Published in final edited form as:

Lupus. 2018 August ; 27(9): 1532–1541. doi:10.1177/0961203318779710.

Depression and Medication Nonadherence in Childhood-onset Systemic Lupus Erythematosus

Alaina M. Davis, MD, MPH^{1,2}, T. Brent Graham, MD, MS^{1,2}, Yuwei Zhu, MD, MS^{3,5}, and Melissa L. McPheeters, PhD, MPH^{4,5}

¹Division of Pediatric Rheumatology, Monroe Carell Junior Children's Hospital

²Vanderbilt University Medical Center

³Department of Biostatistics

⁴Department of Health Policy

⁵Vanderbilt University School of Medicine

Abstract

Objectives—Depression and medication non-adherence are important in managing chronic diseases, but little is known about these factors in childhood-onset systemic lupus erythematosus (cSLE). The objectives of this cross-sectional study were to estimate prevalence of depression and medication non-adherence, describe demographic and disease characteristics associated with depression and medication non-adherence, and evaluate the association between depression and medication non-adherence in cSLE patients.

Methods—Patients with cSLE (n = 51) completed validated screening questionnaires to identify depression and medication non-adherence, Patient Health Questionnaire-9 and Medication Adherence Self-Report Inventory, respectively. Demographic and disease characteristics were obtained via chart abstraction, and compared between groups of depression or medication non-adherence status. A multivariable linear regression model adjusting for propensity scores was conducted to evaluate the association between depression and medication non-adherence.

Results—The prevalence of a positive depression screen was 58.8%, and 7 patients reported suicidal ideation (13.7%). The prevalence of self-reported medication non-adherence was 19.7%. No statistically significant differences for demographic and disease characteristics were found between patients with a positive vs. negative depression screen. Patients reporting medication non-adherence were more likely to have longer disease duration (4.8 vs. 2.6 years, p = 0.035). As the severity of depression symptoms increased, the degree of medication non-adherence also increased (beta = -1.89; p = 0.011).

Corresponding Author: Alaina M. Davis, Monroe Carell Jr. Children's Hospital at Vanderbilt, 2200 Children's Way, Doctor's Office Tower 11240, Nashville, TN 37232, alaina.m.davis@vanderbilt.edu.

Declaration of Conflicting Interests

The authors declare that there is no conflict of interest.

Conclusions—The prevalences of depression and medication non-adherence are high in cSLE, and these factors have a direct relationship. Interventions that better recognize and treat depression and increase rates of medication adherence are needed to improve outcomes in cSLE.

Keywords

Systemic Lupus Erythematosus; depression; medication adherence; pediatrics

Introduction

Childhood-onset systemic lupus erythematosus (cSLE) is characterized by rapid accrual of organ damage with one-third of patients suffering cerebrovascular accidents, renal failure, and/or scarring alopecia within 5 years of disease onset,^{1,2,3,4} making interventions to improve health outcomes for this vulnerable population of children an urgent need. Depression and medication non-adherence are two intervention targets that have the potential to improve outcomes in cSLE, but little is known about depression, medication non-adherence, and the relationship of these two factors in cSLE.

Depression is cited as the most significant predictor of poor health-related quality of life in adults with SLE.⁵ Furthermore, depression is a known risk factor for non9 adherence to chronic medical treatment;^{6,7} and poor adherence has been associated with increased disease activity, increased ambulatory care and emergency room visits, and overall poor prognosis in adults with SLE.^{8,9,10,11} Despite this knowledge, few studies have evaluated rates of depression and factors associated with depression in cSLE.^{12,13,14} Likewise, only one study has measured the rate of medication non-adherence in cSLE, and factors associated with medication non-adherence in this population were not assessed.¹⁵ No known studies have evaluated the association of depression and medication non-adherence in cSLE.

The objectives of this cross-sectional study were to estimate the prevalence of depression and medication non-adherence, describe demographic and disease characteristics associated with depression and medication non-adherence, and evaluate the correlation between depression and medication non-adherence in patients with cSLE.

Methods

Participants and Procedures

For this cross-sectional study participants were recruited between January 11, 2016 and October 20, 2016 from the Pediatric Rheumatology Clinic at Monroe Carell Jr. Children's Hospital at Vanderbilt, a moderate-sized practice within an urban academic institution. The clinic serves a diverse population in terms of age, ethnicity, and insurance status throughout Tennessee and the surrounding states.

Potential participants were identified using a registry created via query of the electronic medical record for all clinic patients billed under the International Classification of Diseases, Ninth Revision (ICD-9) code 710.0 during the prior two years. Patients who had been newly diagnosed with cSLE or who had a known diagnosis of cSLE and were establishing care in the clinic during the study period were manually added to the registry. Eligibility criteria

included a diagnosis of cSLE confirmed using the American College and Rheumatology (ACR) or the Systemic Lupus International Collaborating Clinics (SLICC) classification criteria, presence of prescribed medication for management of SLE for at least 1 month, and ability to complete the consent process and necessary study questionnaires in English.

