Running head: SLE nonadherence and barriers

Title: Development and initial validation of a lupus-specific measure of extent of and reasons for medication nonadherence

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Abstract

Background: Medication nonadherence is common in systemic lupus erythematosus (SLE) and negatively impacts outcomes. To better recognize and address nonadherence, there is need for an easily implemented tool with interpretable scores in this population. Domains of Subjective Extent of Nonadherence (DOSE-Nonadherence) is a measure that captures both *extent of* and *reasons for nonadherence*. We refined and evaluated DOSE-Nonadherence for patients with SLE.

Methods: We refined the *reasons for nonadherence* domain of DOSE-Nonadherence through rheumatologist feedback and patient cognitive interviewing. We then administered the refined instrument to patients prescribed oral SLE medications and compared its results to the Beliefs about Medicines Questionnaire (BMQ), the Medication Adherence Self-Report Inventory (MASRI), medication possession ratios (MPRs), and hydroxychloroquine blood levels via Pearson correlations.

Results: Five rheumatologists provided feedback; 16 patients (median age 43, 100% female, 50% Black) participated in cognitive interviews; 128 (median age 49, 95% female, 49% Black, 88% on anti-malarials, and 59% on immunosuppressants) completed the refined instrument.

Items assessing *extent of nonadherence* produced reliable scores (alpha 0.89) and identified 47% as nonadherent. They showed convergent validity with MASRI (r=-0.57), hydroxychloroquine blood levels (r=-0.55), and to a lesser extent MPRs (r=-0.34 to -0.4), and discriminant validity with BMQ domains (r=-0.27 to 0.32).

Nonadherent patients reported on average 3.5 adherence barriers, the most common being busyness/forgetting (62%), physical fatigue (38%), and pill fatigue (33%).

Conclusion: Our results support the reliability and validity of DOSE-Nonadherence for SLE medications. This instrument can be used to identify, rigorously study, and guide adherence intervention development in SLE.

Systemic lupus erythematosus (SLE) management requires long-term use of immune-altering medications to prevent disease progression and damage. However, nonadherence is as high as 75% and is associated with increased morbidity and mortality(1)(2)(3)(4). Few studies have investigated causes of medication nonadherence in SLE(1). A 2017 systematic review of SLE adherence literature identified eight studies conducted in the United States, among which only one examined determinants of nonadherence, finding that depression and polypharmacy were associated with lower adherence(1). Measuring the extent of and identifying modifiable reasons for nonadherence are crucial steps in developing interventions that optimize adherence to lifesaving SLE medications.

While various methods are used to assess the extent of nonadherence, reasons for nonadherence can be only self-reported. A self-reported measure has the added benefit of providing the necessary information to the clinician at the point of care. To date, there are no easily implemented self-reported tools to assess both the *extent of* and *reasons for nonadherence* among patients with SLE.

Previously, a two-domain, patient-reported instrument had been developed to measure both the *extent of* and *reasons for nonadherence* in hypertension, hyperlipidemia, and hepatitis C(5)(6)(7). We used this existing measure, Domains of Subjective Extent of Nonadherence (DOSE-Nonadherence), as the starting point to build a SLE-appropriate adherence assessment tool (DOSE-Nonadherence-SLE), incorporating concepts of adherence barriers we discovered from literature review and our prior qualitative results(8)(9)(10)(11)(12)(13)(14). We conducted a two-phase study first refining the measure specifically for adults diagnosed with SLE, and then quantitatively evaluating its reliability and validity. The purpose of DOSE-Nonadherence-SLE is to capture both the *extent of* and *reasons for nonadherence* in patients with SLE.

Methods:

Study Setting and Population

The Duke Lupus Registry (DLR) is a prospective cohort of SLE patients followed at the Duke Lupus Clinic. Inclusion criteria for the DLR are age ≥18 years, English fluency, absence of cognitive or physical barriers to provide informed consent, and meeting American College of Rheumatology 1997 or SLE International Collaborating Clinics 2012 SLE classification criteria(15)(16). 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 Duke University institutional review board (study # Pro00008875). The current study was approved under study #Pro00094645.

