American College of Rheumatology
Empowering Rheumatology Professionals

Arthritis Care & Research
Vol. 75, No. 3, March 2023, pp 550–558
DOI 10.1002/acr.24806

Pilot Intervention to Improve Medication Adherence Among Patients With Systemic Lupus Erythematosus Using Pharmacy Refill Data

Kai Sun, Amanda M. Eudy, Jennifer L. Rogers, Lisa G. Criscione-Schreiber, Rebecca E. Sadun, Jayanth Doss, Mithu Maheswaranathan, Ann Cameron Barr, Lena Eder, Amy L. Corneli, Hayden B. Bosworth, and Megan E. B. Clowse

Objective. Despite high rates of medication nonadherence among patients with systemic lupus erythematosus (SLE), effective interventions to improve adherence in SLE are limited. We aimed to assess the feasibility of a pilot intervention and explore its effect on adherence.

Methods. The intervention used pharmacy refill data to monitor nonadherence and prompt discussions surrounding SLE medications during clinic encounters. Over 12 weeks, the intervention was delivered through routine clinic visits by providers to patients with SLE who take SLE-specific medications. We measured acceptability, appropriateness, and feasibility using provider surveys. We also measured acceptability by patient surveys and feasibility by medical record documentation. We explored change in adherence by comparing percent of patients with medication possession ratio (MPR) ≥80% 3 months before and after the intervention visit using the McNemar's test.

Results. Six rheumatologists participated; 130 patients were included in the analysis (median age 43, 95% female, and 59% racial and ethnic minorities). Implementation of the intervention was documented in 89% of clinic notes. Provider surveys showed high scores for feasibility (4.7/5), acceptability (4.4/5), and appropriateness (4.6/5). Among patient surveys, the most common reactions to the intervention visit were feeling determined (32%), empowered (32%), and proud (19%). Proportion of patients with MPR ≥80% increased from 48% to 58% (P = 0.03) after the intervention visit.

Conclusion. Our intervention showed feasibility, acceptability, and appropriateness and led to a statistically significant improvement in adherence. Future work should refine the intervention, assess its efficacy in a controlled setting, and adapt its use among other clinic settings.

INTRODUCTION

Systemic lupus erythematosus (SLE) is a multisystem chronic autoimmune disease that commonly requires long-term use of immune-altering medications to prevent disease progression and damage. However, medication nonadherence in patients with SLE is as high as 75% (1–3). Reasons for such high rates of nonadherence are complex and multifactorial, including factors related to the patient (e.g., medication beliefs and knowledge), the medications (e.g., side effects and pill burden), the clinic (e.g., provider communication), and the health care system (e.g., insurance coverage) (4). Although poor medication adherence is associated with increased hospitalizations, renal failure, and mortality (5–7), little is known about effective means of improving adherence in SLE. Our literature search and 2 recent systematic reviews of patient-directed adherence interventions in rheumatology found just 5 studies targeting adult or adolescent patients with SLE in the US (8,9). Past studies used text message reminders (10), patient navigators (11), electronic pillboxes with automatic reminders and medication education (12), an online

ClinicalTrials.gov identifier: NCT03738826.

This content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

Research reported in this publication was supported by the Duke Center for REsearch to AdvanCe Healthcare Equity (REACH Equity) Career Development Award (NIH grant 5-U-54-MD-012530-02) and NIH/National Center for Advancing Translational Sciences (grant 1-KL-2-TR-002554).

Kai Sun, MD, MS, Amanda M. Eudy, PhD, Jennifer L. Rogers, MD, Lisa G. Criscione-Schreiber, MD, MEd, Rebecca E. Sadun, MD, PhD, Jayanth Doss, MD, MPH, Mithu Maheswaranathan, MD, Ann Cameron Barr, MD, Lena Eder, MD, Amy L. Corneli, PhD, Hayden B. Bosworth, PhD, Megan E. B. Clowse, MD, MPH: Duke University School of Medicine, Durham, North Carolina.

Author disclosures are available at https://onlinelibrary.wiley.com/action/downloadSupplement?doi=10.1002%2Facr.24806&file=acr24806-sup-0001-Disclosureform.pdf.