Patients were invited to participate in the study upon arrival for a scheduled clinic visit by one of two designated clinic nurses who were not directly related to the check-in process or solely responsible for the patient's medical care during that clinic visit. Completion of study procedures while in clinic ensured that health care providers and study personnel were appropriately positioned to intervene should suicidal and/or homicidal ideation be identified on the depression screen. During the consent process participants were asked to acknowledge the required breach of confidentiality should his/her safety or the safety of those around him/her be compromised. Each study participant was also asked to choose whether or not he/she would like to discuss his/her results of the depression screen with a medical provider during the clinic visit. A clinic nurse reviewed the depression screen prior to each participant's discharge from clinic in order to identify and address such information in a time-sensitive manner. Protocol dictated that participants with active suicidal ideation were transferred to the emergency room for urgent evaluation by a mental health team, while those with passive suicidal ideation completed a safety plan with the primary health care provider and/or social worker in clinic and were referred to outpatient mental health services.

Data were collected and stored within REDCap (Research Electronic Data Capture), a secure, HIPAA-compliant web-based application recommended to Vanderbilt researchers by both the Privacy Office and Institutional Review Board (<http://www.projectredcap.org>). Questionnaires used in this study were transcribed in REDCap and administered electronically using an iPad. Demographic and disease activity information for participants was obtained via chart abstraction and transferred directly from the EMR to REDCap. Direct entry of data into the electronic database minimized transcription error and missing data points that could potentially bias the study.

All study procedures were reviewed and approved by the Vanderbilt University Institutional Review Board (#151619). All patients and caregivers, as appropriate based on patient age, provided written informed consent to participate. Access to research materials related to the study may be gained by contacting the corresponding author.

Measures

The Patient Health Questionnaire-9 (PHQ-9) was used to measure the presence or absence of depression symptoms. The PHQ-9 is a 9-item depression screen based on the Diagnostic and Statistical Manual of Mental Disorders, 4th edition criteria for major depression¹⁶ that has been validated for use in an adolescent population.¹⁷ Each symptom criterion is assessed by a question regarding feelings during the last two weeks and is scored on a scale from 0 (not at all) to 3 (nearly every day) generating a total score range 0-27. The categorical scoring algorithm defines mild depression as scores of 5-9, moderate depression as scores of 10-14, moderately severe depression as scores of 15-19, and severe depression as scores of

20-27 with any affirmative response to question 9 regarding suicidal ideation yielding a positive screen regardless of the total score.

Medication non-adherence was measured using the Medication Adherence Self-Report Inventory (MASRI). The MASRI is a 12-item questionnaire of self-reported medication adherence measuring both frequency and timing of medication administration. It includes a visual analog scale (VAS) from 0-100% used to estimate adherence rate during the preceding one month. Higher percentages on the VAS indicate a greater degree of medication adherence.¹⁸ The MASRI has been found to be both reliable and valid in a cohort of patients with SLE that included adolescents.¹⁹ Although all questions regarding the frequency of medication administration were asked in accordance with the validation study methods, only results from the VAS score were used in the primary analysis of this study.

Covariates

Participant demographics, disease characteristics, and medication information were collected directly by the principal investigator from the electronic medical record using a standardized chart abstraction form. Participant demographics included age, sex, race, and insurance type. Disease characteristics included age at diagnosis, disease duration, presence of lupus nephritis, and presence of a known mental health disorder. Presence of lupus nephritis was determined based on documentation of this diagnosis within a rheumatology note or nephrology note in the electronic medical record; renal biopsy results were reviewed when available to confirm this diagnosis. Presence of a known mental health disorder was defined as having had a prior psychiatry appointment at the study site institution or documentation within a rheumatology note of mental health care received at an outside institution during the year preceding study enrollment or the presence of a current prescription for a psychotropic medication. Medication information included a count of all prescribed and scheduled medications (including infusions), names of medications, and weight-based oral glucocorticoid steroid dose.

Disease activity scores were also collected at time of enrollment using the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI). The SLEDAI is a validated tool widely used in SLE research that has been shown to be a sensitive measure of disease activity in both adults and children with SLE.^{20,21} Each SLEDAI form was completed by the participant's primary rheumatology provider and transcribed into the REDCap database by the principal investigator.

Statistical Analysis

The prevalences of depression and medication non-adherence in the study population were calculated. Comparisons of demographic and disease characteristics between groups with and without depression and between groups with and without medication non-adherence were conducted using Wilcoxon rank sum test for continuous variables and chi-square test or Fisher's exact test for categorical variables, as appropriate.

