HHS Public Access

Author manuscript

J Rheumatol. Author manuscript; available in PMC 2024 October 01.

Published in final edited form as:

J Rheumatol. 2023 October ; 50(10): 1302–1309. doi:10.3899/jrheum.2023-0060.

Medication cost concerns and disparities in patient-reported outcomes among a multiethnic cohort of patients with lupus

Alfredo Aguirre, MD[1] **[Assistant Professor]**, **Kimberly DeQuattro, MD**[2] **[Assistant Professor]**, **Stephen Shiboski, PhD**[3] **[Professor]**, **Patricia Katz, PhD**[1] **[Professor]**, **Kurt J. Greenlund, PhD**[4], **Kamil E. Barbour, PhD, MPH, MS**[4], **Caroline Gordon, MD, MA, FRCP**[5] **[Professor]**, **Cristina Lanata, MD**[6], **Lindsey A. Criswell, MD, MPH, DSc**[6], **Maria Dall'Era, MD**[1] **[Professor]**, **Jinoos Yazdany, MD, MPH**[1] **[Professor]**

[1]Division of Rheumatology, University of California, San Francisco

[2]Division of Rheumatology, University of Pennsylvania

[3]Department of Epidemiology & Biostatistics, University of California, San Francisco

[4]Centers for Disease Control and Prevention

[5]Institute of Inflammation and Ageing (IIA), University of Birmingham

[6]Genomics of Autoimmune Rheumatic Disease Section, National Human Genome Research Section NIH

Abstract

Objective: Concerns about the affordability of medications are common in systemic lupus erythematosus (SLE), but the relationship between medication cost concerns and health outcomes is poorly understood. We assessed the association of self-reported medication cost concerns and patient-reported outcomes (PROs) in a multiethnic lupus cohort.

Methods: The California Lupus Epidemiology Study is a cohort of individuals with physician-confirmed SLE. Medication cost concerns was defined as having difficulties affording lupus medications, skipping doses, delaying refills, requesting lower cost alternatives, purchasing medications outside the US, or applying for patient assistance programs. Linear regression and mixed effects models assessed the cross-sectional and longitudinal association of medication cost concerns and PROs, respectively, adjusting for age, sex, race and ethnicity, income, principal insurance, immunomodulatory medications, and organ damage.

Results: Of 334 participants, medication cost concerns were reported by 91 (27%). Medication cost concerns were associated with worse Systemic Lupus Erythematosus Activity Questionnaire (SLAQ, beta coefficient 5.9, 95% CI 4.3 to 7.6, P<0.001), Patient Health Questionnaire Depression Scale (PHQ-8, beta coefficient 2.7, 95% CI 1.4 to 4.0, P<0.001), and Patient-Reported

Corresponding author: Alfredo Aguirre, MD, Department of Medicine, Division of Rheumatology, University of California, San Fancisco, 10 Koret Way, San Francisco, CA 94117, Telephone: 415-353-2497, Fax: 628-246-8279, alfredo.aguirre@ucsf.edu.

Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Conflicts of interest:
None

Outcomes Measurement Information System (PROMIS, beta coefficient for physical function −4.6, 95% CI −6.7 to −2.4, P<0.001) scores after adjusting for covariates. Medication cost concerns were not associated with significant changes in PROs over two-year follow-up.

Conclusion: More than a quarter of participants reported at least one medication cost concern, which was associated with worse patient-reported outcomes. Our results reveal a potentially modifiable risk factor for poor outcomes rooted in the unaffordability of lupus care.

Keywords

Lupus Erythematosus; Systemic; Healthcare Disparities; Drug Costs; Patient Reported Outcome Measures

INTRODUCTION

Although known to suppress disease activity and prevent organ damage in SLE(1–3), chronic use of immunomodulatory medications can pose a significant financial burden for individuals living with lupus(4). Concerns about the affordability of drug costs can result in medication nonadherence and disproportionately affect the minoritized racial and ethnic groups most affected with SLE(5,6). In a study of a population-based cohort of individuals with SLE in Michigan, individuals with SLE were twice as likely to report medication nonadherence due to cost as compared to matched controls(4). Medication-related cost concerns is thus significant problem among at least a subset of patients with SLE that can potentially drive nonadherence and poor health outcomes.

In the general population, medication cost concerns have been described in up to one-third of individuals with chronic illnesses(7–10), and are associated with suboptimal outcomes, including increased hospitalizations(7,10). For instance, among patients with diabetes, cost-related nonadherence—which includes behaviors such as skipping medications, taking less medications, or delaying prescription refills due to costs—was reported in up to 17.6% of individuals and was associated with an increased risk of mortality(10,11). Medication costs and associated affordability concerns are thus potential avenues to optimize the value of treatments for patients with chronic diseases. However, the relationship between medication cost concerns and health outcomes is still poorly understood in the rheumatic diseases. Since individuals with SLE may be particularly susceptible to the impacts of medication costs, it is critical to understand the scope of this problem and its potential effects on health outcomes in this population.

In this study, we describe the prevalence of medication cost concerns among individuals with SLE in the California Lupus Epidemiology Study (CLUES), a cohort based in the San Francisco Bay Area, and assess the relationship between medication cost concerns and patient-reported outcomes (PROs) relevant to SLE patients. Participants were asked about a broad set of medication cost concerns encompassing cost-related nonadherence and other drug-related cost concerns. To capture the widest range of outcomes, we examined several PROs across the domains of disease activity, organ damage, depression, and health-related quality of life. We hypothesized that medication cost concerns are associated with worse PROs. We also examined the impact of medication cost concerns on the change in PRO

scores over time in a longitudinal model, hypothesizing that individuals with medication cost concerns at baseline would experience a decrement in PROs over the course of two-year follow-up relative to those without these concerns.