Address correspondence via email to Kai Sun, MD, MS, at kai.sun@duke.edu.

Submitted for publication June 25, 2021; accepted in revised form October 12, 2021.

SIGNIFICANCE & INNOVATIONS

- We demonstrated the feasibility, acceptability, and appropriateness of an adherence intervention for patients with systemic lupus erythematosus over 12 weeks at an academic lupus clinic.
- After the intervention, patients' medication possession ratios of lupus-specific medications over 3 months improved appreciably.
- This intervention is simple and versatile and requires no additional funding or staffing. By routinely using a readily available and objective proxy of adherence based on pharmacy refill data, the intervention allows more reliable identification of nonadherence as well as potential implementation across many health systems.

educational program with social media discussion (13), and counseling based on hydroxychloroquine (HCQ) blood levels (14). Some of these interventions were resource intensive, and only the latter 2 studies led to an improvement in adherence. We developed an intervention as part of our ongoing research on medication adherence among patients with SLE. The intervention was pilot tested to assess its feasibility, acceptability, and appropriateness, as well as to explore its effect on adherence to SLE medications.

PATIENTS AND METHODS

Intervention development and procedure. The lead and senior authors (KS and MEBC) developed the adherence intervention based on literature review and findings from our initial mixed-methods study (4,15–18). During this process, we found that medication nonadherence among patients with SLE is underrecognized by physicians and underreported by patients (17,18). Additionally, perceived poor provider communication was more commonly reported by Black patients with low adherence in our lupus cohort (15,16). Although understanding the fundamental causes of this finding, which may include systematic racism and implicit bias, are outside the scope of our work, our data suggest that improved patient–provider communication may be especially important among Black patients with low adherence. Our in-depth interviews with lupus patients and providers/staff suggested that interventions that recognize and overcome both logistical (e.g., busyness/forgetting, trouble getting refills) and motivational barriers (e.g., lack of understanding) would be most effective (4). Next, we reviewed these data with an advisory group of lupus clinic stakeholders including patients, clinicians, and staff, who regularly convened to discuss ongoing research in the lupus clinic. The lead and senior authors (KS, MEBC) then developed preliminary intervention steps based on input from the advisory group, and these were finalized after 2 group meetings with all 6 lupus clinic rheumatologists (KS, JLR, LGC-S, RES, JD, and MEBC).

We reached consensus among the 6 lupus clinic rheumatologists that the provider will share his/her computer screen with the patient to review real-time refill data together during the encounter. These data are easily accessible using existing links between the Epic electronic medical record (EMR) system and Surescripts, the largest health information network in the US with access to >80% of all prescription refill data (19) (Figure 1). The provider will then discuss the data with the patient as the provider sees fit. In our group meetings, we brainstormed ways to approach the discussion of refill data with patients. These included validating the patient's experience with empathic statements (e.g., "it is not easy to take this many medications consistently"), praising the patient for regular refills, asking open-ended and nonjudgmental questions about gaps in refill history (e.g., "the refill records here show that you filled two months ago but not last month, what may have happened around that time?"), and addressing barriers on an individual basis. The 6 lupus clinic rheumatologists also broadly discussed potential solutions to common barriers (e.g., social work referral for insurance issues, pillbox or reminder application for busyness and forgetting, and patient education for lack of understanding), but the most appropriate action was left to the discretion of the individual provider during the encounter. This intervention aimed to identify medication nonadherence, improve patient–provider communication, and facilitate logistics for and increase motivation among patients taking SLE medications.

To enable data collection on intervention feasibility and adherence barriers, the lead author (KS) also created an Epic EMR dropdown menu (SmartList) to be embedded in the lupus clinic note template. The SmartList allowed the provider to easily document whether they assessed pharmacy refill data and identified any adherence barriers. The SmartList included common barriers to medication adherence gleaned from in-depth interviews with patients and providers, including cost, insurance, pharmacy issues, busyness or forgetting, pill burden, side effects, concerns about side effects, lack of knowledge, lack of motivation, depression, believing medicines are not needed when feeling well, or other (4). Providers were encouraged to choose all barriers that applied to each patient from the SmartList.

