Research Summary
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Protocol Title: Reducing Disparities in Medication Adherence of Patients with Systemic Lupus Erythematosus (SLE)

Department/Division/Clinical Setting: Division of Rheumatology & Immunology, Duke University Medical Center.

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Purpose of the Study:
The aims of this study are to:

1) Identify key contributors to medication nonadherence among minority SLE patients using mixed methods, including patient self-efficacy, patient-provider communication and racial discordance;
2) Develop a multi-level intervention directed towards providers, clinic staff, and patients based on concepts of self-affirmation and positive affect to increase medication adherence among minority SLE patients by addressing specific findings from Aim 1; and
3) Pilot test the intervention designed in Aim 2 to address barriers that originate in the clinical interaction in the Duke Lupus Clinics.

Background & Significance:

Systemic lupus erythematous (SLE) is more common, severe, and deadly in Hispanics, Asians, and African Americans than in Caucasians. Medication non-adherence is more prevalent in ethnic minorities and may be a significant contributor to known outcome disparities. A range of barriers to adherence have been identified including factors both extrinsic (such as cost, insurance, medication complexity, side effects) and intrinsic (patient level factors, patient-provider relationship) to the patient encounter. This study will focus on two modifiable risk factors intrinsic to the clinical encounter that are especially relevant in the care of minority lupus patients: 1. *self-efficacy*, or confidence in one's own ability to take action to overcome barriers with regards to a specific behavior; and 2. effective *patient-provider communication*. Data suggest that both of these factors are diminished among minority populations, particularly when the patient and provider come from different cultural backgrounds.

Treating lupus, an incurable multisystem autoimmune disease, often requires long term use of immunosuppressive and immunomodulatory medications to prevent disease progression and damage. Barriers to adherence include both unpleasant medication side effects and incomplete efficacy, leading to frequent medication changes. Paradoxically, while troublesome symptoms like fatigue have no effective treatments, severe organ manifestations such as nephritis may be completely asymptomatic, leading patients to question the necessity of treatment escalation.

Additional patient-specific challenges such as self-management of physical activity, nutrition, medications, financial complications from medical care and disability, and stress reduction, make patient self-efficacy a critical management challenge. As a result of these many challenges, medication non-adherence is as high as 75% among patients with SLE. Such complexities make patient-centered lupus care and effective patient-provider communication crucial.

Further complicating medication adherence, the high rate of racial discordance between lupus patients and providers may pose barriers; while African-Americans comprise nearly 40% of SLE patients, they represent only 0.8% of US adult rheumatologists. Racial discordance is associated with stereotypical threat, or apprehension about being negatively stereotyped. This threat impairs patient-provider communication and decreases patient self-efficacy. Also, racial discordance has been linked to implicit bias in providers – unconscious attitudes or stereotypes that affect one's understanding, actions, and decisions, which can further impair communication.

All these factors are important because poor communication and low patient-self efficacy can both undermine patient-centered care, medication adherence and clinical outcomes. Lupus providers also experience stress as a result of patient non-adherence, which creates feelings of powerlessness, helplessness, and frustration that stem from a sense of lack of control. Poor patient outcomes that result from non-adherence may cause providers to question their self-image as a competent health care professional, making them more vulnerable to burnout. Such provider challenges can in turn negatively impact patient adherence. Psychological interventions aimed at *self-affirmation* (the act of affirming one's core values and sources of personal pride) and *positive affect* (feelings that reflect pleasurable engagement with the environment) enhance both patient-physician communication and patient self-efficacy by defusing stereotypical threat, buffering against stress, and reducing defensive rejection of information. Directing psychological interventions towards both lupus providers and patients is a promising strategy to improve adherence and reduce outcome disparities; randomized controlled trials demonstrate that promoting self-affirmation and positive affect improves medication adherence and health behaviors among patients and improves performance among students and professionals.

Despite the clear morbidity that stems from medication non-adherence, few studies have investigated determinants of non-adherence in SLE. This knowledge gap is even wider for minority populations. Our proposal will begin to fill this gap by studying the relationship between race, patient-provider communication, patient self-efficacy in taking lupus medicines, and medication adherence in SLE patients.

Methods:

Aim 1: Mixed Methods Approach to Identify Key Barriers of Medication Adherence

a. Quantitative study: We will analyze data already collected through the Duke Lupus Registry (DLR) (Pro00008875) and Sub-studies of the DLR (Pro00094645). The following table shows cross-sectional data that are collected by self-report. We anticipate analyzing data from 124 consecutively enrolled participants. In addition, the DLR has also collected information from medical records including: insurance, medication details, disease duration, missed visits, hospitalizations/emergency room visits in the past 12 months, comorbidities, medication refill data and drug levels of hydroxychloroquine, azathioprine, and mycophenolate mofetil when available. The Systemic Lupus Activity Questionnaire (SLAQ), a patient reported disease activity

measure, and Systemic Lupus Erythematosus Disease Activity Index (SLEDAI), a provider derived lupus disease activity measure, both routinely collected at each visit in Duke Lupus Clinic, will also be included.