METHODS

Participants:

The California Lupus Epidemiology Study (CLUES) is a cohort study of individuals with physician-confirmed SLE in the San Francisco Bay Area that began enrollment in 2014. As previously described elsewhere, initial recruitment for CLUES was based on a CDC-funded registry of individuals with SLE that aimed to study the regional epidemiology of lupus in the San Francisco Bay Area from 2007 to 2009(5,12). Additional participants were recruited from 2015 to 2018 through community and academic rheumatology clinics and local research networks. SLE diagnoses were confirmed by study physicians, defined as meeting ≥4 of the 11 American College of Rheumatology (ACR) revised criteria for the classification of SLE(13,14), 3/11 ACR criteria plus a rheumatologist's diagnosis of SLE, or a confirmed diagnosis of lupus nephritis(5). Participants in CLUES were evaluated with in-person clinical evaluations, including medical record review, history and physical examination, and collection of biospecimens. In addition, trained interviewers collected sociodemographic data and PROs. 431 individuals with SLE participated in Year 1 of CLUES and 343 completed Year 3 follow-up during which participants were asked about medication cost concerns (hereafter, the Year 3 follow-up will be referred to as the baseline visit). Subsequently, 251 participants completed the Year 4 and 249 completed the Year 5 CLUES study visits. Nine participants died after the Year 3 visit and were excluded from this analysis.

The CLUES study has been approved by the University of California, San Francisco Institutional Review Board (IRB #14–14429), and all participants provided written informed consent.

Medication cost concerns:

Participants were classified as having medication cost concerns if they reported any of the following at any time due to the costs of lupus drugs: 1) having difficulties affording medications, 2) skipping doses or taking less medications than prescribed, 3) delaying refills, 4) requesting lower cost alternatives to prescribed drugs, 5) purchasing medications outside the US, or 6) applying for patient assistance programs. These questions were modeled after a subset of questions from the National Health Interview Survey which asked about cost-related nonadherence and associated affordability concerns(15). Our definition of medication cost concerns includes cost-related nonadherence (items 2 and 3 above), but also encompasses a broader range of patient-reported affordability concerns which could have a variety of impacts on care trajectories and health outcomes.

Patient-reported outcomes (PROs):

Systemic Lupus Erythematosus Activity Questionnaire (SLAQ): A 24-item questionnaire of self-reported symptoms indicative of active SLE, with four response

categories (no problem, mild moderate, severe). SLAQ has a recall period of 3 months and is scored from 0 to 44(16).

Patient Health Questionnaire Depression Scale (PHQ-8): An 8-item questionnaire of depressive symptoms in which each item is scored from 0 (not at all) to 3 (nearly every day), with a total score ranging from 0 to 24(17).

Patient-Reported Outcomes Measurement Information System (PROMIS): PROMIS is group of measures developed by the National Institutes of Health to standardize the assessment of health-related quality of life(18). In this study, we focused on representative domains from the categories of physical health (physical function, pain interference, fatigue, and sleep disturbance) and social health (ability to participate in social roles and activities)(18). As described elsewhere, PROMIS scales were converted to T scores, with a mean (SD) for the general population of 50 (10). For all PROMIS scales, higher scores reflect more of the construct being measured. Thus, for instance, a higher physical function score would be considered to be a better score, while a higher fatigue score would be considered to be worse(19).

Brief Index of Lupus Damage (BILD): A 26-item measure of patient-reported organ damage in SLE that is a proxy for the physician-assessed Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SDI). The BILD items are scored if present, with additional scores for recurrent events; the total score can be 0 to 31(20). BILD score was not measured in Year 3 and was only available in CLUES Years 1 and 4. Of note, the Year 1 BILD score was utilized as the baseline BILD score in this study, under the assumption that relatively little change in organ damage occurred between Year 1 and Year 3.

Figure 1 depicts a timeline of the CLUES cohort study and the relationship between the study visits and the predictor and outcome variables measured.

Covariates:

Additional covariates of interest included age, sex, race and ethnicity (non-Hispanic White, Hispanic, non-Hispanic Black, non-Hispanic Asian), income (<125% federal poverty level according to self-reported annual income and household size vs. ≥ 125% federal poverty level), self-reported principal insurance (private, employer-based insurance, or other; Medicare; Medi-Cal or San Francisco County health plan), total number of self-reported current immunomodulatory medications (including glucocorticoids, hydroxychloroquine, azathioprine, mycophenolate, methotrexate, calcineurin inhibitors, leflunomide, tumor necrosis factor-α inhibitors, rituximab, abatacept, and belimumab), current immunomodulatory regimen (none; glucocorticoids and/or hydroxychloroquine alone; including methotrexate, azathioprine, mycophenolate, and/or calcineurin inhibitors; including biologics), and self-reported nonadherence (number of times any SLE medications were missed in the past 7 days).

Statistical analysis:

Characteristics of participants with and without medication cost concerns were compared with the chi-squared test for categorical variables, the t-test for age, and the Wilcoxon rank-sum test for number of immunomodulatory medications and self-reported nonadherence. First, we examined the cross-sectional relationship between medication cost concerns and PROs at baseline. We constructed linear regression models in which the outcome was the PRO score, and the primary independent variable was the presence (vs. absence) of any medication cost concerns. For the BILD outcome, the BILD at Year 1 was chosen as the dependent variable. These models also adjusted for factors that have previously been shown to be associated with cost-related nonadherence and health outcomes, including age, sex, race and ethnicity, income, and insurance(7,9,21,22), as well as BILD score (for all outcomes except for BILD) to reflect lupus disease severity and the number of immunomodulatory drugs. Marginal means were estimated for the groups with and without medication cost concerns.