Study setting and population. The Duke Lupus Registry (DLR) is a prospective cohort composed of patients with SLE followed at the Duke Lupus Clinic. Inclusion criteria for the DLR are age greater than or equal to 18 years, fluency in English, having no cognitive or other physical barriers to provide informed consent, and meeting American College of Rheumatology 1997 or SLE International Collaborating Clinics 2012 SLE classification criteria (20,21). All enrolled subjects provided signed informed consent to participate in research and are followed regularly as clinically indicated. The DLR has been approved by the institutional review board at Duke University (IRB study Pro00008875).

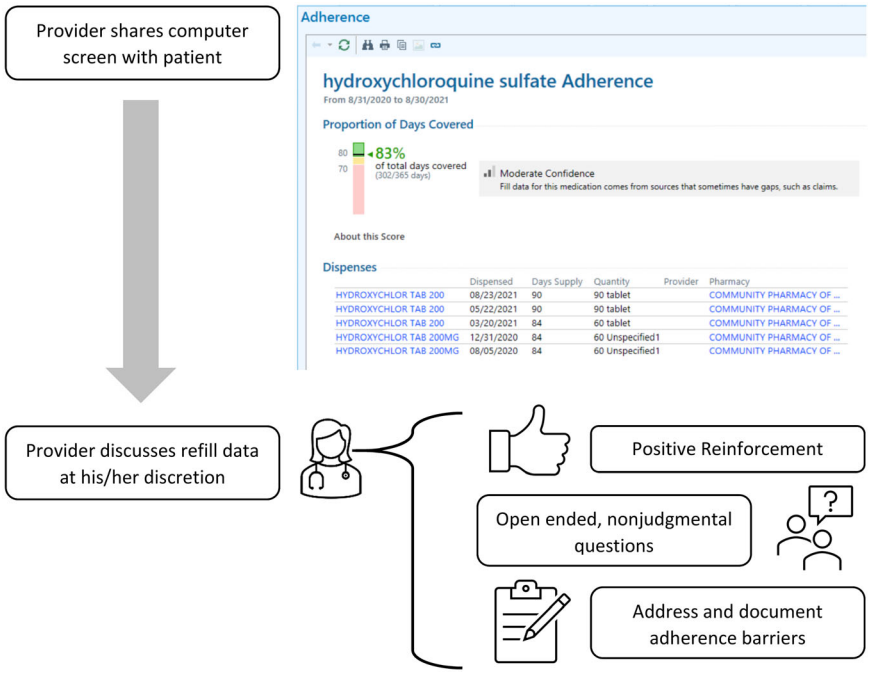

Figure 1. Intervention workflow with screenshot of pharmacy refill data.

This Duke Lupus Clinic takes place 1 half-day a week and is staffed by 6 attending rheumatologists who share the clinical care for all lupus patients. All 6 rheumatologists participated in group meetings to finalize the intervention steps, as well as in the pilot testing of the intervention.

During the pilot intervention period, providers were instructed to perform the adherence intervention on all consecutive follow-up patients taking SLE medications over 12 clinic sessions between September 2019 and January 2020. Only data from DLR participants were included for analysis because these patients already consented for their data to be used for research.

For this analysis, we included patients who were prescribed antimalarials, disease-modifying antirheumatic drugs (DMARDs), or self-administered biologics for SLE (20,21). We excluded patients who were not prescribed any SLE medication or whose only SLE medication was discontinued at the study visit. We also excluded patients who were only prescribed glucocorticoids because in our experience, pharmacy refill data on glucocorticoids tend to be difficult to interpret given the frequent use of steroid tapers. The study was approved by the institutional review board at Duke University (IRB study Pro00100861).

Data collection. *Feasibility, acceptability, appropriateness.* We administered validated questionnaires to measure feasibility, acceptability, and appropriateness to all lupus clinic providers (excluding the lead author) at the end of the intervention period (22). Feasibility, or the extent to which the intervention can be successfully carried out, was assessed using the Feasibility of Intervention Measure (22). Acceptability, or the perception that the intervention is agreeable, palatable, or satisfactory, was assessed using the Acceptability of Intervention Measure (22). Appropriateness, or the perceived fit, relevance, or compatibility of the intervention, was assessed using the Intervention Appropriateness Measure (22). Each of these measures contain 4 items on a 5-point Likert scale. Feasibility was additionally measured by EMR documentation to demonstrate that pharmacy refill data were assessable by the provider.