The propensity score (PS) method was applied to estimate the probability of positive depression screen (PHQ-9 score ≥ 5) using a proportional odds regression model including

all the above listed covariates: age, sex, race, insurance type, age at diagnosis, disease duration, disease activity score, number of medications, weight-based oral glucocorticoid steroid dose, presence of lupus nephritis, and presence of a known mental health disorder. A multivariable linear regression was performed to model MASRI score against PHQ-9 score adjusting for one covariate, the linear predictors of having a positive depression screen from the PS model. Restricted cubic splines with 3 knots were applied on the linear predictors to account for skewed data. The PS method is an accepted data reduction technique that enables adjustment for multiple covariates within the regression analysis despite a small sample size without risking model overfitting.^{22,23,24}

A subgroup analysis limited to participants with age between 12-18 years was conducted using the above described PS method. A sensitivity analysis excluding the two data points defined as statistical outliers was also conducted using the above described PS method. Post-hoc analysis of participants with suicidal ideation was completed; comparisons of demographic and disease characteristics between groups with and without suicidal ideation was conducted using Wilcoxon rank sum test or Fisher's exact test, as appropriate.

All data analyses were conducted using STATA 14.1 statistical software (StataCorp, College Station, TX).

Results

A total of 51 participants were enrolled in the study. The registry included 67 potentially eligible patients, but 11 patients did not present for a clinic appointment at the study site during the study period. An additional 3 patients did not meet ACR and/or SLICC classification criteria for cSLE and were excluded from the study. One patient was excluded from the study because the consenting caregiver was unable to read English. Only 1 invited patient declined to participate (Figure 1). Data from all enrolled participants were included in the analysis. There were no missing data points. Two participants under the age of 10 years completed the study questionnaires with assistance from the accompanying parent.

The mean age of the study participants was 16.2 (3.3) years with an age range from 7-22 years. Most of the participants were female (47, 92.2%). Over half of the study population was black (27, 52.9%). The remainder of reported races were white (15, 29.4%), Asian (5, 9.8%), Hispanic (3, 5.9%), and other (1, 2.0%). Medicaid provided primary insurance for the greatest number of participants (29, 56.9%), followed by commercial insurance (21, 41.2%) and military insurance (1, 2.0%). The mean disease duration for the study participants was 3.0 (2.9) years. Average SLEDAI score was 5.1 (5.5); the median SLEDAI score was 4 with an interquartile range (IQR) of 1.097.0. Lupus nephritis was present in over one-third of the study population (20, 39.2%). The mean number of prescribed and scheduled medications was 6.7 (2.8) with a range between 1 and 14. The majority of the participants were prescribed oral glucocorticoid steroids (44, 86.3%) with a mean prednisone dose of 0.15 (0.10) mg/kg/day. Nearly all participants were prescribed hydroxychloroquine (50, 98.0%). Mycophenolate mofetil was the next most commonly prescribed immunomodulatory medication (35, 68.6%). Other prescribed immunomodulatory medications included azathioprine (4, 7.8%), methotrexate (3, 5.9%), and tacrolimus (2, 3.9%). Few participants

were receiving scheduled immunomodulatory infusions, belimumab (4, 7.8%) and cyclophosphamide (1, 2.0%). Approximately one-third of the population had documentation of receiving mental health services (16, 31.4%).

The prevalence of a positive depression screen, defined as a PHQ-9 score ≥ 5 or any affirmative response to question 9 regarding the presence of suicidal ideation, was 59%. Seven patients reported suicidal ideation. This number represents 14% of the study population and 23% of those individuals with a positive depression screen. The prevalence of medication non-adherence, defined as a MASRI score $\leq 80\%$ on the VAS, was 20%. The mean MASRI score for the entire study population was 88%.

Demographic and disease characteristics for patients with and without a positive depression screen are summarized in Table 1. No statistically significant differences between these groups were found. Demographic and disease characteristics for patients reporting medication adherence and medication non-adherence are summarized in Table 2. Participants who reported medication non-adherence were more likely to have longer disease duration than patients who reported medication adherence (4.8 vs. 2.6 years, $p = 0.035$). No statistically significant differences were found between these groups for the remainder of variables.

A multivariable linear regression adjusting for the linear predictors from the propensity score model incorporating the aforementioned covariates demonstrated that depression was significantly associated with non-adherence (beta coefficient = -1.89 ; $p = 0.011$). The regression model result indicates that as the severity of depressive symptoms increases, the degree of medication non-adherence also increases. Specifically, for every one-point increase in the PHQ-9 score, the MASRI score decreases by approximately two points when controlling for the linear predictors. Figure 2 shows the linear prediction of MASRI score by PHQ-9 score.

The subgroup analysis limited to participants with age between 12-18 years included 36 participants, 70% of the total cohort. Results were consistent with findings from the complete cohort and remained statistically significant (beta coefficient = -2.42 ; $p = 0.013$). Specifically, the direction of the relationship between depression and medication non-adherence was maintained, but the magnitude of the relationship was greater in the subgroup analysis compared to that of the complete cohort. The sensitivity analysis excluding the two statistical outliers with the lowest MASRI scores also produced similar results. The direction of the relationship was again maintained, but the magnitude of the relationship was diminished and did not retain statistical significance (beta -0.34 ; $p = 0.481$).

