ or IS. We defined the index date as receipt of HCQ or IS without use in the prior six months. We measured adherence using the medication possession ratio (MPR), the proportion of days covered by total days supply dispensed, for one-year post-index date. Our outcomes were all-cause and SLE-related emergency department (ED) visits and hospitalizations in the subsequent year. We used multivariable Poisson regression models to examine the association between nonadherence (MPR<80%) and acute care utilization adjusting for sociodemographics and comorbidities.

Results—We identified 9,600 HCQ new users and 3,829 IS new users with SLE. The mean MPR for HCQ was 47.8% (SD 30.3) and for IS, 42.7% (SD 30.7). 79% of HCQ users and 83% of IS users were nonadherent (MPR<80%). In multivariable models, among HCQ users, the incidence rate ratio (IRR) of ED visits was 1.55 (95% CI 1.43–1.69) and the IRR of hospitalizations was 1.37 (95% CI 1.25–1.50), comparing nonadherers to adherers. For IS users,

Corresponding author: Candace H. Feldman, MD, MPH, Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, 75 Francis Street, PBB-3, Boston, MA 02115, chfeldman@partners.org, Office: 617-732-5325, Fax: 617-525-1010.

Author Contributions

All authors were involved in drafting this manuscript or revising it critically for important intellectual content and all authors approved the version submitted. Dr. Feldman and Dr. Costenbader had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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the IRR of ED visits was 1.64 (95% CI 1.42–1.89) and of hospitalizations was 1.67 (95% CI 1.41–1.96) for nonadherers versus adherers.

Conclusion—In this cohort, nonadherence to HCQ and IS was common and was associated with significantly higher subsequent acute care utilization.

Keywords

systemic lupus erythematosus; medication adherence; health services research; disparities; outcome measures; access to care

Medication nonadherence, the failure to take medications as prescribed, is a widespread problem accounting for over $100 billion in preventable healthcare costs in the U.S. annually.(1, 2) Data from systemic lupus erythematosus (SLE) clinical trials demonstrate reduced disease activity and morbidity from use of hydroxychloroquine (HCQ) and immunosuppressive drugs (IS) (3–5). Despite this, studies suggest nonadherence to be a particularly pervasive problem with only 30 to 60 percent of SLE patients taking medications as prescribed.(6–10) Characteristics unique to SLE may render adherence particularly challenging, including frequent disease activity fluctuations, the complexity and toxicity of medication regimens, a high disease burden among lower socioeconomic status groups, and cognitive and psychological manifestations.(8, 10, 11) Adverse outcomes, notably end-stage renal disease, may be more frequent among nonadherent SLE patients.(12, 13)

A number of studies demonstrate high costs of SLE patient care that are in large part due to high health care utilization.(14, 15) Each year, one in four SLE patients are hospitalized, one in six hospitalized patients are readmitted within 30 days of discharge, and one in two SLE patients visit the emergency department (ED).(16–18) Among cardiovascular disease patients, adherence has been shown to significantly impact health care utilization, costs and mortality.(19, 20) In SLE, one cross-sectional study found that patients who reported forgetting to take their medications some of the time had increased odds of ED visits compared to patients who did not report forgetting.(10) A second SLE study demonstrated a potential relationship between poor adherence and increased hospitalizations, however the sample size was small.(21)

To our knowledge, there are no studies to date that examine whether there is a temporal relationship between SLE medication nonadherence and subsequent acute care use. We studied patterns of medication nonadherence in a large, nationwide, racially and ethnically diverse cohort and investigated whether medication nonadherence is associated with high-cost health care utilization. We hypothesized that nonadherers would have a greater number of ED visits and hospitalizations compared to adherers even after adjusting for sociodemographic factors and comorbidities.

Patients and Methods

Patient Population

We utilized the Medicaid Analytic eXtract (MAX), an administrative database that includes billing claims and demographic information for all Medicaid enrollees from 47 states and Washington, D.C. Arizona, Tennessee and Maine do not contribute to MAX. Medicaid is the largest source of health coverage overall in the U.S. and the public health insurance program for low-income individuals and families.(22) It is jointly funded by states and the federal government and covers over 60 million Americans. We included all adults, aged 18–<65 years, continuously enrolled in Medicaid for ≥6 months between January 1, 2000 and December 31, 2006. As more than 90 percent of U.S. adults 65 years and older are enrolled in Medicare, we excluded this group given the potential for incomplete Medicaid claims, and because SLE disproportionately affects younger age groups.(23) We identified all adults with prevalent SLE, defined as ≥3 International Classification of Diseases, ninth revision (ICD-9) codes for SLE (710.0), separated by at least 30 days, from hospital discharge diagnoses or physician visit claims. (24, 25)

Medication New User Identification

In this cohort of SLE patients, we identified new users of an oral immunosuppressive drug (IS) or hydroxychloroquine (HCQ) utilizing the date of first receipt (index date) with no outpatient pharmacy claims for the drug of interest during the prior 6 months of continuous enrollment (Figure 1). We restricted our analyses to incident users in order to minimize differences that may be observed between long-time users of medications and initiators.(26) An incident user cohort also allows for clearly defined temporality of baseline characteristics, medication use and outcomes reducing the potential for reverse causation. Of the new users identified, we included those with ≥2 years of follow-up after the index date. The first 365-day period following the index date was the adherence assessment period and the second 365-day period was the outcome (acute care utilization) assessment period.