Acceptability among patients was measured using a written survey question. The question was developed by the lead author (KS) with input from the advisory group of lupus clinic stakeholders, lending it face validity. To encourage honest feedback and minimize patient burden, the question was voluntarily and anonymously self-administered on paper at the checkout station 1 clinic session per month during the intervention piloting period. All patients, regardless of whether they were included in the DLR, were provided the questionnaire. Patients were asked "if your doctor talked to you today about any barriers you might have to taking your lupus medications, how did the conversation make you feel?" Patients were encouraged to select all the options that applied: "empowered, determined, confused, embarrassed, inspired, worried, ashamed, proud, scared, guilty, upset, angry, excited, other, or did not have a conversation about barriers to taking lupus medications."

Adherence groups. We used medication possession ratio (MPR) as a proxy for adherence to SLE medications (excluding glucocorticoids). Pharmacy refill information from the EMR was reviewed to determine MPR. When EMR refill data were unavailable or appeared inconsistent to the reviewer, these were

Table 1. Comparing characteristics between patients who were adherent and nonadherent at baseline 3 months before intervention visit*

Characteristics	All patients (n = 130)	Nonadherent (n = 67)	Adherent (n = 63)	*P*
Age, median (IQR) years	43 (32–52)	37 (30–51)	46 (34–53)	0.06
Female sex	123 (95)	65 (98)	58 (92)	0.08
Non-White race	77 (59)	48 (72)†	29 (46)†	0.003
<College education	53 (41)	32 (48)	21 (33)	0.09
Married/cohabitating	52 (40)	20 (30)†	32 (51)†	0.02
Medically disabled	38 (29)	23 (34)	15 (24)	0.2
Income ≤$50,000/year	71 (55)	44 (66)†	27 (43)†	0.009
Private insurance	78 (60)	37 (55)	41 (65)	0.3
Medicare/Medicaid	57 (44)	31 (46)	26 (41)	0.6
SLAQ, median (IQR)	9 (4–13)	9 (4–12)	10 (4–13)	0.9
SLEDAI, median (IQR)	2 (0–4)	2 (0–5)	2 (0–4)	0.5
Active nephritis	19 (15)	11 (16)	8 (13)	0.5
PGA, median (IQR)	0.5 (0–1)	0.5 (0–1)	0.25 (0–0.75)	0.1

* Values are the number (%) unless indicated otherwise. IQR = interquartile range; PGA = physician global assessment; SLAQ = Systemic Lupus Activity Questionnaire; SLEDAI = Systemic Lupus Erythematosus Disease Activity Index.
† Significant at $P < 0.05$ between nonadherent and adherent patients.

supplemented by phone calls to the pharmacies. MPRs 3 months before (pre-) and 3 months after (post-) the intervention visit for each SLE medication were calculated as the proportion of days covered by total days' supply dispensed, with MPR greater than or equal to 80% being considered adherent. The 80% cutoff has been consistently applied in prior studies examining SLE medication adherence using pharmacy refill data (6,7,13). We examined adherence to all SLE medications combined and all DMARDs combined (including mycophenolate, azathioprine, methotrexate, and leflunomide). We also examined adherence to antimalarials and mycophenolate separately because these are the 2 most commonly prescribed SLE medications in our cohort (15).

Patients were considered to have either persistent good adherence (MPR ≥80% both pre- and postintervention), improved adherence (MPR <80% preintervention but ≥80% postintervention), or no benefit from the intervention (MPR <80% both pre- and postintervention or MPR ≥80% preintervention but <80% postintervention).