Self-report data:

Demographics	Age, Gender, race/ethnicity, employment status, marital status, living arrangement will be ascertained by self-report
Medication Adherence Self-Report Inventory (MASRI) Part A	A 6-item questionnaire about the amount of medication taken. Provides a numerical estimate of adherence from 0-100%. Validated in lupus.
Patient-Reported Outcomes Measurement Information System (PROMIS) Self-Efficacy for Managing Medications and Treatments – Short Form 8a	An 8-item on a 5-point Likert scale measuring patient confidence in taking medications in a variety of situations.
PROMIS General Self-Efficacy – Short Form 4a	A 4-item on a 5-point Likert scale measuring general level of confidence in managing various situations, problems, and events.
Interpersonal Process of Care Survey (IPC)	A multidimensional instrument measuring communication, patient-centered decision making, and interpersonal style using 29 items on a 5-point Likert scale.
Positive and Negative Affect Schedule (PANAS)	Two 10-item mood scales measuring positive and negative affect on a 5-point scale.
PROMIS-29	Measures 7 domains with 29 items: physical function, anxiety, depression, fatigue, sleep disturbance, social function, and pain. Validated in SLE.

Statistical Analysis: Adherence based on self-report will be analyzed as a continuous variable from 0-100%. Adherence as a binary variable based on a cutoff of ≥80% will also be explored. Patient self-efficacy and patient-physician communication will be analyzed as continuous variables. We will also explore analyzing them as binary variables dichotomized at the median to high vs. low. Disease activity will be categorized as remission, low, medium, and high. The association between medication adherence as a continuous variable and 1) patient self-efficacy and 2) patient-provider communication will be assessed using linear regression models.

b. Qualitative study: We will conduct individual interviews with minority lupus clinic patients, clinical staff and providers to better understand facilitating factors and barriers to adherence with a focus on patient-physician communication and patient self-efficacy. We will also measure provider stress and implicit bias using the implicit association test (https://implicit.harvard.edu/implicit/). Prior to start of interviews, each participant will compete a brief questionnaire that include basic demographic information from the participants including age, gender, race/ethnicity, education, years since disease diagnosis for patients, years of being a rheumatologist for providers.

Inclusion: Patients are eligible if they are non-Caucasian, have an established diagnosis of SLE, actively followed in the Duke Lupus Clinic for at least 6 months, and are prescribed at least 1 scheduled oral or injectable disease modifying medication for lupus. All clinic staff and providers are eligible.

Exclusion: we will exclude patients who are pregnant or nursing, seen for the first time in Duke Lupus Clinic, and those with significant cognitive impairment as determined by treating rheumatologist.

Sampling Strategy and recruitment: Two purposeful samples of 1) lupus clinical staff and providers, and 2) patients with SLE will be studied. Recruitment will continue until idea

saturation, typically by 12 subjects in a group. We will review patients' records to identify potential participants to invite them for the interview based on demographics and adherence data (obtained from their pharmacy). A recruitment phone script will be used, and potential participants will be contacted prior to their visit to lupus clinic.

Research Design and Subject Compensation: Semi-structured interviews will be conducted using an IRB approved interview guide.

In-person Consent: Consenting patients will complete the interview, before, on or after the day of the lupus clinic visit, in person or either over the phone. If the patient interview is conducted over the phone, consent will take place at the time of the lupus clinic appointment and the interview will be scheduled as a phone call using the IRB approved interview document. Regardless of when the interview takes place, the consent will occur in person prior to the interview.

Email consent: In order to facilitate recruitment in a timely manner, the consent and the IRB disclosure form may be emailed to the participant. If the participant elects to complete the in-person interview, the consent and IRB disclosure form will be returned to the study staff on the day of the interview. A member of the study team will sign the consent and provide the participant with their signed and dated copy prior to the interview. If the participant elects to complete a phone interview, the interview will not be scheduled until the consent and IRB disclosure form have been emailed to the study PI. The study PI will sign the consent and send a signed and dated copy back to the participant. Once the consent and IRB disclosure form are printed, the PI will delete the email. Clinic staff and providers will complete their interviews either in-person or over the phone. Each interview will take 30-60 minutes.

Compensation: A $25 stipend will be offered to each patient as an appreciation of his/her time. Clinic staff and providers will not be compensated.

Data Analysis & Statistical Considerations: We will use qualitative, thematic analysis. Interviews will be audio-recorded and transcribed verbatim. The recordings will be transcribed by GMR Transcription. Nvivo, a qualitative research software, will be used to facilitate analysis. Two analysts from Duke QualCore will apply deductive, structural codes, followed by inductive, thematic codes to the data. We will then identify the most salient themes, further explore the nuances of each theme and how they relate to each other as well as identify sub-themes, primarily based on salience.