Qualitative evaluation and refinement

DOSE-Nonadherence is based on a 7-day recall period. The *extent of nonadherence* domain contains three items (I missed my medicine, I skipped a dose of my medicine, and I did not take a dose of my medicine) on a 5-point Likert scale that are scored by computing their mean, with higher scores indicating greater nonadherence(5). Patients who endorse nonadherence on any of the *extent of nonadherence* items (score >1) then go on to complete the *reasons for nonadherence* domain. The *extent of nonadherence* items were not meant to be modified as they were designed to be disease-agnostic and have been extensively evaluated through cognitive interviews(5)(6)(7). In contrast, the *reasons for nonadherence* domain was designed to be tailored to specific diseases and medication regimens, and each reason stands alone as a descriptor. Therefore, we focused our efforts in this phase on the latter items.

The first author (KS) formulated a preliminary version of the *reasons for nonadherence* by augmenting the existing DOSE-Nonadherence items with concepts discovered from literature

review and our prior qualitative study and removing concepts that were not relevant to patients with SLE(8)(9)(10)(11)(12)(13)(14). These concepts and preliminary items were reviewed with a standing lupus advisory group generally attended by 2-8 patients, 2-3 clinicians, and 2 clinic staff, who selected the most salient items (Supplemental table 1).

The resulting draft questionnaire was reviewed by lupus clinic providers (JR, LC, RS, JD, MC) who commented on whether the *reasons for nonadherence* items were comprehensive in addressing nonadherence issues encountered in clinical practice.

Next, we conducted two rounds of semi-structured individual cognitive interviews with 16 DLR patients to evaluate and refine the *reasons for nonadherence* items, revising them between rounds(17). We purposefully sampled patients prescribed SLE medications for at least 6 months and 50% Black patients. Common practice and the literature indicated that relatively little new information is learned with more than 12 interviews within a relatively homogenous sample of interview participants(18)(19)(20). To account for diversity of experiences, we added four interviews, yielding a total of 16.

Interviews were conducted via Zoom by two interviewers (KS, DA) using a semi-structured interview guide. During the interviews, participants first completed the self-administered DOSE-Nonadherence-SLE online using Research Electronic Data Capture (REDCap)(21). The interviewers then shared their screen and reviewed the participant's response processes and answers together retrospectively(17). Patients reporting perfect adherence on the *extent of nonadherence* items were asked to consider hypothetical reasons for missing doses. We used think aloud and verbal probing techniques to ascertain how an item was interpreted and a response formed. Patients were also encouraged to comment on questionnaire structure, item stem, and missing or redundant concepts to ensure that the instrument comprehensively and

parsimoniously captured most important barriers patients face in taking SLE medications, and that respondents' understanding of items was consistent with their intended meanings. Patients were not asked to comment on the instructions, 7-day recall period, response scale, or formatting, which had been extensively evaluated and were not meant to be modified(5). Interviews were recorded and took approximately 30 minutes each. The interviewers took detailed structured notes to systematically track issues that arose for each item and added, removed, or edited items in response to feedback between rounds. The rationales for revising items were also documented. Matrix analysis was performed to summarize information across interviews.

Quantitative evaluation

After qualitative refinement, we assessed DOSE-Nonadherence-SLE by administering it to DLR patients who were prescribed oral medications for SLE. This phase of the study focused on evaluating the reliability and validity of the *extent of nonadherence* items in patients with SLE.

Data collection

Cross-sectional data were obtained through questionnaire and electronic medical record (EMR) review. Due to COVID-19 restrictions on research, questionnaires were initially sent as an email link to all 362 DLR patients, and later administered in person during clinic visits to patients who did not respond to the initial email until sample size goal was reached. Clinical information was extracted from the most recent visit for patients who completed questionnaires via email, and from the same day encounter for patients who completed questionnaires in person. Self-reported socio-demographic information including race and ethnicity was collected. SLE medications prescribed were obtained through chart review. In addition to the refined DOSE-Nonadherence-SLE, the following instruments and information were obtained.