Table 2. Feasibility, acceptability, and appropriateness based on provider surveys (n = 5)*

Domain	Score
Feasibility	
The adherence intervention is implementable	4.7/5
The adherence intervention is possible	4.9/5
The adherence intervention is doable	4.9/5
The adherence intervention is easy to use	4.4/5
Acceptability	
The adherence intervention meets my approval	4.3/5
The adherence intervention is appealing	4.4/5
I like the adherence intervention	4.4/5
I welcome the adherence intervention	4.6/5
Appropriateness	
The adherence intervention is fitting	4.6/5
The adherence intervention is suitable	4.6/5
The adherence intervention is applicable	4.6/5
The adherence intervention is a good match	4.6/5

* Scores range from 1–5, with 5 being best.

Prescribed SLE medications and documented adherence barriers were collected from EMR review.

SLE disease activity. We used the Systemic Lupus Activity Questionnaire (SLAQ) (23), a validated patient-reported SLE disease activity measure. The provider-derived SLE Disease Activity Index (SLEDAI) (24) and physician global assessment (PGA) (25) were completed at the study visit by the attending rheumatologist.

Statistics. Categorical variables were described with percentages, and continuous variables were summarized with either mean (SD) or median (interquartile range), depending upon distribution. The Wilcoxon rank sum test was used to examine differences in distribution of nonparametric variables between adherent and nonadherent patients at baseline. The Kruskal-Wallis test was used to examine differences in distribution of nonparametric variables across adherence groups after the intervention. The McNemar's test was used to compare the percentage of patients who were adherent (MPR ≥80%) before and after the intervention visit. Statistical analyses were performed using STATA (version 14.2).

RESULTS

Study population. Pilot testing of the intervention was conducted between September 25, 2019 and January 15, 2020, during which 134 follow-up encounters were conducted with unique patients who are also DLR participants. Of these, 130 patients were included in the analysis after excluding 2 patients who were not prescribed any SLE medications, 1 for medication discontinuation at the intervention encounter, and 1 for being only prescribed prednisone. Median age was 43 years (interquartile range 32–52 years) 123 (95%) were female, 77 (59%) were racial and ethnic minorities (69 Black, 4 Asian, 3 Hispanic, 1 Native American), and 52 (40%) were married or

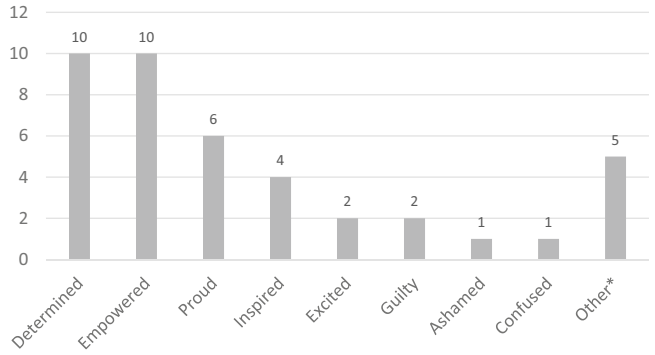

Figure 2. Patient acceptability survey results (n = 49). Patients were asked "if your doctor talked to you today about any barriers you might have to taking your lupus medications, how did the conversation make you feel?" * = Of the 5 patients who indicated "other" feelings, 1 each reported feeling pleasant and truthful, and 3 did not specify.

living with a partner. A substantial proportion of patients had less than a 4-year college education (41%) and were medically disabled (29%), and the majority had an annual household income lower than $50,000 a year (55%) (Table 1). During the 3-month periods before and after the intervention visit, 92% patients were prescribed an antimalarial, 28% mycophenolate, 22% azathioprine, 12% methotrexate, 7% belimumab, and 2% leflunomide. Most patients (62%) were prescribed at least 2 SLE medications including antimalarials, DMARDs, or self-injected belimumab.

Feasibility, acceptability, appropriateness. Of the 130 intervention encounters, 116 (89%) contained documentation that the provider reviewed pharmacy refill data with the patient during the encounter. The average scores for acceptability among providers was 4.4/5, appropriateness 4.6/5, and feasibility 4.7/5 (Table 2).