Aim 2: Intervention Development

Based on findings from the first aim of the study, a multi-disciplinary team will develop a multi-level intervention. We will invite some clinic patients to be part of the advisory group that will develop the intervention. The patients will be collaborators as opposed to research subjects. The PI will present the data learned from Aim 1 and get their input on the intervention that will be developed. Since the patients are the true stakeholders, their input is extremely valuable on what would work/not work. We will seek to identify new approaches physicians can use to communicate with minority patients more effectively. Any component of the intervention directed at the patient will be delivered at the beginning of the clinical encounter after obtaining informed consent. The intervention will most likely focus on provider-patient communication and self-efficacy, but will be driven by data from Aim 1. The target population will also be determined based on Aim 1 data.

Study Team: The intervention will be developed in collaboration with lupus clinic providers, staff, and patients. We will convene 3-6 monthly meetings to review results from Aim 1, identify targets for intervention, and develop feasible and acceptable interventions.

Intervention Targets: We hypothesize that an intervention that involves self-affirmations and positive affect for physicians, staff, and patients will improve provider-patient communication and enhance patient self-efficacy. It is possible, however, that Aim 1 will not demonstrate these factors as important in the racial disparities in medication adherence. If this were to happen, we would work with the multi-disciplinary team to identify different targets and interventions that would be more effective, based on the results of Aim 1.

Aim 3: Pilot Testing of Intervention
The intervention developed from Aim 2 of the study will be implemented in clinic, focusing on a small cohort of providers, clinic staff, and African American SLE patients. The baseline measures collected in the Aim 1 surveys will be collected at the time of the intervention and again 3 months later. Feasibility and acceptability of the intervention will be assessed. At the completion of this pilot, we will have feasibility and outcomes measures to adjust or expand the intervention project.

IRB amendment 15Jan2020

Based on our findings from Aim 1, our intervention will involve all providers in the Duke Lupus Clinic and will not need informed consent. When the protocol was first written we thought the intervention would enroll patients, but instead we have decided to apply our intervention through the Duke Lupus Clinic.

INTERVENTION:
During a routine standard of care clinic visit, the provider is prompted by a smartphrase in Epic EMR to share the screen with their patient and review their lupus medication refill information available through connection with Surescript. Positive feedback is provided to patients with proportion of days covered in the goal range of 80-100%. For those with proportion of days covered <80%, barriers are explored with open-ended questions. Adherence barriers elicited during this conversation are then addressed and documented in Epic. Acceptability is assessed using anonymous provider surveys, and feasibility is measured by percentage of visits with adherence documentation in Epic EMR. We will also explore effect on patient-reported adherence and pharmacy refill rates 3 months after the intervention. The intervention will be conducted from October 1, 2019 to January 31, 2020. Chart review of patients enrolled in the Duke Lupus Registry from this period and 3 months after will be performed to assess the intervention.

Consent Process

Quantitative data analysis: The consent form for the DLR includes use of medical information.

Qualitative study: Participants will provide signed informed consent prior to participation in individual interviews. The consent process will include an explanation of the project design and intent, an assurance of confidentiality and data security, and a reminder that participation is voluntary. When each participant is invited, it will be clear that this is a research study and their responses will be used for research. Consent will be conducted by Study PI, study interviewer and/or CRC's.

Pilot intervention: Details of the intervention will be dependent on our findings from Aim 1. An addendum to the IRB with details of the intervention will be submitted prior to start of this phase of the study. If consent is applicable, it will also be submitted through process of an amendment.

Subject's Capacity to Give Legally Effective Consent: Patients who are not competent to provide informed consent in English will not be included.

Study Interventions: To be determined based on findings from Aim 1. Updated 15Jan2020 as above.

Risk/Benefit Assessment: Being included in this study does not pose any increased risk to participants involved. There is minimal potential risk for loss of confidentiality, Patients who participate in the intervention may experience improved patient-physician communication, self-efficacy, and/or medication adherence. The data obtained, may improve the care for patients with SLE in the future. The risk to each participant in this study is no greater than minimal, making it reasonable given the potential benefit to future patients.

Costs to the Subject: None

Data & Safety Monitoring: A data monitoring committee will not be used.

Privacy, Data Storage & Confidentiality: All data including the audiotapes and transcriptions will be maintained on a secure server. Participants will be assigned a unique identification number that will not be related to their name, date of birth, social security number, or medical record number. For data analysis, the unique ID number will be the only patient identifier used.

IRB Amendment 06Jun2024

We will assess change in medication adherence by comparing Medication Possession Ratio (MPR) of patients seen during the intervention period by participating providers. To do this, we will obtain medication fill data using chart review and by pulling data directly from the EMR. We will use the Analytics Center of Excellence (ACE) to pull data from the EMR to include encounter date, patient demographics, medications, and Surescripts refill data.

Data will include return patients seen by the following participating providers on the dates specified:

Lisa Carnago: 2/16, 2/23, 3/1, 3/8

Cassy Sims: 2/26, 2/28, 3/4, 3/11, 3/13, 3/18, 3/20

Ankoor Shah: 2/13, 2/15, 2/20, 2/22, 2/27, 2/29, 3/5, 3/7

Brian Andonian: 2/15, 2/22, 2/29, 3/7

Stephen Balevic: 2/23, 3/8, 3/22

Isaac Smith: 2/15, 2/29, 3/14, 3/21

Data will be delivered securely via Box.