Oral IS included mycophenolate mofetil, mycophenolic acid, azathioprine, leflunomide, methotrexate, tacrolimus and oral cyclophosphamide. We restricted our analysis to oral immunosuppressives for a number of reasons. First, a limitation of Medicaid claims data is that inpatient intravenous medications are billed differently depending on the state and thus we might not be able to account for all infusions given during hospitalization. Second, while there is a standard of care associated with dosing schedules of oral medications for SLE, protocols for intravenous therapy, for example cyclophosphamide, differ and therefore adherence assessment using pharmacy refill claims data becomes challenging. Studies in rheumatoid arthritis have assigned days' supply of medications such as infliximab based on a recommended dosing schedule.(27) However for SLE patients, recommended dosing schedules for cyclophosphamide and rituximab vary significantly and therefore we would not be able to follow this strategy without biasing our adherence estimate. Third, we hypothesize that adherence to oral medications may be influenced by different factors than adherence to hospital-based or outpatient appointments for intravenous therapy. Issues such as lack of transportation, inability to miss work, or lack of childcare, may be obstacles specific to adherence to intravenous therapy that are especially relevant in this low-income

vulnerable population. Due to the use of claims data, we would not have been able to appropriately incorporate these factors in our analyses.

Medication Adherence: Medication Possession Ratio

We used prescription refill claims to assess medication adherence for a one-year period beginning at the index date. We calculated the mean medication possession ratio (MPR) separately for HCQ and IS. We defined MPR as the total medication days, according to the prescription fill date and the days supplied, divided by the 365-day adherence assessment period beginning on the index date (date of first prescription). We excluded any hospitalization days from both the numerator and the denominator. We dichotomized the MPR as <80% and ≥80% (28) and MPR≥80% was considered adherent.(29) This standard, dichotomized measure has been used to assess medication adherence among Medicaid beneficiaries in prior studies.(20, 30) We conducted secondary analyses utilizing three MPR thresholds, 0–49%, 50–79% and ≥80%, to determine whether there was a relationship between degree of nonadherence and the outcomes of interest. These cutoffs have also been previously used to evaluate adherence behavior among Medicaid beneficiaries.(31, 32)

Outcome: Acute Care Utilization

We assessed our primary outcome, acute care utilization, by examining the number of ED visits and the number of hospitalizations during the one-year follow-up period (Figure 1). We assessed all-cause hospitalizations and ED visits, and SLE-related ED visits and hospitalizations utilizing SLE discharge diagnosis codes (ICD-9 710.0).

Covariates

We collected all covariates during the six months of continuous enrollment prior to the index date (Figure 1). We determined age at the index date, sex, U.S. geographic region (Northeast, Midwest, South, West) and race/ethnicity. We used Medicaid's categorizations of race/ethnicity based on self-report. Due to small numbers that would prevent reporting in accordance with Centers for Medicare and Medicaid Services (CMS) policies, we described combined categories: White, Black or African American, Hispanic or Latino (including Hispanic or Latino and one or more races), Asian (including Native Hawaiian or other Pacific Islander), Native American (including American Indian or Alaskan Native) and Other (including unknown).(33)

Area-level socioeconomic status (SES) was determined using a previously validated composite score of seven U.S. Census variables: median household income, proportion with income below 200% of federal poverty level, median home value, median monthly rent, mean education level, proportion of people age ≥25 who were college graduates, and proportion of employed persons with a professional occupation.(34) We obtained U.S. Census data by ZIP code for each patient and aggregated this to the county level and then divided it into binary categories of higher versus lower area-level SES.

We used a previously developed SLE-specific risk adjustment index to characterize comorbidities. This index utilizes ICD-9 codes for comorbidities particularly relevant to SLE patients and was shown to account for more variation in the risk of mortality among

SLE patients than the traditionally used Charlson comorbidity index.(35) We used the median score in our population to divide patients into higher or lower risk categories. We also determined the number of different medication prescriptions and overall health care utilization (number of outpatient visits, hospitalizations and ED visits) during the six month baseline period.