The anonymous survey was completed by 49 patients (Figure 2). Of these, 18 reported that they did not have a discussion about adherence with the provider. Of the remainder, the most frequent responses were that the intervention visit made them feel determined (n = 10, 32%), empowered (n = 10, 32%), proud (n = 6, 19%), and inspired (n = 4, 13%). Very few patients reported negative feelings from the intervention visit; 2 felt guilty, and 1 each felt confused and ashamed.

Change in adherence and adherence barriers. Among 130 patients who were prescribed any SLE medications, phone calls were made to 47 pharmacies to verify refill status. Although the majority of the phone calls (n = 25) confirmed that the EMR refill data were correct, they were inaccurate for 16 and unavailable for 6.

At baseline, 67 (52%) patients did not refill SLE medications regularly (MPR <80%) 3 months before the intervention visit. These patients were more likely to be younger, be of minority racial and ethnic groups, have annual household income less than $50,000, and were less likely to be married or cohabitating (Table 1). For those who did not refill regularly at baseline, lupus clinic providers identified and documented at least 1 adherence barrier for 35 (52%) patients, and the most frequent barriers were busyness or forgetting (n = 19, 54%), cost (n = 6, 17%), side effects (n = 6, 17%), pill burden (n = 4, 11%), and insurance (n = 4, 11%). In comparison, among the 63 patients who refilled regularly at baseline, 18 (29%) had at least 1 adherence barrier documented, with busyness or forgetting (n = 11, 61%) and cost (n = 5, 28%) being the most common.

Comparing adherence rates before and after the intervention visit, 53 (41%) had persistent good adherence, 35 (27%) had improved adherence, and 42 (32%) had no benefit from the intervention. Compared with those who had no benefit, those who

Table 3. Comparing characteristics between patients who had persistent good adherence, improved adherence, and no benefit from the adherence intervention*

Characteristics	Persistent good adherence (n = 53)	Improved adherence (n = 35)	No benefit (n = 42)	*P*
Age, median (IQR) years	46 (38–53)	38 (31–51)	35 (29–51)	0.03†
Female sex	48 (91)	34 (97)	41 (98)	0.09
Non-White race	24 (45)	20 (57)	33 (79)	0.004†
<College education	18 (34)	14 (40)	21 (50)	0.3
Married/cohabitating	28 (53)	13 (37)	11 (26)	0.03†
Medically disabled	13 (25)	13 (37)	12 (29)	0.4
Income ≤$50,000	22 (42)	19 (54)	30 (71)	0.01†
Private insurance	34 (64)	21 (60)	23 (55)	0.7
Medicare/Medicaid	24 (45)	16 (46)	17 (40)	0.9
SLAQ, median (IQR)	9 (4–13)	9 (4.5–14)	9 (5–12)	0.9
SLEDAI, median (IQR)	2 (0–4)	2 (0–4)	2 (0–6)	0.2
Active nephritis	7 (13)	4 (11)	8 (19)	0.6
PGA, median (IQR)	0.25 (0–0.75)	0.5 (0–1)	0.75 (0.25–1)	0.04†

* Values are the number (%) unless indicated otherwise. IQR = interquartile range; PGA = physician global assessment; SLAQ = Systemic Lupus Activity Questionnaire; SLEDAI = Systemic Lupus Erythematosus Disease Activity Index.
† Significant at $P < 0.05$ among patient groups.

Table 4. Distribution of adherence groups for patients taking any SLE medication, any DMARDs, antimalarials, and mycophenolate*

Class of SLE medication	Persistent good adherence	Improved adherence	No benefit
Any SLE medication (n = 130)	53 (41)	35 (27)	42 (32)
DMARDs (n = 85)	34 (40)	15 (18)	36 (42)
Antimalarials (n = 120)	62 (52)	23 (19)	35 (29)
Mycophenolate (n = 37)	18 (49)	4 (11)	15 (41)

* Values are the number (%). DMARDs = disease-modifying antirheumatic drugs (including methotrexate, azathioprine, mycophenolate, leflunamide); SLE = systemic lupus erythematosus.

had improved adherence were more likely to be older, married or cohabitating, White, and have annual household income greater than $50,000. There were no differences in lupus activity measures among the adherence groups except for lower PGA among patients with persistent good adherence (Table 3).