Demographic and disease characteristics for patients with and without suicidal ideation are summarized in Table 3. All patients reporting suicidal ideation had PHQ-9 scores ≥ 5 (i.e. no patients had a positive depression screen solely based on an affirmative response to question 9 regarding the presence of suicidal ideation). Participants who reported suicidal ideation were diagnosed with cSLE at a younger age compared to participants who did not report suicidal ideation (9.0 vs 13.8 years, $p = 0.001$). No statistically significant differences were found between these groups for the remainder of variables.

Discussion

The prevalence of a positive depression screen in this study population of patients with cSLE was high (59%). This finding is only slightly higher than the prevalence of depression in cSLE reported in prior studies (20-57%).^{12,13,14} Prevalence in this study may be higher due to use of a positive depression screen as a surrogate marker for depression. Screening tools are designed to be particularly sensitive and as a result may identify some false positives. Perhaps even more striking than the high rate of depression in cSLE is the high rate of reported suicidal ideation. Nearly one-quarter (23%) of participants in this study who had a positive depression screen reported suicidal ideation at the time of the screen. This number represents 14% of the total study population. Again, this estimate is similar to that reported in previous studies where the prevalence of suicidal ideation in pediatric patients with SLE ranges between 14-34%.^{14,25,26} These prevalences are disproportionately higher than those observed in healthy controls^{14,27,28} and those reported for children with special health care needs and other chronic diseases such as Type I diabetes mellitus and asthma.²⁹⁻³¹ Although none of the participants in this study posed an immediate suicide risk, the results support a need for increased awareness and capacity to identify and intervene in patients with cSLE, who appear to be at particular risk for depression and suicidal ideation.

Predictors of a positive depression screen were not identified, as there were no significant differences between patients with and without a positive depression screen. This lack of predictive patient characteristics with the above noted high prevalence supports the need for universal depression screening in this population. A study conducted by The Childhood Arthritis and Rheumatology Research Alliance (CARRA) showed that 77% of pediatric rheumatologists agreed routine depression screening in pediatric rheumatology patients should be conducted, but only 2% of the surveyed pediatric rheumatologists reported completing routine screening using standardized tools and protocols, with limited staff resources and time being cited as the most frequent barrier to routine screening.³² Participants who had presence of suicidal ideation were more likely to have been diagnosed with cSLE at a younger age. Thus, patients diagnosed with cSLE at a young age may represent a subpopulation that warrants more frequent screening for depression and suicidal ideation or other forms of intervention. Interestingly, participants receiving mental health services were not necessarily more likely to have higher or lower depression screen scores nor presence or absence of suicidal ideation. This may relate to current efficacy of mental health interventions, but remains an area largely unexplored in patients with cSLE.

The prevalence of medication non-adherence in this study population of patients with cSLE was also notable with 20% of the participants reporting less than 80% adherence with SLE medications during the preceding month. This percentage is likely to be an underestimation of the true rate of medication non-adherence given that it was measured using a tool that relies on patient self-report. In addition, patients who did not present for a clinic visit during the study period were potentially non-adherent to the suggested frequency of clinic visits. This subset of patients may be at increased risk for medication non-adherence, but would not have been captured in the analysis. A previously published study used drug blood levels, pharmacy refill data, and the MASRI to measure adherence to hydroxychloroquine in cSLE. This study found that medication adherence estimates using hydroxychloroquine blood

levels correlated with rates measured using pharmacy refill data and the MASRI. However, the mean adherence rates measured with the MASRI were the highest at 80%, which is a similar estimate to our study and supports the idea that MASRI results tend to overestimate adherence.¹⁵ Additionally, a recently published review of medication adherence in adults with SLE reported a prevalence of non-adherence measured by varying methods ranging from 43-75%.³³

Patients who reported medication non-adherence in this study were more likely to have longer disease duration than those who reported medication adherence. Given the relatively large number of statistical tests completed on this small sample size, the risk that this statistical significance was due to chance must be considered. Nonetheless, this finding is consistent with studies looking at medication non-adherence in adults with SLE³³ and aligns with clinical experience where patients with cSLE become less attentive to disease management as their initial presenting symptoms are not as vividly recollected.

Additional predictors of medication non-adherence were not identified, even with inspection of the two outliers with the lowest MASRI scores. As with depression, this lack of predictive patient characteristics and the above noted high prevalence support the need for universal medication adherence assessment in patients with cSLE.