Statistical Analysis

We used Chi-square tests and Student's t-tests to compare sociodemographic characteristics of adherent (MPR≥80%) and nonadherent (MPR<80%) patients with SLE, separately for HCQ and IS. We determined the number of HCQ and IS users with zero, one or two or more hospitalizations or ED visits, all-cause and SLE-related, during the follow-up period, and compared them by prior adherence category using Chi-square tests. To assess the association between nonadherence (MPR<80% versus MPR ≥80%) and acute care utilization, we used multivariable Poisson regression adjusting for calendar year, sociodemographic factors (age, gender, race/ethnicity, region and SES), comorbidities using the SLE risk adjustment index, and baseline number of medications. We also examined models that additionally adjusted for healthcare utilization during the baseline period. We conducted secondary analyses utilizing three categories for the MPR (0– 49%, 50–79% and ≥80%) in multivariable Poisson regression models to determine whether degree of nonadherence behavior was associated with acute care utilization. The objective of these analyses was to investigate whether there was a temporal association between adherence behavior, as measured by the MPR, and acute care utilization, not to infer causality.

In sensitivity analyses, we utilized a six-month period for adherence assessment, rather than the one-year period we used in our primary analysis, with a subsequent one-year period to ascertain acute care utilization. We chose to do this because immunosuppressive medications, particularly for lupus nephritis, may be prescribed as induction therapy for a six-month period and we hoped to differentiate between medication discontinuation and nonadherence.

All analyses were conducted using SAS, Version 9.3 (Cary, NC). Data were obtained from the Centers for Medicare and Medicaid Services through an approved data use agreement. Results are presented in accordance with their policies; cell sizes <11 are suppressed. The Partners Healthcare Institutional Review Board approved this study.

Results

Hydroxychloroquine and Immunosuppressive New User Characteristics

We identified 9,600 patients with prevalent SLE who filled a new prescription for HCQ. Their mean age was 39.8 years (SD 11.4), 9,150 (95.3%) were female, 3,866 (40.3%) were Black, 3,190 (33.2%) were White, and 1,492 (15.5%) were Hispanic, 454 (4.7%) were Asian (Table 1). Among the new HCQ users, 69.2% had low SLE risk-adjustment index scores. The mean number of medications at baseline was 11.9 (SD 8.6). The mean MPR for HCQ use was 47.8% (SD 30.3); 2,048 (21.3%) were adherent with MPR ≥80% and 7,552 (78.7%) were nonadherent with MPR<80%.

There were 3,829 new users of IS drugs with a mean follow-up time of 3.6 years (SD 1.2) (Table 1). The mean age was 38.7 years (SD 11.7), 95% were female, 29.4% were White, and 40.6% were Black. The mean SLE risk-adjustment index was 1.3 (SD 2.1) and the mean number of baseline medications was 13.3 (SD 9.5). The mean MPR was 42.7% (SD 30.4) and 3,178 (83%) were nonadherent.

HCQ nonadherers were younger, with a mean age of 39 (SD 11.3) years compared to the mean age of 42.8 (SD 11.3) years among the adherers ($p<0.0001$) (Table 2). A greater percentage of nonadherers were Black ($p<0.0001$), and Hispanic ($p<0.0001$), and fewer were White ($p<0.0001$). Nonadherers also had a lower mean SLE-risk adjustment index ($p=0.05$), and on average, were taking fewer medications at baseline compared to adherers ($p<0.0001$).

Similarly, IS nonadherers were younger on average than adherers, 40.3 years (SD 11.8) compared to 38.3 years (SD 11.7) ($p<0.0001$) (Table 2). A greater percentage of nonadherers were Black compared to adherers ($p<0.0001$). Nonadherers had a lower mean socioeconomic status score ($p=0.0005$), a lower mean SLE risk-adjustment index ($p=0.004$) and, on average, fewer baseline medications compared to nonadherers ($p<0.0001$).

Acute Care Utilization

During the follow-up period, 2,375 (31.5%) HCQ nonadherers had two or more all-cause ED visits (mean number of visits 1.70, SD 3.72), compared to 461 (22.5%) adherers (mean 1.13, SD 2.71) (Table 3). Among IS nonadherers, 1,110 (34.9%) had two or more all-cause ED visits (mean 1.94, SD 3.89) compared to 164 (25.2%) adherers (mean 1.15, SD 2.06). In terms of SLE-related visits, 7.4% of HCQ nonadherers had two or more visits compared to 4.3% of adherers. Among IS users, 9.1% of nonadherers had two or more visits that were SLE-related compared to 6.5% of adherers. In addition, 13.7% of HCQ nonadherers had two or more all-cause hospitalizations compared to 10.4% of adherers. Among IS nonadherers, 17.4% had two or more all-cause hospitalizations (mean 0.84, SD 1.88), compared to 12.8% of adherers (mean 0.52, SD 1.17).