Second, we undertook a longitudinal analysis that assessed the relationship between medication cost concerns at baseline and subsequent changes in PROs in the following two years (i.e., in the fourth and fifth years of CLUES, see Figure 1) using linear mixed effects models with subject-specific random intercepts and accounting for repeated measures. In these models, the outcome was again the individual PRO score, and we adjusted for the covariates listed above, including visit year, interactions between visit year and medication cost concerns, and interactions between visit year and time-invariant variables. Mean PRO scores for participants with and without medication cost concerns were estimated and plotted, adjusting for the above covariates and relevant interactions. For the BILD outcome, only two time points were available for analysis, so a change score was calculated (Year 1 score subtracted from Year 4 score), and a linear regression model adjusting for above covariates analyzed the relationship between medication cost concerns and the change score. Statistical analyses were performed using STATA, version 17.0 (StataCorp, College Station, TX).

RESULTS

CLUES cohort characteristics at baseline

Of the 334 participants who completed a baseline evaluation, medication cost data was available for 332. The mean age was 49 years, of whom 91% were female. Regarding self-reported race and ethnicity, 31% of participants were White, 34% were Asian, 11% were Black, and 22% were Hispanic. Medication cost concerns were reported by 91 (27%): 38 (11%) reported difficulties affording lupus medications, 25 (8%) reported skipping doses/taking less lupus medications, 29 (9%) reported delayed refills, 29 (9%) reported requesting lower cost alternatives to prescribed drugs, 6 (2%) reported purchasing drugs outside the US, and 31 (9%) reported applying for patient assistance programs. Of those reporting medication cost concerns, 39 (43%) reported >1 medication cost concern.

As shown in Table 1, age, sex, race and ethnicity, income, number of immunomodulatory drugs, and self-reported nonadherence were not significantly different between participants

with and without medication cost concerns. The distribution of self-reported principal insurance was significantly different between participants with and without medication cost concerns, with the former more likely to report Medicare insurance (P<0.001). In addition, participants with medication cost concerns more frequently reported a current biologic-containing immunomodulatory regimen (P<0.001) as compared to those without cost concerns.

Medication cost concerns and PROs: Cross-sectional regression analysis

After adjustment for covariates, participants with medication cost concerns had higher scores on the SLAQ (beta coefficient 5.9, 95% CI 4.3 to 7.6, P<0.001), PHQ-8 (beta coefficient 2.7, 95% CI 1.4 to 4.0, P<0.001), PROMIS pain interference (beta coefficient 4.4, 95% CI 2.1 to 6.8, P<0.001), PROMIS fatigue (beta coefficient 7.1, 95% CI 4.4 to 9.7, P<0.001), and PROMIS sleep disturbance scores (beta coefficient 2.3, 95% CI 0.04 to 4.5, P=0.046) as compared to those without medication cost concerns. PROMIS physical function (beta coefficient −4.6, 95% CI −6.7 to −2.4, P<0.001) and PROMIS ability to participate in social roles and activities scores (beta coefficient −4.7, 95% CI −7.4 to −1.9, P=0.001) were significantly lower in those with medication cost concerns as compared to those without those concerns. Medication cost concerns were not significantly associated with BILD score (beta coefficient 0.3, 95% CI −0.23 to 0.83, P=0.264). Table 2 shows the marginal means for these patient-reported outcomes in participants with and without medication cost concerns after adjustment for confounders.

Longitudinal association of medication cost concerns and PROs

Including the baseline CLUES visit, participants had a median of 3 visits (range 1–3). PRO data was complete for at least two visits in >80% of participants for all outcomes except the PROMIS ability to participate in social roles and activities outcome, where PRO data was available for at least two visits in 61% participants. In mixed effects models adjusting for covariates, visit year, and interactions between time-invariant variables and visit year, medication cost concerns were not associated with significant between-visit changes in PRO scores. These relationships were further explored graphically by plotting the mean PRO scores over time in participants with and without medication cost concerns, adjusted for the covariates above. These graphs (Figure 2) show that the disparities in PROs between those with and without medication cost concerns remained stable over the course of follow up. For the BILD change score, which analyzed two time points, medication cost concerns were not associated with significant changes in BILD over time after adjusting for covariates (0.14, 95% CI −0.12 to 0.41, P=0.293).

DISCUSSION

In this study, more than one-quarter of participants in CLUES reported at least one medication cost concern, which encompassed financial concerns related to lupus drugs and cost-related medication nonadherence. We found marked differences in PROs among those with medication cost concerns in our cross-sectional analysis at baseline, with worse SLE disease activity, depressive symptoms, and health-related quality of life among those with drug-related affordability concerns. In this longitudinal cohort, the differences in outcomes

we observed at baseline persisted over the course of follow-up. This highlights the urgent need to better understand and ameliorate these concerns among our patients, who often depend on long-term medication use for proper control of their disease.

Our research confirms the high burden of medication cost concerns among individuals with rheumatic diseases and SLE. Prior studies have investigated medication cost concerns from the perspective of cost-related nonadherence, which has been reported in approximately 20% of individuals with SLE(4) and RA(23). Indeed, persons with SLE often identify medication affordability concerns as a major reason for missing medication doses or discontinuing altogether, along with other reasons such as side effects(24,25). Qualitative research points to copays, high deductibles, and insurance lapses as prominent cost-related barriers(25). In a study on individuals with lupus nephritis, medication costs also emerged as a leading barrier to medication-related decision making(26). Medication costs can thus have a variety of impacts on care trajectories; accordingly, in this study, we defined medication costs concerns broadly to encompass a range of affordability concerns, including cost-related nonadherence, as well as reported difficulties affording medications and behaviors such as requesting lower cost alternatives from clinicians.