Existing measures of adherence. To establish convergent validity of the *extent of nonadherence* domain, or degree to which its score correlates with another instruments meant to measure the same construct, we assessed related constructs. The Medication Adherence Self Report Inventory (MASRI) part A is a 6-item instrument which asks about the amount of medication taken in the past month and provides a numerical estimate of adherence from 0-100% on a visual analog scale. In patients with SLE, this measure showed internal consistency, reliability, and concurrent and predictive validity when compared to pharmacy refill data(22). We used a cutoff of 90% indicating adherence given known ceiling effect(22). Medication possession ratios (MPRs) for all SLE medications three months prior to the date of questionnaire completion were obtained by EMR review, supplemented by phone calls to pharmacies. MPR was calculated as the proportion of days covered by total days' supply dispensed(23), and we used a cutoff of 80% indicating adherence(3)(4)(24). Available Hydroxychloroquine blood levels measured using liquid chromatography coupled with mass spectrometry within 2 weeks of questionnaire completion were included(25)(26). Therapeutic range is 500-2000ng/ml. Reduced levels have been associated with worse SLE disease activity, supporting its validity in measuring adherence(25)(26)(27)(28)(29).

Medication beliefs. To establish discriminant validity, or degree to which the scores diverge from instruments meant to measure different constructs, we administered the 18-item Beliefs about Medicines Questionnaire (BMQ), which measures beliefs about the necessity of prescribed medication (Specific-Necessity); beliefs about the danger of dependence, long-term toxicity, and disruptive effects of medication (Specific-Concerns); beliefs that medicines are harmful and/or addictive and should not be taken continuously (General-Harm); and beliefs that medicines are overused by doctors (General-Overuse)(30)(31). Scores range 5-25 for Specific-Necessity and

Specific-Concerns, and 4-20 for General-Harm and General-Overuse, with higher scores indicating stronger beliefs (Table 1).

Statistics

Descriptive statistics were performed. A score >1 on any of the three *extent of nonadherence* items was considered to indicate nonadherence, and scores of the three items were averaged. We used Cronbach's alpha to assess reliability of the *extent of nonadherence* items and examined their relationships using inter-item correlations(32). We computed Pearson correlations between *extent of nonadherence* item scores and comparison measures (MASRI, MPR, hydroxychloroquine blood levels, and BMQ subscale scores) to examine convergent and discriminant construct validity. Correlation >0.50 was considered evidence of convergent validity(6), which was expected between *extent of nonadherence* scores and MASRI and hydroxychloroquine blood levels. Given that taking and refilling medications are different adherence constructs and the difference in the time period measured (7 vs 90 days)(33), we expected a weaker correlation (0.3-0.5) between *extent of nonadherence* scores and MPRs. We expected a weak correlation (<0.30) between *extent of nonadherence* scores and BMQ subscale scores as evidence of discriminant validity, because medication beliefs may impact, but are distinct from, medication-taking behavior(34).

A target sample size of 123 provides 80% power and 5% alpha error to detect the significance of a correlation of 0.25, which estimates the correlation strength for discriminant validity. This sample size is consistent with ones previously shown to be sufficient in validating patient-reported measures in SLE(35)(36)(37)(38). Statistical analyses were performed using STATA (version 14.2 College Station, TX).

Results:

Qualitative evaluation and refinement

Reactions to the initial draft of DOSE-Nonadherence-SLE from five lupus clinic providers (mean age 43, 80% female, 80% White, on average 7 years in practice) were overall positive. Providers queried whether items should be combined to reduce response burden or be asked as separate questions, in particular, "I forgot" or "I was busy", "I was physically too tired" or "too stiff", and "I was too depressed" or "overwhelmed". These questions were explored in the cognitive interviews with patients.

Among 16 patients who participated in cognitive interviews, the median age was 43, all were female, 50% were Black, and 31% reported perfect adherence. Supplemental table 2 shows concepts covered in the original DOSE-Nonadherence questionnaire, new concepts incorporated that are relevant for patients with SLE, and actions taken based on feedback from the advisory group and cognitive interviews.

During cognitive interviews, most patients indicated that being "too stiff" and "too tired" to take medications were different concepts; therefore, these became separate items. One patient indicated that "medicine is not working because I still felt bad" and "when I skip a dose I don't feel any difference" were redundant. Exploring this further, several patients felt that they were different when thinking deeper, and therefore these remained separate items.

Most participants indicated that "I forgot" and "I was busy" go hand in hand and required similar types of intervention, and therefore these were combined into one descriptor.

Most participants indicated that being "depressed" and "overwhelmed" were distinct ideas, but a sense of being overwhelmed is reflected by being "tired of taking medicines". Therefore, "overwhelmed" was removed.

One participant during the first round of interviews suggested adding "it is hard to open pill bottles" and "I have no one to help me". During the second round of interviews, most participants indicated that "hard to open bottles" is a concept covered by "too stiff" and "I have no one to help me," so it was not included.