In our multivariable Poisson regression models, we adjusted for calendar year, age, gender, race/ethnicity, geographic region, socioeconomic status, SLE-risk adjustment index, and baseline number of medications (Table 4). We found statistically significant greater acute care utilization among HCQ and IS nonadherers compared to adherers. Comparing HCQ nonadherers to adherers, the IRR for all-cause ED visits was 1.55 (95% CI 1.43–1.69) and the IRR of SLE-related ED visits was 1.60 (95% CI 1.43–1.80). The IRR of all-cause hospitalizations for HCQ nonadherers compared to adherers was 1.37 (95% CI 1.25–1.50) and for SLE-related hospitalizations, 1.30 (95% CI 1.18–1.44). For IS nonadherers compared to adherers, the IRR of all-cause ED visits was 1.64 (95% CI 1.42–1.89), and of SLE-related was 1.69 (95% CI 1.38–−2.05). In terms of hospitalizations, the IRR for all-cause hospitalizations was 1.67 (95% CI 1.41–1.96) and SLE-related was 1.60 (95% CI 1.34–1.91), comparing IS nonadherers to adherers.

For both HCQ and IS users, we additionally adjusted for health care utilization (ED visits, hospitalizations and outpatient visits) during the baseline period and similarly found

statistically significant greater acute care utilization among nonadherers versus adherers with IRRs in line with our aforementioned results.

Secondary Analyses

In secondary analyses, we divided HCQ and IS nonadherers into two categories, MPR 0–49% and MPR 50–79%, and compared each group to adherers (MPR≥80%) in adjusted Poisson models (Table 5). We found the highest IRRs for all-cause and SLE-related ED visits and hospitalizations both for HCQ and IS users, comparing those with the poorest adherence (MPR 0–49%) to adherers (MPR ≥80%). The IRRs were incrementally lower but still statistically significant for moderate nonadherers (MPR 50–79%) with the exception of the HCQ group for which the IRR of SLE-related hospitalizations was comparable to adherers.

Sensitivity Analysis

We conducted a sensitivity analysis using a six-month period, instead of the one-year period in our primary analysis, to assess adherence (as measured by MPR) and the subsequent one-year to evaluate acute care utilization (Supplemental Table 1). In our fully adjusted model, we found IRRs in line with our primary analysis with statistically significantly greater acute care utilization among nonadherers compared to adherers.

Discussion

In this study, we demonstrated that nonadherence to hydroxychloroquine and to immunosuppressive medications among individuals with SLE was associated with significantly higher acute care utilization in the subsequent year. Nonadherent SLE patients who were new users of HCQ had more than a 55% greater incidence rate of ED visits, and nearly 40% increased rate of hospitalizations compared to adherent patients. New users of IS drugs who were nonadherent also had nearly 65% greater incidence of ED visits and nearly 70% greater incidence of hospitalizations compared to adherent patients. We also demonstrated that individuals with the poorest level of adherence (MPR 0–49%) had the highest rates of acute care utilization, and for all categories except HCQ SLE-related hospitalizations, moderate nonadherence (MPR 50–79%) was also associated with statistically significant increases in utilization.

While this is the first longitudinal study to investigate the relationship between adherence and acute care utilization in SLE patients, our findings are in line with prior cross-sectional studies. One study demonstrated that SLE patients who self-reported difficulty with adherence were 45% more likely to visit the ED.(10) Although this study did not find a difference in hospitalizations between adherent and nonadherent patients, both adherence and health care utilization were self-reported measures. In addition, the prior study was cross-sectional and therefore a temporal relationship could not be investigated. It is also plausible, however, that there is a stronger relationship between adherence and ED visits that may or may not result in hospitalization, compared to planned and direct hospitalizations, for which other factors may dominate. However, one prior small study of 180 patients with SLE who visited an ED over the course of eight months, did find an association between

poor adherence and increased hospitalization.(21) In other chronic diseases including diabetes and cardiovascular disease, nonadherence has been associated with increased acute care utilization, specifically increased number of hospitalizations, and with greater net health care costs and higher mortality.(36–41)

In this low-income high-risk cohort of Medicaid beneficiaries with SLE, we found extremely poor adherence overall; only 21% of HCQ new users and 17% of IS new users were adherent to their medications (MPR≥80%). While it is challenging to compare rates of adherence across SLE studies because many different measures and adherence thresholds are used, our study confirms prior findings that adherence to SLE medications overall is very poor.(8–10, 42, 43) While it was beyond the scope of this study to examine predictors of nonadherence in this population, we did note that disproportionately greater percentages of HCQ and IS nonadherers compared to adherers were young (aged 18–30 years) or Black. Prior studies have similarly shown that young age and Black race were associated with increased rates of SLE medication nonadherence.(9, 11)