A striking finding in our study was that individuals with SLE and medication cost concerns had worse PRO scores across a variety of domains, such as disease activity, but also including depression, and diverse aspects of health-related quality of life, even after adjustment for demographic factors, income, insurance, SLE organ damage, and number of immunomodulatory drugs. The disparity in PRO scores was particularly notable for the SLAQ outcome, with the mean patient-reported disease activity score nearly twice as high in those with medication cost concerns as compared to those without those concerns. Participants with medication cost concerns also had worse depression scores and health-related quality of life, as indicated by the PHQ-8 and PROMIS measures. For the PROMIS measures, the differences were especially pronounced for the fatigue, pain interference, physical function, and social roles/activities domains, exceeding estimates of minimally important differences(27). Interestingly, there were no significant differences for the BILD outcome at baseline; the effects of affordability concerns and other socioeconomic factors such as poverty, on damage accrual may take longer to manifest(28). These data suggest that clinicians should be alerted to the possibility of affordability concerns when treating patients with either high disease activity or poor health-related quality of life.

A compelling mechanistic link between the unaffordability of drugs used in SLE and worse health outcomes is nonadherence, which is associated with increased risk of flare and acute care utilization(29,30) and forms the basis of our definition of medication cost concerns. Another potential mediating factor is psychosocial stress. In our longitudinal analysis, we attempted to further examine the association between medication cost concerns and PROs, although we did not observe worsening in PROs in those with medication cost concerns as compared to those without these concerns over follow-up as hypothesized. This may be due to a variety of reasons. For instance, the observation time of two years may have been too limited; prior studies have shown that other sociodemographic variables have an impact on outcomes such as organ damage in SLE, but when observed over longer time intervals(28). Medication cost concerns are likely dynamic over time, although in our study were only

measured at baseline. We did observe, though, that the disparities in PROs between those with and without medication cost concerns at baseline persisted over the course of follow-up (Figure 2), suggesting that this subgroup of individuals with affordability concerns continues to have unmet needs over time and may benefit from interventions, either directed at reducing out-of-pocket costs, medication nonadherence, or suboptimal disease outcomes.

A surprising finding was that many sociodemographic factors, such as age, sex, race and ethnicity, and income were not significantly associated with medication cost concerns (Table 1), as has been shown in other studies of chronically ill or older adults(9,21,22). Self-reported nonadherence did not differ between groups either, although our study was limited in asking participants for the number of missed doses in the last 7 days. This suggests that, in the absence of clear risk factors, potentially any patient with SLE could be susceptible to drug affordability concerns, regardless of their sociodemographic background or recent adherence level. Our results did show a higher proportion of Medicare beneficiaries and current biologic users among those with medication cost concerns. These findings merit further investigation, especially from the context of cost-sharing and drug-related out-of-pockets costs, which have been shown to be important determinants of affordability concerns and subsequent nonadherence in the general population(21,31) and in patients with rheumatoid arthritis receiving biologic therapy(32).

Although we are still beginning to understand the scope of medication cost concerns in SLE, there are several potential tools that the rheumatology community can use to begin to address this problem. Clinicians can engage patients in discussing their medication costs on a more routine basis, since affordability concerns often impacts medication decision making and adherence. Research has documented a willingness on the part of both patients and clinicians to discuss medication costs, although only a fraction ever do in clinical encounters(33). In a study of patients with RA, clinicians discussed drug costs in only one-third of encounters, despite medication changes being made in more than half of visits(34). Uncovering medication cost concerns may point to solutions such as finding lower cost alternatives or opportunities for changes in policy that enable dependable healthcare coverage and reduce out-of-pocket drug costs. For instance, implementation of the Medicare Part D prescription drug benefit in 2006 was associated with a decrease in cost-related nonadherence among beneficiaries(35). In parts of the world with universal prescription drug coverage, medication costs are not a major cause of medication nonadherence in patients with SLE(36). Medication coverage and out-of-pocket costs are particularly relevant in the context of biologics and newly approved agents entering the lupus treatment armamentarium, although even relatively low drug cost burdens of common immunosuppressants can exacerbate nonadherence in individuals with SLE(37). Addressing medication cost concerns effectively will thus entail interventions in the clinic as well as in the domain of policy to improve both access and outcomes among patients with SLE.

The are several important strengths to highlight in this study. It is one of the largest investigations of medication cost concerns among individuals with SLE and benefits from the CLUES cohort’s population-based study design and diverse representation of Asian and Hispanic participants. We purposefully employed a broad definition of medication cost concerns to capture a wide variety of financial concerns; we also studied a diverse array

of PROs and performed longitudinal analyses to understand the relationship between cost concerns and outcomes.

This study also has several limitations. The questions about medication cost concerns may have lacked precision because no recall time was defined; medication cost concerns were not necessarily current or even recent. In addition, the questions referred to SLE medications in general and not to specific medications or classes of medications. Disease activity and organ damage in this study were assessed by means of patient report and were not verified by physician-assessed measures, which may be less susceptible to non-inflammatory symptoms or bias(38). Other factors that likely impact medication affordability concerns, such as out-of-pocket expenses and medical debt, were not measured in CLUES but warrant further investigation. We considered the possibility of reverse causality in our cross-sectional model and for this reason undertook a longitudinal model; additional studies investigating medication cost concerns from a longitudinal perspective with longer follow-up time should be conducted. Future study should focus on the long-term effect of advances in policy, such as upcoming capping out-of-pocket expenses for Medicare Part D beneficiaries(39).

In summary, medication cost concerns were associated with worse patient-reported outcomes across diverse domains in this multiethnic cohort of people with SLE, even after adjustment for important sociodemographic and clinical variables. These differential outcomes persisted over time in this longitudinal cohort, highlighting the unmet need to address these concerns among people with SLE in general.