One participant suggested adding an open-ended question to capture any additional barriers, and several agreed. Therefore, we added a final free-response question. Another participant suggested having patients mark their top three barriers. Several participants agreed because it would show that the doctor cares and allow patients to prioritize which barriers to address. Therefore, we added the instruction, "Of the reasons listed above, please mark 3 that you feel are the biggest challenges for you."

All participants understood all items as intended and indicated that all items were relevant to patients with SLE. All except for one indicated that the questionnaire was the appropriate length. Results became redundant by approximately 14 interviews. The resulting SLE-specific measure containing 25 reasons for nonadherence was used in the quantitative evaluation (Supplemental table 3).

Quantitative evaluation

Among 128 participants enrolled, 85% completed questionnaires via email, and 15% in person. Median age was 49, 95% were female, 49% were Black, and 40% had Medicaid/Medicare insurance. On average, patients completed the questionnaire 42 days from their most recent clinic visit. Median disease duration was 14 years. Patients were on average prescribed 2 SLE medications: 88% anti-malarials, 59% a synthetic disease modifying anti-rheumatic drug

(DMARD) (30% mycophenolate, 15% azathioprine, and 13% methotrexate, 2% leflunomide), and 7% belimumab (Table 2).

Extent of nonadherence

The three items assessing *extent of nonadherence* produced reliable scores (alpha 0.89) and had inter-item correlations between 0.83 and 0.96. These items classified 47% of patients as nonadherent. In comparison, 21% of patients were nonadherent based on the MASRI cutoff of 90%, and 43% based on the MPR cutoff of 80% (Table 3).

Reasons for nonadherence

Patients defined as nonadherent based on the *extent of nonadherence* items on average had 3.5 reasons for missing doses [interquartile range 1-5].

The most common reasons were “I forgot or I was busy” (n=37, 62%), “I was too tired” (n=23, 38%), and “I was tired of taking medicines every day” (n=20, 33%). These three reasons were also most frequently chosen as most challenging to overcome, and together were present in 75% of nonadherent patients. Barriers with the highest scores, indicating greatest impact on adherence, were “I forgot or I was busy” (median 4), “I was too tired” (median 4), and “I do not have a regular schedule” (median 4) (Table 4).

The least common reasons for missing doses were “I heard someone had a bad experience taking them” (n=1), “my family or friends suggested I not take them” (n=2), and “the medication instructions were hard to follow” (n=2).

Six patients provided an answer to the final free-response question. One respondent reported that they forgot, and one each reported reflux, headache, can't keep anything down, stomach pain, and felt ill due to other reasons.

Construct validity

As expected, the *extent of nonadherence* scores were most strongly correlated with MASRI (r=-0.57, n=118) and HCQ blood levels (r=-0.55, n=14), moderately correlated with anti-malarial MPR (r=-0.39, n=113) and DMARD MPR (r=-0.40, n=76), and weakly correlated with BMQ subscales (r=-0.27 to 0.32, n=128). In comparison, the MASRI was moderately correlated with anti-malarial MPR (r=0.34) and weakly correlated with BMQ Specific Necessity (r=0.23) and Specific Concerns (r=-0.25) but was not statistically significantly correlated with other comparison measures (Table 5).

Discussion

We developed, refined, and psychometrically tested DOSE-Nonadherence-SLE, the first self-reported instrument to assess both the *extent of* and *reasons for nonadherence* in patients with SLE. By incorporating feedback from lupus clinic stakeholders in the questionnaire refinement process, the lupus-specific *reasons for nonadherence* items were perceived to cover the concepts they purport to measure, i.e., exhibited face validity. Quantitative evaluation of the disease-agnostic *extent of nonadherence* items showed that the items produced consistent results and measure what they intend to measure in the SLE population, supporting their reliability and construct validity.

Although self-reported measures are known to underestimate nonadherence, our instrument identified more nonadherent patients than the MASRI, suggesting greater sensitivity. It also

performed better than the MASRI in psychometric testing when compared to HCQ blood levels and pharmacy refills, supporting its use in patients with SLE. Further, it has an advantage over existing measures used in rheumatic diseases, including the MASRI and MPR, which only assess degree of nonadherence without considering barriers.