About half of the patients in both the improved adherence and no benefit groups had at least 1 adherence barrier identified and documented, and the distribution of barriers were similar between the 2 groups. Table 4 shows adherence groups for the different SLE medications classes.

The proportion of patients who regularly refilled SLE medications (3-month MPR ≥80% for all SLE medications) increased from 48% preintervention to 58% postintervention (P = 0.03). Similarly, the proportion of patients refilling antimalarials increased from 60% to 71% (P = 0.02). There is a nonsignificant trend for an increased proportion of patients refilling mycophenolate (50% to 59%; P = 0.1) and DMARDs as a whole (49% to 59%; P = 0.09).

DISCUSSION

We present a simple adherence intervention for patients taking SLE medications with promising preliminary results demonstrating feasibility, acceptability, and appropriateness. The intervention did not incur additional costs in resources or staff to our current care and allowed providers to identify, document, and address a range of adherence barriers. Medication adherence improved appreciably after the intervention visit when examining patients taking any SLE medications and those taking antimalarials. Those benefiting from the intervention included a higher proportion of patients identifying as White, reporting an annual household income over $50,000, and having more social support.

This intervention was beneficial for several reasons. By sharing the screen, the provider and the patient together discovered the patient's refill status. This increased recognition of nonadherence through routine use of readily available refill information. It also provided an opportunity for the provider to ask open-ended and nonjudgmental questions. If done with sensitivity and respect, these questions can lead to honest discussions about adherence barriers with the patient, thereby improving patient–provider communication, shared decision-making, and patient education. Allowing patients to view their own refill data and praising the patient for regular refills could enhance patient motivation. Devising individualized solutions with each patient can help decrease their logistical burdens in obtaining and taking medications, particularly for patients reporting busyness and forgetting as a barrier. These are all mechanisms suggested by existing literature on SLE medication adherence and are in line with recently published EULAR studies on the overarching principles for the assessment and management of nonadherence among patients with rheumatic diseases (26–30).

The most common barrier observed was busyness and forgetting, which has previously been recognized as a common obstacle to adherence (4,31). However, our prior qualitative work suggested that when patients express busyness and forgetting as a barrier, sometimes it may be driven by a lack of motivation or priority (4). This could partially explain why a substantial portion of patients did not benefit from the intervention if logistical but not motivational barriers were specifically addressed during the intervention visit. Future qualitative studies should determine how providers can effectively ask about adherence barriers and assess whether they adequately understand and address patients' barriers. Training providers in motivational interviewing could further enhance the effectiveness of the intervention (32).

Our study confirms prior work that nonadherence disproportionally affects patients who are younger, belong to racial and ethnic minority groups, and have lower income and less social support (2,3,15,33–35). Unfortunately, patients with these characteristics were also less likely to derive benefit from the intervention. This suggests that the intervention needs to be refined to minimize disparities in nonadherence and poor outcomes. It is also important to note that certain barriers, particularly related to affordability and insurance, would require sustained structural changes to rectify. Nonetheless, our intervention can help identify patients in need of additional support so existing resources can be applied appropriately.

Our literature search found only 5 studies that examined adherence interventions specifically in a US lupus population, of which only 2 demonstrated improvement in adherence (10–14). Our intervention is most similar in concept to one described by Durcan et al (14), who followed Costedoat-Chalumeau et al (36) in using HCQ levels to inform adherence counseling. Durcan et al monitored patients' HCQ levels at each visit, and those with low levels received an email and adherence counseling at the next

visit (14). Attributing the mechanism for change to education and behavior support, Durcan et al observed that the proportion of patients with adequate HCQ levels increased with each visit at which HCQ level was assessed, from 56% at baseline to 69% after 1 visit, 77% after 2, and 80% after 3 or more. Although we used MPR, a less robust proxy of adherence than HCQ levels, the improvement we observed is comparable to that in the Durcan study after 1 visit. It is possible that our intervention effect may be even stronger after several consecutive intervention visits. The optimal frequency and duration to conduct our intervention warrant further study.