Interestingly, in our unadjusted analyses, we found that both HCQ and IS adherers had, on average, more baseline medications and higher SLE-specific risk adjustment indices compared to nonadherers, suggesting that SLE patients with more severe disease and more comorbidities were more adherent in this cohort. The literature to date presents conflicting findings regarding these relationships. One study by Daleboudt and colleagues demonstrated no association between nonadherence and numbers of comorbidities, extent of organ involvement and number of medications.(9) Other studies have shown that increased number of medications and more comorbidities may be associated with poorer adherence; however these studies were cross-sectional in nature and therefore subject to reverse causation.(8, 10, 11) We hypothesize that in this cohort, patients with more severe disease may have greater incentive to adhere to their medications in order to alleviate symptoms (e.g. joint pain, rash, edema) or may be more motivated to prevent complications (e.g. skin scarring, renal damage). Prior studies in other chronic diseases have similarly shown that individuals with a higher perceived risk of disease-related complications and with symptomatic disease were more likely to adhere to their medications compared to those with asymptomatic disease.(44, 45) Qualitative studies among SLE patients should be considered to further investigate this issue.

There are several noteworthy strengths to this study. First, this study was conducted in a large, nationwide population of racially and ethnically diverse Medicaid beneficiaries with SLE, shown to have a high burden of disease, and an increased risk of adverse outcomes.(25, 46) Prior studies note that patients with frequent ED visits and hospitalizations generate a disproportionate share of health care costs.(47) Particularly among Medicaid beneficiaries, significant efforts are underway to identify, target and improve care for the highest cost patients.(48) Interventions to improve medication adherence may provide an opportunity to decrease health care costs for this vulnerable population. Second, this is the first adherence study in SLE patients to use a new medication user design, as opposed to a prevalent user design. Prevalent user designs are subject to healthy survivor bias; patients must have “survived” and adhered during the initial, often critical time when a medication is started in order to be included, which overestimates adherence.(49) Third, this is a longitudinal study,

which allowed us to examine whether there was temporal relationship between adherence and the outcomes of interest. Prior studies in SLE that investigated this question have been cross-sectional, and thus subject to reverse causation. In addition, separate periods were used to assess baseline covariates, adherence and outcomes, to limit over-adjustment by factors that may lie on the causal pathway. Fourth, in addition to a dichotomized MPR cutoff of 80 percent, we examined levels of nonadherence and demonstrated a dose-response relationship between degree of nonadherence and increased acute care utilization.

There are limitations to this study. We used administrative claims data for these analyses, which lack clinical information regarding disease activity or duration. We therefore cannot assess whether medications were initiated or discontinued because of SLE flares, adverse reactions or ineffectiveness. In addition, there may be misclassification of SLE cases. However, we used a conservative definition of ≥3 ICD-9 codes to increase specificity and to exclude individuals who were seen once for “rule-out” SLE and once in follow-up. This definition was used previously to examine the prevalence and incidence of SLE in the Medicaid population and yielded results in line with prior studies.(24, 50) Further, medication adherence is a complex behavior that is challenging to measure. While the MPR is considered to be among the best measures, it may not be able to accurately predict long-term use patterns or differentiate between patients who stop medication entirely versus those with a gap in use.(51) In addition, adherence may not be a static behavior and may have changed after the period in which it was assessed during which outcomes were measured. We also restricted our analyses to oral immunosuppressives and therefore our findings may not be reflective of the relationship between intravenous immunosuppressive adherence and acute care utilization.

Finally, there is the possibility of residual confounding from a healthy adherer effect. This refers to the phenomenon whereby adherence may be associated with other healthy behaviors and thus patients who are more likely to adhere may be at lower risk for adverse outcomes for these same reasons.(52) Prior studies suggest that patients who adhere to one medication for a chronic disease are more likely to adhere to other therapies as well and may be more likely to obtain cancer screening and vaccinations.(53, 54) Residual confounding from a healthy adherer effect may overestimate the preventive value of adherence behavior itself and is a potential limitation of this study.(55) However, in our study population, on average, adherers had higher SLE-specific risk adjustment indices and more baseline medications compared to nonadherers suggesting that in terms of comorbidities, they were not healthier overall. In addition, a large study of post-myocardial infarction patients specifically examined the degree to which the healthy adherer effect played a role in the relationship between medication adherence and outcomes and did not find significant evidence to support this.(19)

We acknowledge that there are multiple measures used to assess both medication adherence and persistence in the literature to date. Two measures, the MPR and the proportion of days covered (PDC) are among the most widely used particularly in administrative data. The MPR has been used in multiple Medicaid database studies.(20, 30) In one study among Medicaid beneficiaries, both the MPR and the PDC had the highest predictive validity for hospitalization episodes, one of the main outcomes in our study.(56) The definition we used

for MPR in the context of a new user design and a 365-day adherence assessment period beginning on the date of first prescription yields a value almost identical to an interval-based approach for PDC calculation.(57) While adherence is a complex behavior the full extent of which is challenging to capture regardless of the method, we feel that the measure of adherence utilized here accurately reflects days covered by medication prescription refills during the study period.