Our study addresses a dearth in the literature in quantifying barriers to adherence among patients with SLE. Hardy, et. al. also assessed adherence barriers in patients with SLE but used a questionnaire developed in cardiovascular disease prevention not adapted or validated for SLE(39). Common adherence barriers discovered in that study overlapped with our findings, including busyness or forgetting and concerns about side effects. Additionally, a common barrier found by Hardy et. al was "having personal reasons for not taking medications", which can be interpreted broadly and thus has unclear implications. In contrast, our *reasons for nonadherence* items, having been refined for SLE, are more concrete and specific, and therefore more actionable.

DOSE-Nonadherence-SLE could be valuable in both clinical and research settings. Clinically, it offers a structured approach to ascertaining degree of and barriers to adherence at the point of care, which can guide individualized adherence plans and improve patient-centered care. In research, it can be used to study adherence barriers on a population level, e.g. identifying racial differences in barriers, as patients from racial and ethnic minority backgrounds are more likely to be nonadherent(40). It can also be used to identify the most impactful adherence barriers and serve as an intermediate outcome measure in adherence intervention trials. For example, in our cohort, the three most common and most challenging barriers reported by patients with SLE were busyness or forgetting, being physically too tired, and being tired of taking medications. The prevalence and impact of these barriers make them attractive targets on which to focus

intervention efforts which may include use of reminders, social support, and simplifying the medication regimen.

Our results suggest possible changes that can be made to the *reasons for nonadherence* items as we work to improve this measure. For example, only 1-2 nonadherent patients reported "I heard someone had a bad experience taking [lupus medications]", "my family or friends suggested I not take [lupus medications]", and "the medication instructions were hard to follow." All patients except for one who reported "I do not have a regular schedule" also reported "I forgot or I was busy", suggesting that the former may be redundant. These items can be deleted to reduce response burden if larger studies confirm our findings. Considering the tradeoff between comprehensiveness and response burden, we suggest retaining the free-response question to capture rarer barriers, particularly if those aforementioned items were removed. Additionally, based on the responses to the free-response question, we decided to retain the item "I missed my lupus pills because I was feeling too sick". We also suggest retaining the instruction for patients to mark the most challenging adherence barriers. The ability to focus on the most impactful barriers would increase the clinical utility of this questionnaire, particularly in resource-limited settings or when patients report similar scores on multiple adherence barriers.

Our study has several limitations. First, our questionnaire assesses adherence in the past 7 days, which may not represent patients' behavior over longer periods of time, and may be more strongly influenced by white-coat adherence effect, where adherence improves immediately surrounding an appointment. This recall period was chosen after previous extensive cognitive interviews showing that the extent of and reasons for nonadherence were more easily and accurately recalled in the last 7 days compared to 14 or 30 days(5)(6). The measure could be administered repeatedly to obtain information over longer time periods. Second, a small number

of the patients who underwent cognitive interviews reported perfect adherence and considered hypothetical reasons for missing doses. Third, most patients completed surveys through email, and those patients may be more engaged with medical care and therefore more adherent than the average lupus patient, possibly impacting the number or selection of reported adherence barriers, affecting the generalizability of our findings. Generalizability may also be impacted by the patient population of our academic lupus clinic located in the Southeastern United States. Future studies should consider its evaluation in and adaptation to other organizational and cultural contexts. Fourth, the number of HCQ blood levels taken within 2 weeks of the questionnaire administration was small, as blood work was typically performed during a clinic visit. However, we still detected significant correlation with the *extent of nonadherence* items. Although MPR and HCQ blood levels are objective measures of adherence, their use may be limited by availability and cost. Additionally, *reasons for nonadherence* covered in this questionnaire apply to oral medications, and barriers to taking self-injections can overlap with but are distinct from oral medications. However, this questionnaire is still very relevant, as only a small percentage of patients with SLE take self-injections, and almost all of them also take oral medications. Lastly, we were not able to meaningfully assess validity correlations among *reasons for nonadherence* to identify redundant items or to correlate those reasons with other measures due to small numbers of patients reporting each adherence barrier.

In conclusion, our results support the reliability and validity of DOSE-Nonadherence-SLE in assessing the *extent of* and *reasons for nonadherence* among patients with SLE. In comparison to the MASRI and MPR, DOSE-Nonadherence-SLE offers a structured approach to recognizing adherence barriers. As such, this instrument can be used to identify and rigorously study the most common reasons for nonadherence in SLE and guide interventions development to target them.