Financial support:

This work was funded by a grant from the Centers for Disease Control and Prevention (5U01DP006486). Additional support from NIH/NIAMS P30AR070155, K24AR074534, and the Russell/Engleman Medical Research Center for Arthritis.

REFERENCES

1. Bruce IN, O'Keeffe AG, Farewell V, Hanly JG, Manzi S, Su L, et al. Factors associated with damage accrual in patients with systemic lupus erythematosus: results from the Systemic Lupus International Collaborating Clinics (SLICC) Inception Cohort. Ann Rheum Dis 2015;74:1706–13. [PubMed: 24834926]
2. Zen M, Fuzzi E, Loredo Martinez M, Depascale R, Fredi M, Gatto M, et al. Immunosuppressive therapy withdrawal after remission achievement in patients with lupus nephritis. Rheumatology (Oxford) 2022;61:688–95. [PubMed: 33909900]
3. Jourde-Chiche N, Costedoat-Chalumeau N, Baumstarck K, Loundou A, Bouillet L, Burtey S, et al. Weaning of maintenance immunosuppressive therapy in lupus nephritis (WIN-Lupus): results of a multicentre randomised controlled trial. Ann Rheum Dis 2022;81:1420–7. [PubMed: 35725295]
4. Minhas D, Marder W, Harlow S, Hassett AL, Zick SM, Gordon C, et al. Access and Cost-Related Nonadherence to Prescription Medications Among Lupus Patients and Controls: The Michigan Lupus Epidemiology and Surveillance Program. Arthritis Care Res (Hoboken) 2021;73:1561–7. [PubMed: 32741110]
5. Dall'Era M, Cisternas MG, Snipes K, Herrinton LJ, Gordon C, Helmick CG. The incidence and prevalence of systemic lupus erythematosus in San Francisco County, California: The California Lupus Surveillance Project. Arthritis & Rheumatology 2017;69:1996–2005. [PubMed: 28891237]
6. Izmirly PM, Parton H, Wang L, McCune WJ, Lim SS, Drenkard C, et al. Prevalence of systemic lupus erythematosus in the United States: Estimates from a meta-analysis of the Centers for Disease Control and Prevention National Lupus Registries. Arthritis Rheumatol 2021;art.41632.

7. Heisler M, Choi H, Rosen AB, Vijan S, Kabeto M, Langa KM, et al. Hospitalizations and deaths among adults with cardiovascular disease who underuse medications because of cost: a longitudinal analysis. Med Care 2010;48:87–94. [PubMed: 20068489]
8. Naci H, Soumerai SB, Ross-Degnan D, Zhang F, Briesacher BA, Gurwitz JH, et al. Persistent medication affordability problems among disabled Medicare beneficiaries after Part D, 2006–2011. Med Care 2014;52:951–6. [PubMed: 25122530]
9. Kang H, Lobo JM, Kim S, Sohn M-W. Cost-related medication non-adherence among U.S. adults with diabetes. Diabetes Res Clin Pract 2018;143:24–33. [PubMed: 29944967]
10. Van Alsten SC, Harris JK. Cost-Related Nonadherence and Mortality in Patients With Chronic Disease: A Multiyear Investigation, National Health Interview Survey, 2000–2014. Prev Chronic Dis 2020;17:E151. [PubMed: 33274701]
11. Taha MB, Valero-Elizondo J, Yahya T, Caraballo C, Khera R, Patel KV, et al. Cost-Related Medication Nonadherence in Adults With Diabetes in the United States: The National Health Interview Survey 2013–2018. Diabetes Care 2022;45:594–603. [PubMed: 35015860]
12. Aguirre A, Izadi Z, Trupin L, Barbour KE, Greenlund KJ, Katz P, et al. Race, Ethnicity, and Disparities in the Risk of End-Organ Lupus Manifestations Following a Systemic Lupus Erythematosus Diagnosis in a Multiethnic Cohort. Arthritis Care & Research 2023;75:34–43.
13. Tan EM, Cohen AS, Fries JF, Masi AT, McShane DJ, Rothfield NF, et al. The 1982 revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 1982;25:1271–7. [PubMed: 7138600]
14. Hochberg MC. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 1997;40:1725.
15. Patel MR, Piette JD, Resnicow K, Kowalski-Dobson T, Heisler M. Social Determinants of Health, Cost-related Nonadherence, and Cost-reducing Behaviors Among Adults With Diabetes: Findings From the National Health Interview Survey. Med Care 2016;54:796–803. [PubMed: 27219636]
16. Karlson EW, Daltroy LH, Rivest C, Ramsey-Goldman R, Wright EA, Partridge AJ, et al. Validation of a Systemic Lupus Activity Questionnaire (SLAQ) for population studies. Lupus 2003;12:280–6. [PubMed: 12729051]
17. Kroenke K, Strine TW, Spitzer RL, Williams JBW, Berry JT, Mokdad AH. The PHQ-8 as a measure of current depression in the general population. J Affect Disord 2009;114:163–73. [PubMed: 18752852]
18. Witter JP. The Promise of Patient-Reported Outcomes Measurement Information System-Turning Theory into Reality: A Uniform Approach to Patient-Reported Outcomes Across Rheumatic Diseases. Rheum Dis Clin North Am 2016;42:377–94. [PubMed: 27133496]
19. Katz P, Yazdany J, Trupin L, Rush S, Helmick CG, Murphy LB, et al. Psychometric Evaluation of the National Institutes of Health Patient-Reported Outcomes Measurement Information System in a Multiracial, Multiethnic Systemic Lupus Erythematosus Cohort. Arthritis Care Res (Hoboken) 2019;71:1630–9. [PubMed: 30354017]
20. Yazdany J, Trupin L, Gansky SA, Dall'era M, Yelin EH, Criswell LA, et al. The Brief Index of Lupus Damage (BILD): A patient-reported measure of damage in SLE. Arthritis Care Res (Hoboken) 2011;63:1170–7. [PubMed: 21584946]
21. Briesacher BA, Gurwitz JH, Soumerai SB. Patients at-risk for cost-related medication nonadherence: a review of the literature. J Gen Intern Med 2007;22:864–71. [PubMed: 17410403]
22. Khera R, Valero-Elizondo J, Das SR, Virani SS, Kash BA, de Lemos JA, et al. Cost-Related Medication Nonadherence in Adults With Atherosclerotic Cardiovascular Disease in the United States, 2013 to 2017. Circulation 2019;140:2067–75. [PubMed: 31760784]
23. Harrold LR, Briesacher BA, Peterson D, Beard A, Madden J, Zhang F, et al. Cost-related medication nonadherence in older patients with rheumatoid arthritis. J Rheumatol 2013;40:137–43. [PubMed: 23322458]
24. Garcia Popa-Lisseanu MG, Greisinger A, Richardson M, O'Malley KJ, Janssen NM, Marcus DM, et al. Determinants of treatment adherence in ethnically diverse, economically disadvantaged patients with rheumatic disease. J Rheumatol 2005;32:913–9. [PubMed: 15868630]
25. Sun K, Corneli AL, Dombeck C, Swezey T, Rogers JL, Criscione-Schreiber LG, et al. Barriers to Taking Medications for Systemic Lupus Erythematosus: A Qualitative Study of Racial Minority