The association between depression and medication non-adherence has been unexplored in cSLE. To our knowledge, this is the first study to assess for an association between depression and medication non-adherence in this specific population. Results from the multivariable linear regression in this study showed a small but significant relationship between depression and medication non-adherence. The model showed that as the severity of depression symptoms increased the degree of medication non-adherence also increased. Specifically, for every one point increase in the PHQ-9 score, the MASRI score decreased by nearly two points. Similar relationships between depression and medication non-adherence have been reported in other chronic diseases,⁶ including childhood-onset diseases such as Type I diabetes mellitus and inflammatory bowel disease.^{34,35} In addition, depressive symptoms have been found to be a predictor of medication non-adherence in adults with SLE.^{7,36,37}

The relationship between depression and medication non-adherence was slightly more pronounced for participants with age between 12-18 years. Specifically, the subgroup analysis demonstrated that for every one point increase in the PHQ-9 score, the MASRI score decreased by two and a half points. In addition, the direction of the relationship between depression and medication adherence was maintained even when excluding the two participants with the lowest MASRI scores, though the magnitude of the relationship was smaller and did not retain statistical significance given the reduced sample size. While these two data points are statistically defined as outliers, we believe they actually reflect the spectrum of results expected for this population. Additional chart review was completed to check the validity of the data to ensure the outliers were neither inaccurate nor implausible. No data entry errors were found and both participants were confirmed to have had poor medication adherence - one had documented discussions regarding poor medication adherence within clinic notes preceding the study date and the other subsequently had

undetectable mycophenolate mofetil blood levels. Furthermore, no discrete demographic or disease characteristic differences were identified in these two participants compared to the remainder of the cohort, thereby supporting the conclusion that there is a need for universal medication adherence assessment, possibly by multiple methods, in patients with cSLE. Alternatively, larger studies to better determine who is most at risk for medication nonadherence are needed.

The primary limitation of this study is an inability to discern the directionality of the relationship observed. The cross-sectional study design can only be used to identify associations, not to determine causality. Given that depression is a known symptom of neuropsychiatric SLE, the alternative temporal relationship must be considered. The small sample size and single-site design is also a limitation, as it may affect the accuracy of the regression model and generalizability of the study results. However, the sample size was sufficient to detect a statistically significant difference between groups, as was predicted by a priori power calculations. In addition, the sample size in this study is similar to that reported in prior studies addressing rates of depression and medication non-adherence in cSLE.^{12,14} Furthermore, nearly 80% of the convenience sample was recruited with only 1 patient declining to participate, thereby limiting selection bias. Another limitation is that only covariates available within the EMR could be measured in this preliminary study. Specifically, potentially relevant psychosocial factors could not be assessed (i.e. household income, household education level, caregiver marital status, presence of siblings). However, measuring the types of insurance could be considered as a proxy for socioeconomic status, and no statistically significant difference between insurance groups was found.

The tools used to define the exposure and outcome (PHQ-9 and MASRI, respectively) of the study each have inherent limitations. The PHQ-9 is a screening tool, and while the tool was designed based on diagnostic criteria for major depression, it is not a diagnostic tool. Rather, the results from the PHQ-9 are used as a proxy measure for a diagnosis of depression. As a result, there is a potential for exposure misclassification. The MASRI relies on self-report of medication non-adherence. While efforts are made to promote accurate reporting, there remains a risk for recall bias and social desirability bias. Nonetheless, the tools used in this study are standardized and validated in the population of interest, thereby limiting the overall risk of misclassification and information bias. In addition, the ability to use them within the clinical setting allowed for capture of information regarding suicidal ideation that might not have been ethical to obtain using other study designs.

This study adds to the literature reporting high rates of depression and suicidal ideation in patients with cSLE; is one of the only studies reporting rates of medication non-adherence in this population; and is the first known study that provides preliminary evidence that depression and medication non-adherence are related in cSLE. Furthermore, this study has demonstrated feasibility of administering depression and medication non-adherence screens within a clinical setting. Feasibility is important because developing and evaluating interventions to improve depression and medication non-adherence first requires measurement of these factors at the point of service. Prospective multicenter cohort studies are needed to better understand the relationship of depression and medication non-adherence and to identify potential risk factors for depression and medication non-adherence. Such

research will help inform the development of improved systems of care to ameliorate depression and medication non-adherence, thereby improving health outcomes for this vulnerable population of children.

Acknowledgments

We thank all the patients and their parents for their participation in this study. We also thank Manda Mitchell and Amber Bullington for their contributions to survey collection.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors. Dr. Davis received support from the National Institutes of Health via a training grant [2T32AR059039-06A1] and resources from the Vanderbilt Clinical and Translational Science Award [1UL1RR024975] including access to REDCap [UL1 TR000445].