Using MPR as an adherence proxy costs less than measuring HCQ blood levels and can be applied to all SLE medications regardless of the availability of blood levels. However, pharmacy refill data are not universally available or accurate, and we did have to directly call pharmacies to confirm data for a subset of patients. An intervention combining refill data with medication blood levels for those with unreliable refill data may provide a solution for improved accuracy while limiting cost.

Strengths of the study include the intervention's simplicity and versatility and the use of existing resources in the Epic EMR. It does not require additional staff or visits and can be easily integrated into clinic flow. Additionally, instead of relying on self-reported adherence, the intervention uses objective refill data through Surescripts, which connects nearly all US EMRs and pharmacies (19), allowing more reliable identification of nonadherence as well as potential implementation across many health systems. Lastly, the intervention was developed based on constructs that enhance adherence from literature review, our formative mixed-methods data, and input from lupus clinic stakeholders.

Our study has several limitations. First, this was a pilot study aimed primarily at assessing feasibility and acceptability. It was not powered to detect differences in adherence, and the relatively small sample size limits statistical power in comparing adherence groups, different classes of SLE medications, and impacts of specific adherence barriers. Yet, we found meaningful improvement in adherence, underscoring its potential. Such improvement in adherence may be particularly important for a drug such as mycophenolate, for which better adherence even for a subset of patients can potentially lead to less renal failure, acute care utilization, and health care costs. Second, because all providers share clinical care for all lupus patients in our clinic, controlled testing of the intervention was logistically challenging. Therefore, we assessed adherence before and after the intervention visit without using a control group. It is possible that the observed improvement in adherence would have occurred regardless of the intervention or because of the white-coat adherence effect, in which adherence improves simply by seeing the physician. However, this is unlikely because the baseline adherence rates before intervention were similar to those previously reported in our clinic despite a significant passage of time (15). Also, the white-coat adherence effect is mainly observed immediately surrounding an appointment and is not expected to persist for 3 months (37). Third, acceptability assessment using anonymous patient surveys only captured a portion of patients who underwent the intervention and may have been composed of patients who were not included in this analysis. This may explain why many reported not having discussed adherence with their provider. Additionally, anonymous surveys did not allow us to compare acceptability across different providers to identify ones who may need more training. We were also not able to compare patient satisfaction between adherence groups. However, we felt it was necessary to encourage honest feedback, and we find it reassuring that those who reported having a discussion gave overwhelmingly positive feedback. Fourth, refill data are only a surrogate for adherence, but they have been shown to correlate well with HCQ levels and predict outcomes in patients with SLE (6,10,38), supporting its use as a proxy for adherence. Additionally, dichotomizing MPR may have missed patients who made a substantial improvement from baseline but did not meet the 80% threshold for adherence. This is overall a conservative bias, further underscoring the potential of this intervention.

Despite the limitations of pharmacy refill data, routine use of a readily available, objective, and free proxy of adherence is valuable. Pharmacy refill data can be combined with patient-reported adherence or available drug-level testing to enhance its accuracy. Another limitation is that our analysis included both oral and injectable medications, and adherence barriers for the 2 groups of medicines are likely to be distinct. However, only a small proportion of the patients were on self injections, and most of them also took an oral medication. Furthermore, the pilot testing was conducted in a tertiary academic lupus center and will likely require adaptation to other clinical settings. Finally, there are several unanswered questions about this intervention. For example, we did not measure how long it took to perform the intervention, assess fidelity in performing the intervention by each provider, examine the frequency needed for intervention, verify that the adherence barriers documented were comprehensive and adequately addressed, or measure longer-term clinical outcomes affected by adherence, and these are areas for future research.

In conclusion, we developed and pilot tested an adherence intervention for patients taking SLE medications with promising initial data. However, additional research is needed to refine the intervention to best serve patients with the greatest needs, adapt it for other clinical settings, and assess its effectiveness in a controlled setting.

AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be submitted for publication. Dr. Sun had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. Sun, Corneli, Bosworth, Clowse.
Acquisition of data. Sun, Eudy, Rogers, Criscione-Schreiber, Sadun, Doss, Maheswaranathan, Barr, Eder, Clowse.
Analysis and interpretation of data. Sun, Eudy, Clowse.

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