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Table legends:

Table 1. Comparison measures collected with DOSE-Nonadherence-SLE and their score interpretations.

Table 2. Sociodemographic and clinical characteristics of 128 survey participants.

Table 3. Rates of nonadherence and scores of comparison measures among survey participants.

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Supplemental table 1. Concepts, preliminary versions, and final version of items on reasons for nonadherence chosen by the lupus clinic advisory group.

Supplemental table 2. Reasons for nonadherence concepts covered in the original DOSE-Nonadherence questionnaire, concepts relevant for patients with SLE, and actions taken based on feedback from the advisory group meeting and patient cognitive interviews.

Supplemental table 3. Final version of DOSE-Nonadherence-SLE.

Table 1. Comparison measures collected with DOSE-Nonadherence-SLE and their score interpretations.

Comparison Measures	Theoretical Range	Score Interpretation Higher scores indicate…
Medication Adherence Self Report Inventory (MASRI)	0-100%	Better adherence; cut off 90% used to dichotomize adherent vs nonadherent
Medication possession ratio (MPR)	0-100%	Better adherence; cut off 80% used to dichotomize adherent vs nonadherent
Hydroxychloroquine blood levels	0 - >2000ng/ml	Higher blood concentration; therapeutic range 500-2000ng/ml
Beliefs about Medicines Questionnaire (BMQ) Specific Necessity	5-25	Greater belief about necessity
BMQ Specific Concerns	5-25	Greater concerns
BMQ General Harm	4-20	Greater beliefs about harm
BMQ General Overuse	4-20	Greater beliefs about overuse

Table 2. Sociodemographic and clinical characteristics of 128 survey participants.

Characteristics	**Value**
Age, years, median [IQR]	49 [40-59]
Female gender, n (%)	122 (95%)
Race	
White, n (%)	59 (46%)
Black, n (%)	63 (49%)
Other race, n (%)	7 (6%)
Hispanic ethnicity, n (%)	6 (5%)
Household income ≤$50,000/year, n (%)	60 (47%)
College education or higher, n (%)	79 (62%)
Private insurance, n (%)	72 (56%)
Medicare/Medicaid insurance, n (%)	51 (40%)
Medically disabled, n (%)	33 (26%)
Disease duration in years, median, [IQR]	14 [7-23]
Number of SLE medications prescribed, median, [IQR]	2 [1-3]
Prescribed medications	
Anti-malarial, n (%)	112 (88%)
DMARD, n (%)	75 (59%)
Mycophenolate, n (%)	38 (30%)
Methotrexate, n (%)	17 (13%)
Azathioprine, n (%)	19 (15%)
Leflunomide, n (%)	2 (2%)

Biologic/small molecule, n (%)	11 (9%)
Prednisone, n (%)	40 (31%)
Days between questionnaire completion and clinic visit, median, [IQR]	42 [15-105]

DMARD = disease modifying anti-rheumatic drug; IQR = interquartile range; SLE = systemic lupus erythematosus; *biologic/small molecule 9 belimumab, 1 etanercept, 1 tofacitinib

Table 3. Rates of nonadherence and scores of comparison measures among survey participants.

Adherence Measure (Number Completed)	Rate of Non-adherence, n (%)	Score Indicating Nonadherence	Median Score [IQR]
Self-reported adherence			
DOSE-Nonadherence *extent of nonadherence* (128)*	60 (47%)	>1	1[1-2]
MASRI (118)^	25 (21%)	<90	96[90-100]
Pharmacy refill data			
HCQ MPR (113)^	37 (33%)	<80	100[66-100]
MMF MPR (38) ^	14 (37%)	<80	92[60-100]
AZA MPR (20) ^	10 (50%)	<80	77[36-100]
DMARD MPR (76)^	34 (45%)	<80	92[46-100]
Belimumab MPR (9)^	2 (22%)	<80	100[82-100]
All SLE medications MPR (128)^	55 (43%)	<80 for all SLE medications	NA
Drug level			
HCQ blood level (14)	3 (21%)†	<500ng/dL	1080 [604-1288]

AZA = azathioprine; DOSE-Nonadherence = Domains of Subjective Extent of Nonadherence; DMARD = disease modifying anti-rheumatic drug; HCQ = hydroxychloroquine; IQR = interquartile range; MASRI = Medication Adherence Self Report Inventory; MMF = mycophenolate; MPR = medication possession ratio; SLE = systemic lupus erythematosus; *Score range 1-5, higher score indicates greater nonadherence; ^Score range 0-100, lower score indicates greater nonadherence; †HCQ blood levels were 70 ng/dL, 491 ng/dL, and 491ng/dL

Table 4. *Reasons for nonadherence* reported by 60 patients who were considered nonadherent based on the *extent of nonadherence* items.