References

1. Lim LS, Pullenayegum E, Lim L, Gladman D, Feldman B, Silverman E. From Childhood to Adulthood: the trajectory of damage in patients with childhood-onset systemic lupus erythematosus. *Arthritis Care Res.* Epub ahead of print 24 Jan 2017.
2. Hiraki LT, Benseler SM, Tyrrell PN, Herbert D, Harvey E, Silverman ED. Clinical and laboratory characteristics and long-term outcome of pediatric systemic lupus erythematosus: A longitudinal study. *J of Pediatr.* 2008; 152:550–556. [PubMed: 18346514]
3. Brunner HI, Gladman DD, Ibanez D, Urowitz MD, Silverman ED. Difference in disease features between childhood-onset and adult-onset systemic lupus erythematosus. *Arthritis Rheum.* 2008; 58:556–562. [PubMed: 18240232]
4. Watson L, Leone V, Pilkington C, et al. Disease activity, severity, and damage in UK Juvenile-Onset Systemic Lupus Erythematosus Cohort. *Arthritis Rheum.* 2012; 64:2356–2365. [PubMed: 22294381]
5. Moldovan I, Katsaros E, Carr FN, et al. The patient Reported Outcomes in Lupus (PATROL) study: role of depression in health-related quality of life in Southern California lupus cohort. *Lupus.* 2011; 20:1285–1292. [PubMed: 21813589]
6. DiMatteo MR, Lepper HS, Croghan TW. Depression is a risk factor for noncompliance with medical treatment: Meta-analysis of the effects of anxiety and depression on patient adherence. *Arch Intern Med.* 2000; 160:2101–2107. [PubMed: 10904452]
7. Julian LJ, Yelin E, Yazdany J, et al. Depression, medication adherence, and service utilization in systemic lupus erythematosus. *Arthritis Rheum.* 2009; 61:240–246. [PubMed: 19177526]
8. Petri M, Perez-Gutthann S, Longenecker JC, Hochberg M. Morbidity of systemic lupus erythematosus: role of race and socioeconomic status. *Am J Med.* 1991; 91:345–353. [PubMed: 1951378]
9. Adler M, Chambers S, Edwards C, Neild G, Isenberg D. An assessment of renal failure in an SLE cohort with special reference to ethnicity, over a 25-year period. *Rheumatol.* 2006; 45:1144–1147.
10. Rojas-Serrano J, Cardiel MH. Lupus patients in an emergency unit. Causes of consultation, hospitalization, and outcome. A cohort study. *Lupus.* 2000; 9:601–606. [PubMed: 11035435]
11. Costedoat-Chalumeau N, Pouchot J, Guettrot-Imbert G, et al. Adherence to treatment in systemic lupus erythematosus patients. *Best Pract Res Clin Rheumatol.* 2013; 27:329–340. [PubMed: 24238690]
12. Sibbitt WL, Brandt JR, Johnson CR, et al. The incidence and prevalence of neuropsychiatric syndromes in pediatric onset systemic lupus erythematosus. *J Rheumatol.* 2002; 29:1536–1542. [PubMed: 12136916]
13. Kohut SA, Williams TS, Jayanthikumar J, et al. Depressive symptoms are prevalent in childhood-onset systemic lupus erythematosus. *Lupus.* 2013; 22:712–720. [PubMed: 23704369]
14. Knight A, Weiss P, Morales K, Gerdes M, Gutstein A, Vickery M, et al. Depression and anxiety and their association with healthcare utilization in pediatric lupus and mixed connective tissue