Overall, in this study we demonstrated significantly increased acute care utilization among SLE patients who were shown to be nonadherent to either HCQ or IS medications compared to those who were adherent. Patients with the poorest level of adherence had the highest rates of utilization. Further studies are needed to understand whether interventions that improve adherence will reduce acute care utilization and improve outcomes particularly for the most vulnerable groups. In addition, given the higher costs of some SLE medications, and the burden of multiple essential medications and copayments, additional research is needed to understand whether improving adherence results in net cost saving for the patient and for the health care system, especially for a high-risk, low-income population.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Significance and Innovation

- We demonstrated that adherence to hydroxychloroquine and immunosuppressive medications was poor among U.S. Medicaid beneficiaries with systemic lupus erythematosus (SLE), a racially/ethnically diverse, low-income population at high risk for adverse health outcomes.
- Patients who were nonadherent had significantly greater all-cause and SLE-related emergency department visits and hospitalizations even after adjusting for sociodemographic factors and comorbidities.
- This increased acute care utilization among nonadherers suggests that there may be an opportunity to intervene to reduce avoidable morbidity and health care costs by improving adherence behavior.

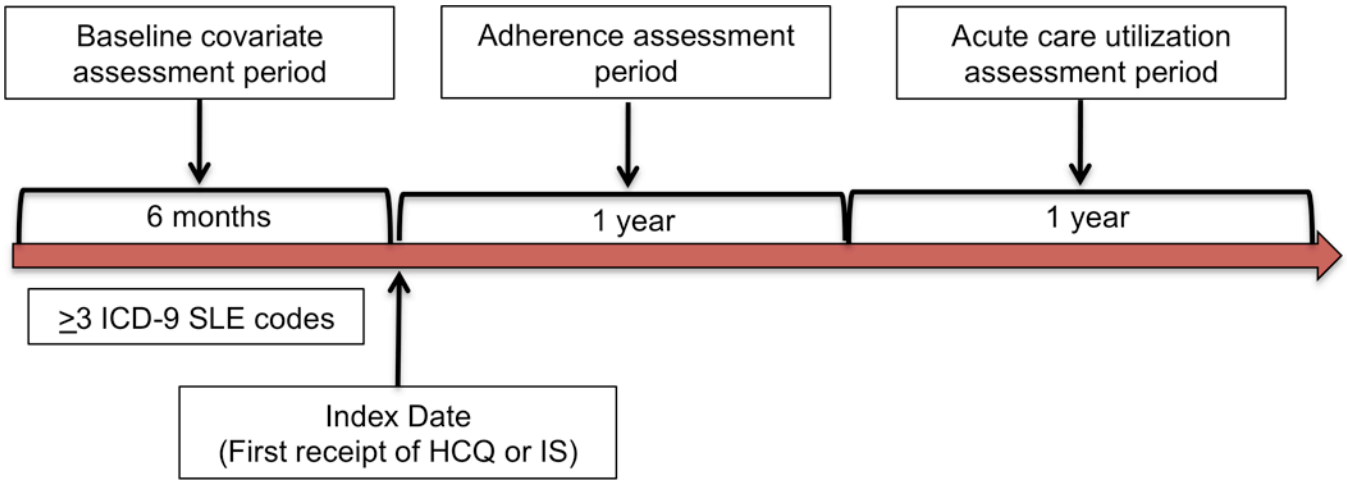

Figure 1.

New users of hydroxychloroquine (HCQ) or immunosuppressive medications (IS) were identified among SLE patients with six months of prior continuous enrollment in Medicaid and no use of these drugs during that time. Adherence was assessed using the Medication Possession Ratio (MPR) during the year following the index date and the outcome (acute care utilization) was measured during the subsequent year.