Patients, Lupus Providers, and Clinic Staff. Arthritis Care Res (Hoboken) 2022;74:1459–67. [PubMed: 33662174]

26. Singh JA, Qu H, Yazdany J, Chatham W, Dall'era M, Shewchuk RM. Barriers to Medication Decision Making in Women with Lupus Nephritis: A Formative Study using Nominal Group Technique. J Rheumatol 2015;42:1616–23. [PubMed: 26178276]
27. Katz P, Pedro S, Alemao E, Yazdany J, Dall'Era M, Trupin L, et al. Estimates of Responsiveness, Minimally Important Differences, and Patient Acceptable Symptom State in Five Patient-Reported Outcomes Measurement Information System Short Forms in Systemic Lupus Erythematosus. ACR Open Rheumatol 2020;2:53–60. [PubMed: 31943975]
28. Yelin E, Trupin L, Yazdany J. A prospective study of the impact of current poverty, history of poverty, and exiting poverty on accumulation of disease damage in systemic lupus erythematosus. Arthritis Rheumatol 2017;69:1612–22. [PubMed: 28480630]
29. Rojas-Serrano J, Cardiel MH. Lupus patients in an emergency unit. Causes of consultation, hospitalization and outcome. A cohort study. Lupus 2000;9:601–6. [PubMed: 11035435]
30. Julian LJ, Yelin E, Yazdany J, Panopalis P, Trupin L, Criswell LA, et al. Depression, medication adherence, and service utilization in systemic lupus erythematosus. Arthritis Rheum 2009;61:240–6. [PubMed: 19177526]
31. Eaddy MT, Cook CL, O'Day K, Burch SP, Cantrell CR. How patient cost-sharing trends affect adherence and outcomes: a literature review. P T 2012;37:45–55. [PubMed: 22346336]
32. Heidari P, Cross W, Crawford K. Do out-of-pocket costs affect medication adherence in adults with rheumatoid arthritis? A systematic review. Semin Arthritis Rheum 2018;48:12–21. [PubMed: 29496225]
33. Alexander GC, Casalino LP, Meltzer DO. Patient-physician communication about out-of-pocket costs. JAMA 2003;290:953–8. [PubMed: 12928475]
34. Beard AJ, Sleath B, Blalock SJ, Roth M, Weinberger M, Tudor G, et al. Predictors of rheumatoid arthritis patient-physician communication about medication costs during visits to rheumatologists. Arthritis Care Res (Hoboken) 2010;62:632–9. [PubMed: 20191466]
35. Madden JM, Graves AJ, Zhang F, Adams AS, Briesacher BA, Ross-Degnan D, et al. Cost-related medication nonadherence and spending on basic needs following implementation of Medicare Part D. JAMA 2008;299:1922–8. [PubMed: 18430911]
36. Chambers SA, Raine R, Rahman A, Isenberg D. Why do patients with systemic lupus erythematosus take or fail to take their prescribed medications? A qualitative study in a UK cohort. Rheumatology (Oxford) 2009;48:266–71. [PubMed: 19151034]
37. Lomanto Silva R, Swabe GM, Magnani JM. Medication Co-pay Modifies Treatment Adherence in Patients with Systemic Lupus Erythematosus. [abstract] Arthritis Rheumatol 2022; 74 (suppl 9):2215–6.
38. Askanase AD, Castrejón I, Pincus T. Quantitative data for care of patients with systemic lupus erythematosus in usual clinical settings: a patient Multidimensional Health Assessment Questionnaire and physician estimate of noninflammatory symptoms. J Rheumatol 2011;38:1309–16. [PubMed: 21459938]
39. Hwang TJ, Kesselheim AS, Rome BN. New Reforms to Prescription Drug Pricing in the US: Opportunities and Challenges. JAMA 2022;328:1041–2. [PubMed: 35984652]