- disease patients: a cross-sectional study. *Pediatr Rheumatol Online J*. 2014; 12:42. [PubMed: 25242900]
15. Ting TV, Kudalkar D, Nelson S, et al. Usefulness of cellular text messaging for improving adherence among adolescents and young adults with systemic lupus erythematosus. *J Rheumatol*. 2012; 39:174–179. [PubMed: 22089460]
 16. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med*. 2001; 16:606–613. [PubMed: 11556941]
 17. Richardson LP, McCauley E, Grossman DC, et al. Evaluation of the PHQ-9 Item for detecting major depression among adolescents. *Pediatrics*. 2010; 126:1117–1123. [PubMed: 21041282]
 18. Walsh JC, Mandalia S, Gazzard BG. Responses to a 1 month self-report on adherence to antiretroviral therapy are consistent with electronic data and virological treatment outcome. *AIDS*. 2002; 16:269–277. [PubMed: 11807312]
 19. Koneru S, Shishov M, Ware A, et al. Effectively Measuring Adherence to Medications for Systemic Lupus Erythematosus in a Clinical Trial. *Arthritis Rheum*. 2007; 57:1000–1006. [PubMed: 17665465]
 20. Bombardier C, Gladman DD, Urowitz MB, Caron D, Chang CH. Derivation of the SLEDAI. A disease activity index for lupus patients. The Committee on Prognosis Studies in Lupus. *Arthritis Rheum*. 1992; 35:630–640. [PubMed: 1599520]
 21. Brunner HI, Feldman BM, Bombardier C, Silverman ED. Sensitivity of the Systemic Lupus Erythematosus Disease Activity Index, British Isles Lupus Assessment Group Index, and Systemic Lupus Activity Measure in the evaluation of clinical change in childhood-onset systemic lupus erythematosus. *Arthritis Rheum*. 1999; 42:1354–1360. [PubMed: 10403262]
 22. Rosenbaum PR, Rubin DB. The central role of the propensity score in observational studies for causal effects. *Biometrika*. 1983; 70:41–55.
 23. d'Agostino RB. Tutorial in biostatistics: propensity score methods for bias reduction in the comparison of a treatment to a non-randomized control group. *Stat Med*. 1998; 17:2265–2281. [PubMed: 9802183]
 24. Leon AC, Mueller TI, Solomon DA, Keller MB. A dynamic adaptation of the propensity score adjustment for effectiveness analyses of ordinal doses of treatment. *Stat Med*. 2001; 20:1487–1498. [PubMed: 11343369]
 25. Nassi L, Punaro L, Morton A, et al. Suicidal ideation common in childhood-onset systemic lupus erythematosus (cSLE): Genetic expression and depressive symptoms in cSLE. *Arthritis Rheum*. 2009; 60:1532.
 26. Lim LS, Lefebvre A, Benseler S, Peralta M, Silverman ED. Psychiatric illness of systemic lupus erythematosus in childhood: spectrum of clinically important manifestations. *J Rheumatol*. 2013; 40:506–512. [PubMed: 23242179]
 27. Krause M, Zamora-Legoff JA, Crowson CS, Wampler Muskardin T, Mason T, Matteson EL. Population-based study outcomes of patients with juvenile idiopathic arthritis (JIA) compared to non-JIA subjects. *Semin Arthritis Rheum*. 2017; 46:439–443. [PubMed: 27522464]
 28. Knight AM, Xie M, Mandell DS. Disparities in psychiatric diagnosis and treatment for youth with systemic lupus erythematosus: analysis of a national US Medicaid sample. *J Rheumatol*. 2016; 43:1427–1433. [PubMed: 27134262]
 29. Child and Adolescent Health Measurement Initiative, Data Resource Center on Child and Adolescent Health. National Survey of Children with Special Health Care Needs. 2010. <http://www.childhealthdata.org/browse/ata-snapshots/cshcn-profiles/condition-specific?rpt=12&cond=15&geo=1&ind=144>. Accessed 21 Sept 2017
 30. Child and Adolescent Health Measurement Initiative, Data Resource Center on Child and Adolescent Health. National Survey of Children with Special Health Care Needs. 2010. <http://childhealthdata.org/browse/data-snapshots/cshcn-profiles/condition-specific?rpt=12&cond=7&geo=1&ind=144>. Accessed 21 Sept 2017
 31. Child and Adolescent Health Measurement Initiative, Data Resource Center on Child and Adolescent Health. National Survey of Children with Special Health Care Needs. 2010. <http://childhealthdata.org/browse/data-snapshots/cshcn-profiles/condition-specific?cond=1&geo=1&rpt=12&ind=144>. Accessed 21 Sept 2017

32. Knight AM, Vickery ME, Muscal E, et al. Identifying Targets for Improving Mental Health Care of Adolescents with Lupus: Perspectives from Pediatric Rheumatology Clinicians in the United States and Canada. *J Rheumatol*. 2016; 43:1136–1145. [PubMed: 27036378]
33. Mehat P, Atiquzzaman M, Esdalle JM, Avina-Zubieta A, De Vera MA. Medication non-adherence in systemic lupus erythematosus: a systemic review. *Arthritis Care Res*. 2017; 69:1706–1713.
34. Spekhorst LM, Hummel TZ, Benninga MA, van Rheenen PF, Kindermann A. Adherence to Oral Maintenance Treatment in Adolescents with Inflammatory Bowel Disease. *J Pediatr Gastroenterol Nutr*. 2016; 62:264–270. [PubMed: 26230905]
35. Khandelwai S, Sengar GS, Sharma M, Choudhary S, Nagaraj N. Psychosocial Illness in Children with Type I Diabetes Mellitus: Prevalence, Pattern, and Risk Factors. *J Clin Diagn Res*. 2016; 10:SC05–SC08.
36. Abdul-Sattar AB, Abou El Magd SA. Determinants of medication non-adherence in Egyptian patients with systemic lupus erythematosus: Sharkia Governorate. *Rheumatol Int*. 2014; 35:1045–1051. [PubMed: 25424491]
37. Marengo MF, Waimann CA, de Achaval S, Zhang H, Garcia-Gonzalez A, Richardson MN, et al. Measuring therapeutic adherence in systemic lupus erythematosus with electronic monitoring. *Lupus*. 2012; 21:1158–1165. [PubMed: 22588588]

Figure 1.

Of the 67 potentially eligible patients identified, a total of 51 patients were enrolled in the study. Only 1 patient declined to participate, and only 1 patient was excluded due to the patient caregiver's inability to complete the consent process in English.

Figure 2.

The regression analysis shows that as the severity of depressive symptoms increases, the degree of medication non-adherence also increases when controlling for the linear predictors from the propensity score analysis.