Over the past 7 days, I missed my lupus pills because…	**Number reporting barrier, n (%)**	**Average score, median [IQR]^**	**Number picked as 3 most challenging, n (%)**
I forgot or I was busy	37 (62%)	4.0[2.0-5.0]	29 (48%)
I was too tired	23 (38%)	4.0[2.0-5.0]	10 (17%)
I was tired of taking medicines every day	20 (33%)	3.0[2.0-3.0]	14 (23%)
I felt well	16 (27%)	3.0[2.0-3.0]	4 (7%)
I do not have a regular schedule	15 (25%)	4.0[2.0-4.0]	5 (8%)
when I skip a dose I don't feel any difference	13 (22%)	3.0[2.0-4.0]	4 (7%)
I needed to take them with food but could not eat at the time	12 (20%)	3.5[3.0-4.0]	5 (8%)
I am worried about side effects	11 (18%)	3.0[2.0-3.5]	2 (3%)
I could not fill the medicine on time	11 (18%)	3.0[2.0-4.0]	6 (10%)
I was too stiff	10 (17%)	2.5[2.0-3.0]	0 (0%)
I felt too depressed	9 (15%)	2.0[2.0-3.0]	1 (2%)
they caused side effects	9 (15%)	3.0[2.0-5.0]	5 (8%)
I take too many pills	8 (13%)	2.0[2.0-2.5]	2 (3%)

I feel that nothing will get better even if I take them	6 (10%)	2.5[2.0-3.0]	0 (0%)
I still felt so bad I thought the medicine was not working	6 (10%)	2.0[2.0-3.0]	0 (0%)
I do not understand why I need to take them	5 (8%)	3.0[2.0-3.0]	0 (0%)
it cost too much	5 (8%)	2.5[2.0-5.0]	3 (5%)
I am worried that they would affect my ability to have children in the future	5 (8%)	3.0[3.0-4.0]	2 (3%)
I had no one to help me	5 (8%)	3.0[2.0-3.0]	2 (3%)
I am worried that my doctor did not prescribe the right medicine for me	3 (5%)	2.0[2.0-3.0]	0 (0%)
I had a hard time swallowing them	3 (5%)	3.0[2.0-4.0]	1 (2%)
the medication instructions were hard to follow	2 (3%)	2.5[2.0-3.0]	0 (0%)
my family or friends suggested I not take them	2 (3%)	3.0[2.0-4.0]	1 (2%)
I heard someone had a bad experience taking them	1 (2%)	2.0[2.0-2.0]	0 (0%)

^score range 1-5 with higher score indicating greater perceived impact on adherence; IQR = interquartile range

Table 5. Evaluating construct validity of *extent of nonadherence* items by correlating with other adherence measures and comparing with MASRI.

Comparison measures (Number completed)	**Pearson's correlation with *extent of nonadherence***	**Pearson's correlation with MASRI**
Adherence measures		
MASRI (n=118)	-0.57*	--
HCQ blood level (n= 14)	-0.55*	0.50
HCQ MPR (n=113)	-0.39*	0.34*
DMARD MPR (n=76)	-0.40*	0.16
MMF MPR (n=38)	-0.34*	0.25
Beliefs in Medicines Questionnaire (BMQ)		
Specific Necessity (n=128)	-0.27*	0.23*
Specific Concern (n=128)	0.24*	-0.25*
General Overuse (n=128)	0.20*	-0.10
General Harm (n=128)	0.32*	-0.17

HCQ = hydroxychloroquine; DMARD = disease modifying anti-rheumatic drugs; MASRI = medication adherence self-report inventory; MMF = mycophenolate; MPR = medication possession ratio; *indicates statistically significant correlations

Correction

Development and Initial Validation of a Systemic Lupus Erythematosus–Specific Measure of the Extent of and Reasons for Medication Nonadherence

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In the article, the Acknowledgment is incomplete and should be corrected as follows:

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