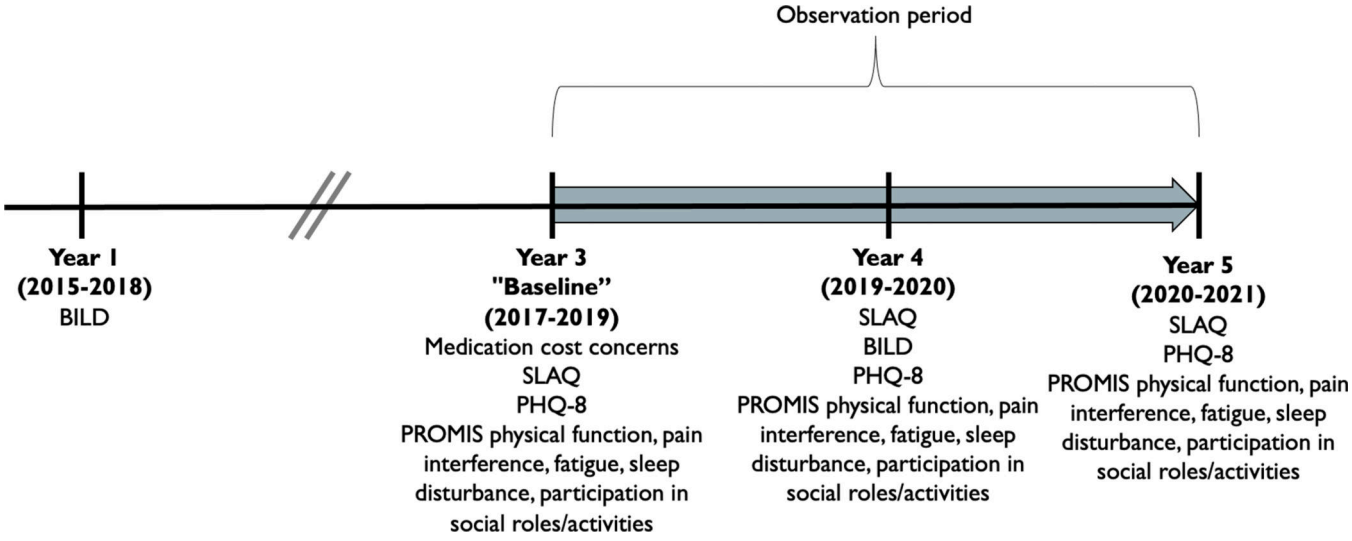

Figure 1: Timeline of the CLUES study, showing relevant study visits and predictor and outcome variables:

This figure depicts a schematic of the timeline of CLUES, showing the observation period for this study, which began in Year 3 of the cohort when participants were asked about medication cost concerns. Shown here are also the relationship between the study visits and the predictor and outcome variables collected. BILD, Brief Index of Lupus Damage; PHQ-8, Personal Health Questionnaire Depression Scale 8; PROMIS, Patient-Reported Outcomes Measurement Information System; SLAQ, Systemic Lupus Erythematosus Activity Questionnaire.