Table 1

Baseline characteristics of SLE new users of hydroxychloroquine (HCQ) and immunosuppressive drugs (IS)

Characteristics	HCQ New Users N=9600	IS New Users N=3829
Years of follow-up – Mean (SD)	4.0 (1.3)	3.6 (1.2)
Age – Mean (SD)	39.8 (11.4)	38.7 (11.7)
Age group – N (%)		
18–30 years	2429 (25.3)	1146 (29.9)
31–45 years	4111 (42.8)	1552 (40.5)
46–64 years	3060 (31.9)	1131 (29.5)
Gender – N (%)		
Female	9150 (95.3)	3638 (95.0)
Male	50 (4.7)	191 (5.0)
Race/Ethnicity – N (%)		
White	3190 (33.2)	1127 (29.4)
Black	3866 (40.3)	1555 (40.6)
Hispanic	1492 (15.5)	691 (18.1)
Asian	454 (4.7)	212 (5.5)
Native American	126 (1.3)	63 (1.7)
Other	472 (4.9)	181 (4.7)
Geographic Region – N (%)		
Midwest	1718 (17.9)	704 (18.4)
Northeast	2372 (24.7)	921 (24.1)
South	3265 (34.0)	1206 (31.5)
West	2245 (23.4)	998 (26.1)
Socioeconomic Status		
Mean (SD)	1.2 (1.8)	1.3 (1.8)
Median	1.1	1.2
Lower	4834 (50.4)	1922 (50.2)
Higher	4766 (49.7)	1907 (49.8)
SLE Risk Adjustment Index		
Mean (SD)	1.0 (1.8)	1.3 (2.1)
Low	6643 (69.2)	2283 (59.6)
High	2957 (30.8)	1546 (40.4)
Number of Medications – Mean (SD)	11.9 (8.6)	13.3 (9.5)
Medication Possession Ratio (MPR)		
Mean % (SD)	47.8 (30.3)	42.7 (30.4)
MPR ≥80% (Adherent)	2048 (21.3)	651 (17)
MPR <80% (Nonadherent)	7552 (78.7)	3178 (83)
Baseline Health Care Utilization – Mean (SD)		
Emergency Department Visits	1.6 (3.5)	1.8 (3.7)
Inpatient Visits	0.6 (1.5)	0.78 (1.8)

Characteristics	HCQ New Users N=9600	IS New Users N=3829
Outpatient Visits	9.0 (9.0)	10.3 (9.9)

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Table 2

Characteristics of SLE Hydroxychloroquine and Immunosuppressive New Users by Adherers (MPR≥80%) versus Nonadherers (MPR<80%)

	Hydroxychloroquine New Users			Immunosuppressive New Users		
	MPR≥80% (Adherers) N=2048	**MPR<80% (Nonadherers) N=7552**	**p-value**	**MPR≥80% (Adherers) N=651**	**MPR<80% (Nonadherers) N=3178**	**p-value**
Age – Mean (SD)	42.8 (11.3)	39.0 (11.3)	<0.0001	40.3 (11.8)	38.3 (11.7)	<0.0001
Age group – N (%)						
18–30 years	346 (16.9)	2083 (27.6)	<0.0001	165 (25.4)	981 (30.9)	0.005
31–45 years	863 (42.1)	3248 (43.0)	0.48	255 (39.2)	1297 (40.8)	0.43
46–64 years	839 (41.1)	2221 (29.4)	<0.0001	231 (35.5)	900 (28.3)	0.0003
Gender – N (%)						
Female	1934 (94.4)	7216 (95.6)	0.03	614 (94.3)	3024 (95.2)	0.37
Male	114 (5.6)	336 (4.5)		37 (5.7)	154 (4.9)	
Race/Ethnicity – N (%)						
White	912 (44.5)	2278 (30.1)	<0.0001	208 (32.0)	919 (28.9)	0.12
Black	620 (30.3)	3246 (43.0)	<0.0001	217 (33.3)	1338 (42.1)	<0.0001
Hispanic	240 (11.7)	1252 (16.6)	<0.0001	135 (20.7)	556 (17.5)	0.05
Asian	112 (5.5)	342 (4.5)	0.07	38 (5.8)	174 (5.5)	0.71
Native American	26 (1.3)	100 (1.3)	0.84	11 (1.7)	52 (1.6)	0.92
Other	138 (6.7)	334 (4.4)	<0.0001	42 (6.5)	139 (4.4)	0.02
Geographic Region – N (%)						
Midwest	295 (14.4)	1423 (18.8)	<0.0001	84 (12.9)	620 (19.5)	<0.0001
Northeast	593 (29.0)	1779 (23.6)	0.41	212 (32.6)	709 (22.3)	<0.0001
South	681 (33.3)	2584 (34.2)	0.99	178 (27.3)	1028 (32.4)	0.01
West	479 (23.4)	1776 (23.4)	<0.0001	177 (27.2)	821 (25.8)	0.47
Socioeconomic Status – Mean (SD)	1.14 (1.86)	1.25 (1.77)	0.01	1.56 (1.82)	1.29 (1.80)	0.0005
SLE Risk Adjustment Index – Mean (SD)	1.05 (1.91)	0.96 (1.83)	0.05	1.53 (2.33)	1.27 (2.05)	0.004
Medications- Mean (SD)	14.05 (8.69)	11.26 (8.52)	<0.0001	14.78 (9.07)	13.03 (9.51)	<0.0001