Table 1

Demographics and Disease Characteristics by Depression Screen

	PHQ-9 score < 5 N = 21	PHQ-9 score 5 N = 30	p-value
Age (years)	17.0 (15.0–18.0)	16.5 (15.0–18.0)	0.725
Sex			
Male	3 (14.3)	1 (3.3)	0.293
Female	18 (85.7)	29 (96.7)	
Race/Ethnicity			
Caucasian	8 (38.1)	7 (23.3)	
Black	8 (38.1)	19 (63.3)	0.098
Hispanic	3 (14.3)	0 (0)	
Asian	2 (9.5)	3 (10.0)	
Other	0 (0)	1 (3.3)	
Insurance			
Commercial	8 (38.1)	13 (43.3)	0.639
Medicaid	12 (57.1)	17 (56.7)	
Tricare	1 (4.8)	0 (0)	
Age at diagnosis (years)	14.0 (13.0–15.0)	14.0 (9.3–15.0)	0.607
Disease duration (years)	2.0 (1.0–4.0)	1.9 (0.8–4.0)	0.843
SLEDAI score	4.0 (2.0–6.0)	4.0 (0.5–8.0)	0.954
No. of medications	6.0 (5.0–8.0)	7.0 (6.0–8.8)	0.155
Oral Steroids			
No	5 (23.8)	2 (6.7)	0.109
Yes	16 (76.2)	28 (93.3)	
Prednisone dose (mg/kg/day)	0.11 (0.08–0.14)	0.11 (0.06–0.19)	0.643
Presence of lupus nephritis	6 (28.6)	14 (46.7)	0.193
Receives mental health services	4 (19.0)	12 (40.0)	0.112

Values are presented as median (IQR) or N (%).

Table 2

Demographics and Disease Characteristics by Medication Adherence

	MASRI score N = 41	80 MASRI score < 80 N = 10	p-value
Age (years)	17.0 (15.0–18.0)	17.0 (15.3–18.8)	0.596
Sex			
Male	4 (9.8)	0 (0)	0.573
Female	37 (90.2)	10 (100)	
Race/Ethnicity			
Caucasian	11 (26.8)	4 (40.0)	
Black	21 (51.2)	6 (60.0)	0.788
Hispanic	3 (7.3)	0 (0)	
Asian	5 (12.2)	0 (0)	
Other	1 (2.4)	0 (0)	
Insurance			
Commercial	17 (41.5)	4 (40.0)	1.00
Medicaid	23 (56.1)	6 (60.0)	
Tricare	1 (2.4)	0 (0)	
Age at diagnosis (years)	14.0 (12.0–16.0)	12.0 (9.5–14.8)	0.096
Disease duration (years)	1.8 (0.6–3.0)	5.0 (2.0–7.0)	0.033 *
SLEDAI score	4.0 (2.0–8.0)	4.0 (0.0–6.0)	0.364
No. of medications	6.0 (5.0–8.0)	7.0 (6.3–8.0)	0.146
Oral Steroids			
No	4 (12.2)	2 (20.0)	0.612
Yes	36 (87.8)	8 (80.0)	
Prednisone dose (mg/kg/day)	0.11 (0.08–0.21)	0.08 (0.04–0.13)	0.162
Presence of lupus nephritis	15 (36.6)	5 (50.0)	0.486
Receives mental health services	10 (24.4)	6 (60.0)	0.054

Values are presented as median (IQR) or N (%).

* An asterisk indicates statistical significance ($p < 0.05$).

Table 3

Demographics and Disease Characteristics by Presence or Absence of Suicidal Ideation

	(-) Suicidal Ideation N = 44	(+) Suicidal Ideation N = 7	p-value
Age (years)	17.0 (15.0-18.0)	15.0 (12.0-17.0)	0.223
Sex			
Male	4 (9.1)	0 (0)	1.000
Female	40 (90.9)	7 (100)	
Race/Ethnicity			
Caucasian	14 (31.8)	1 (14.3)	
Black	23 (52.3)	4 (57.1)	0.382
Hispanic	3 (6.8)	0 (0)	
Asian	3 (6.8)	2 (28.6)	
Other	1 (2.3)	0 (0)	
Insurance			
Commercial	18 (40.9)	3 (42.9)	1.000
Medicaid	25 (56.8)	4 (57.1)	
Tricare	1 (2.3)	0 (0)	
Age at diagnosis (years)	14.5 (13.0-16.0)	9.0 (7.5-9.0)	< 0.001 *
Disease duration (years)	2.0 (0.7-4.0)	5.0 (1.7-8.0)	0.077
SLEDAI score	4.0 (1.5-6.0)	6.0 (1.0-11.0)	0.501
No. of medications	6.0 (5.0-8.0)	7.0 (6.0-9.0)	0.341
Oral Steroids			
No	7 (15.9)	0 (0)	0.573
Yes	37 (84.1)	7 (100)	
Prednisone dose (mg/kg/day)	0.11 (0.06-0.15)	0.13 (0.09-0.36)	0.160
Presence of lupus nephritis	15 (34.1)	5 (71.4)	0.096
Receives mental health services	13 (29.6)	3 (42.9)	0.664

Values are presented as median (IQR) or N (%).

* An asterisk indicates statistical significance (p < 0.05).