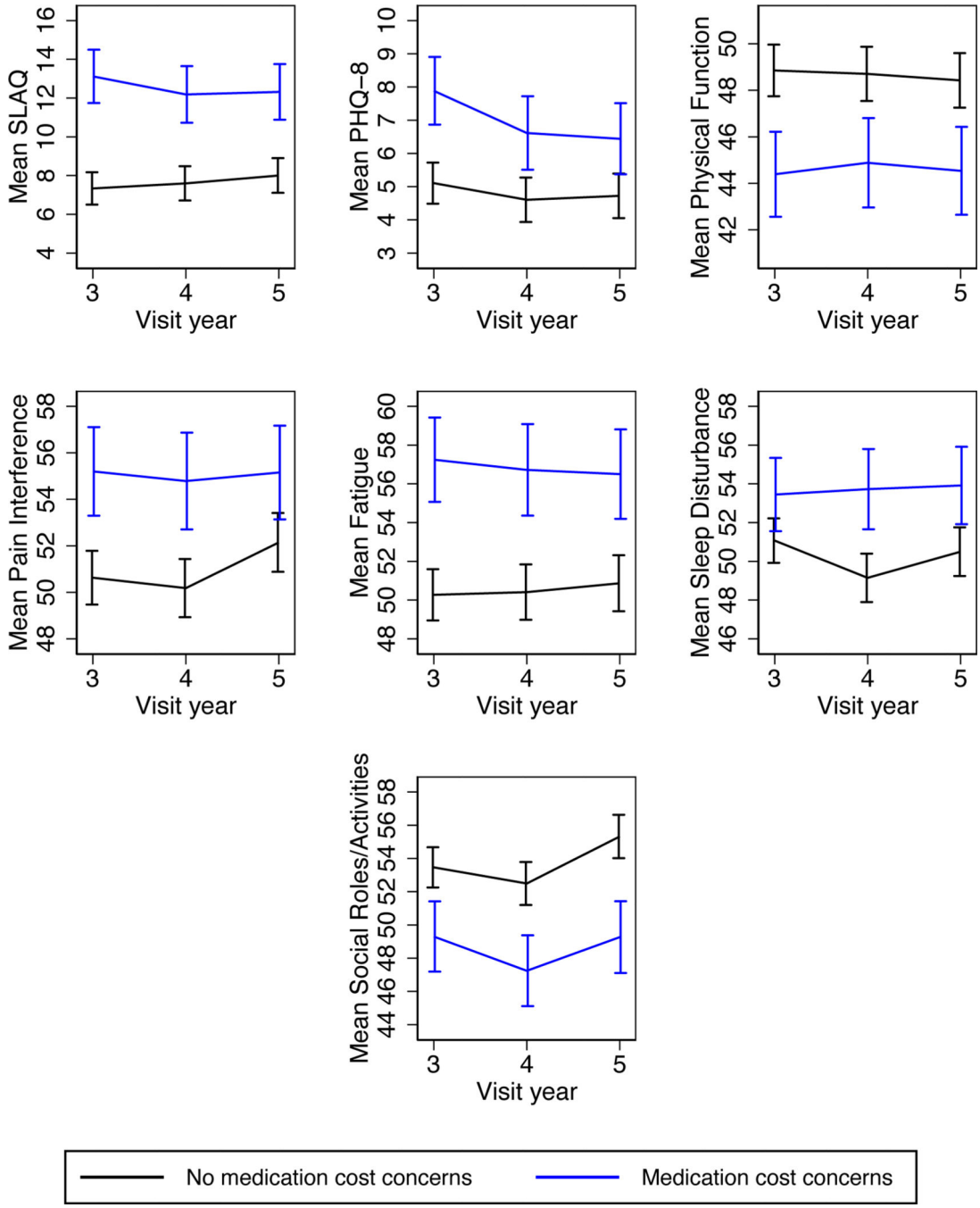

Figure 2: The association between medication cost concerns and change in PROs over time: Depicted here is the relationship between medication cost concerns at baseline and mean PRO scores (95% CI) over the course of follow-up. Medication cost concerns did not predict clinically significant worsening in PROs over the two-year follow-up in CLUES. PROMIS scales are converted to T scores with a mean±SD population of 50±10. Higher scores reflect more of the construct being measured (e.g., a higher physical function score would be considered to be a better score, while a higher fatigue score would be considered to be worse). Mean PRO scores were adjusted for age, sex, race and ethnicity, income, insurance,

number of immunomodulatory medications, BILD score, visit year, interactions between visit year and medication cost concerns, and significant interactions between visit year and other time-invariant variables in mixed effects models for each PRO score. BILD, Brief Index of Lupus Damage; PHQ-8, Personal Health Questionnaire Depression Scale 8; SLAQ, Systemic Lupus Erythematosus Activity Questionnaire.

Table 1:

Sociodemographic and clinical factors in CLUES participants with and without medication cost concerns

Characteristic*	No medication cost concerns n=241	Medication cost concerns n=91	P-value
Age, mean (SD)	49.0 (14.4)	49.8 (13.7)	0.645
Female sex	221 (92)	82 (90)	0.647
Race and ethnicity			0.368
Non-Hispanic White	69 (29)	34 (39)	
Hispanic	54 (23)	19 (22)	
Non-Hispanic Black	27 (11)	10 (11)	
Non-Hispanic Asian	87 (37)	25 (28)	
Low income†	45 (21)	16 (19)	0.730
Principal insurance			<0.001
Private or other	130 (54)	45 (49)	
Medicare	52 (22)	36 (40)	
Medi-Cal or SF Health Plan	59 (24)	10 (11)	
Number of immunomodulatory drugs, mean (SD)††	1.6 (1.1)	1.9 (1.1)	0.076
Current immunomodulatory drug(s)			<0.001
None	40 (17)	9 (10)	
Glucocorticoids and/or HCQ alone	90 (37)	30 (33)	
MTX, MMF, AZA, and/or CNI§	102 (42)	36 (40)	
Biologic§§	9 (4)	16 (18)	
Self-reported nonadherence, mean (SD)†	0.4 (0.9)	0.5 (0.8)	0.096

AZA, azathioprine; CNI, calcineurin inhibitor; HCQ, hydroxychloroquine; MTX, methotrexate; MMF, mycophenolate.

*Values are n (%) unless otherwise specified

†Defined as <125% of the federal poverty level according to self-reported annual income and household size

††Including glucocorticoids, hydroxychloroquine, azathioprine, mycophenolate, methotrexate, calcineurin inhibitors, leflunomide, rituximab, tumor necrosis factor-α inhibitors, abatacept, and/or belimumab

§CNI includes cyclosporine or tacrolimus

§§Biologic includes rituximab, tumor necrosis factor-α inhibitors, abatacept, or belimumab

†Number of times any SLE medications were missed in the past 7 days

Table 2:

Adjusted baseline PROs for participants with and without medication cost concerns

Characteristic*	No medication cost concerns	Medication cost concerns	P-value
SLAQ score	7.3 (6.5–8.2)	13.2 (11.7–14.6)	<0.001
BILD score†	1.9 (1.6–2.2)	2.2 (1.7–2.6)	0.264
PHQ-8 score	5.2 (4.5–5.8)	7.9 (6.8–9.0)	<0.001
PROMIS Physical function††	48.8 (47.7–49.9)	44.2 (42.4–46.0)	<0.001
PROMIS Pain interference	50.7 (49.6–51.9)	55.2 (53.2–57.2)	<0.001
PROMIS Fatigue	50.3 (48.9–51.6)	57.3 (55.1–59.5)	<0.001
PROMIS Sleep disturbance	51.1 (50.0–52.3)	53.4 (51.5–55.3)	0.046
PROMIS Ability to participate in social roles and activities	53.9 (52.6–55.2)	49.2 (46.9–51.6)	0.001

BILD, Brief Index of Lupus Damage; PHQ-8, Personal Health Questionnaire Depression Scale 8; PROMIS, Patient-Reported Outcomes Measurement Information System; SLAQ, Systemic Lupus Erythematosus Activity Questionnaire.

*Marginal means (95% CI) estimated using multivariable linear regression adjusting for age, sex, race and ethnicity, income, insurance, number of immunomodulatory drugs, and Year 1 BILD score (for all outcomes except for BILD).

†Year 1 BILD score.

††PROMIS scales were converted to T scores with a mean ±SD population of 50±10. Higher scores reflect more of the construct being measured (e.g., a higher physical function score would be considered to be a better score, while a higher fatigue score would be considered to be worse).