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Table 3

Acute care utilization among SLE hydroxychloroquine (HCQ) and immunosuppressive (IS) new users by adherers (MPR≥80%) versus nonadherers (MPR<80%) during follow-up year

	Number of Visits	Emergency Department Visits		Hospitalizations	
		All-cause N (%)	SLE-related N (%)	All-cause N (%)	SLE-related N (%)
HCQ Adherers N=2048	**0**	1188 (58.0)	1783 (87.1)	1551 (75.7)	1674 (81.7)
	1	399 (19.5)	177 (8.6)	284 (13.9)	227 (11.1)
	≥2	461 (22.5)	88 (4.3)	213 (10.4)	147 (7.2)
	Mean (SD)	1.13 (2.71)	0.21 (0.70)	0.49 (1.28)	0.32 (0.92)
HCQ Nonadherers N=7552	**0**	3789 (50.1)	6113 (81.0)	5378 (71.2)	5924 (78.4)
	1	1388 (18.4)	882 (11.7)	1143 (15.1)	952 (12.6)
	≥2	2375 (31.5)	557 (7.4)	1031 (13.7)	676 (9.0)
	Mean (SD)	1.70 (3.72)	0.36 (1.13)	0.65 (1.61)	0.42 (1.12)
IS Adherers N=651	**0**	367 (56.4)	551 (84.6)	471 (72.4)	514 (79.0)
	1	120 (18.4)	58 (8.9)	97 (14.9)	88 (13.5)
	≥2	164 (25.2)	42 (6.5)	83 (12.8)	49 (7.5)
	Mean (SD)	1.15 (2.06)	0.25 (0.77)	0.52 (1.17)	0.33 (0.77)
IS Nonadherers N=3178	**0**	1465 (46.1)	2465 (77.6)	2114 (66.5)	2400 (75.5)
	1	603 (19.0)	423 (13.3)	512 (16.1)	418 (13.2)
	≥2	1110 (34.9)	290 (9.1)	552 (17.4)	360 (11.3)
	Mean (SD)	1.94 (3.89)	0.46 (1.36)	0.84 (1.88)	0.53 (1.36)

All p-values <0.05 from Chi-square tests comparing adherers to nonadherers for all-cause and SLE-related emergency department visits and hospitalizations

Table 4

Adjusted incidence rate ratios (IRR) of acute care utilization (emergency department (ED) visits and hospitalizations), comparing nonadherers (MPR<80%) to adherers (MPR ≥80%)

		All-cause		SLE-related	
		IRR*	95% CI	IRR*	95% CI
ED Visits	**HCQ**	1.55	1.43–1.69	1.60	1.43–1.80
	IS	1.64	1.42–1.89	1.69	1.38–2.05
Hospitalizations	**HCQ**	1.37	1.25–1.50	1.30	1.18–1.44
	IS	1.67	1.41–1.96	1.60	1.34–1.91

*Incidence Rate Ratios (IRR) compare nonadherers (medication possession ratio, MPR<80%) to adherers (MPR≥80%) with 95% confidence intervals. Multivariable Poisson regression models adjusted for calendar year, age, gender, race/ethnicity, geographic region, socioeconomic status, SLE risk-adjustment index and baseline number of medications

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Table 5

Secondary analysis of the incidence rate ratio (IRR) of emergency department (ED) visits and hospitalizations for hydroxychloroquine (HCQ) and immunosuppressive (IS) nonadherers at two levels (MPR 0–49% and 50–79%) compared to adherers (MPR ≥80%)

		ED Visits IRR* (95% CI)		Hospitalizations IRR* (95% CI)	
		All-Cause	SLE-related	All-Cause	SLE-related
HCQ	MPR 0–49%	1.71 (1.57–1.86)	1.75 (1.56–1.97)	1.50 (1.36–1.65)	1.43 (1.29–1.58)
	MPR 50–79%	1.26 (1.14–1.39)	1.31 (1.15–1.50)	1.13 (1.01–1.26)	1.07 0.95–1.21)
IS	MPR 0–49%	1.42 (1.26–1.59)	1.71 (1.40–2.09)	1.75 (1.48–2.07)	1.65 (1.38–1.98)
	MPR 50–79%	1.18 (1.04–1.34)	1.62 (1.30–2.03)	1.47 (1.21–1.77)	1.48 (1.20–1.81)

*Incidence Rate Ratios (IRR) compare each nonadherence category (MPR 0–49% and MPR 50–79%) to adherers (MPR ≥80%) with 95% confidence intervals. Poisson regression models adjusted for calendar year, age, gender, race/ethnicity, geographic region, socioeconomic status, SLE risk-adjustment index and baseline number of medications.