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RESEARCH ARTICLE

Multidisciplinary care in patients with systemic lupus erythematosus: a randomized controlled trial in China

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Abstract

Background For the large number of systemic lupus erythematosus (SLE) patients in China, it is critical to carry out effective disease management to improve the treatment effect and reduce disease burden. A pharmacist-led multidisciplinary care model has not been reported in Chinese SLE patients before. *Objective* To assess the effect of patient-centered, pharmacist-led, multidisciplinary care on clinical outcomes and satisfaction with health care in Chinese SLE patients. Setting: The South Campus, Renji Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China. *Method* Participants were 143 systemic lupus erythematosus patients randomly assigned to either the intervention group (multidisciplinary care: physician, pharmacist and nurse) or the control group (usual care only). *Main outcome measures* The primary outcome was scores on the systemic lupus erythematosus disease activity index-2000, the satisfaction with information about medicines scale, and the EuroQol five-dimension questionnaire, assessed at baseline and 12 months. *Results* Between October 1, 2017 and October 1, 2018, 42 participants were included in the intervention group and 40 in the control group. At 12 months, results for the systemic lupus erythematosus disease activity index-2000 differed significantly between the intervention group and the control group (0 vs. 2, $P=0.027$). Patient satisfaction with health care was also significantly greater in the intervention group than in the control group (92.9 vs. 0%, $P=0.000$). According to the EuroQol five-dimension questionnaire, health quality was also improved (0.94 vs. 0.85, $P=0.006$). *Conclusion* Our multidisciplinary care team significantly improved clinical outcomes and satisfaction with drug information in Chinese systemic lupus erythematosus patients.

Keywords China · Patient-centered · Pharmacist-led care · Satisfaction with medicines information · Systemic lupus erythematosus

Impacts on practice

- Low treatment adherence and satisfaction with medication counselling are barriers to remission in systemic lupus erythematosus patients in China.
- If pharmacists take an active role in the multidiscipline team to improve disease management of lupus patients, they help to reduce the unnecessary use of medical resources.

Introduction

The systemic lupus erythematosus (SLE), an autoimmune disease defined by a vast amount of different autoantibodies in the blood and involves multiple various organ systems (e.g., joints, skin, lungs, brain, kidneys) [1].

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Approximately 1.3 million people in China live with SLE, where the average prevalence is 0.0975–0.376% [2, 3]. At present, although there is no cure for SLE, medication can minimize organ damage and control disease activity [4]. Therefore, effective disease management, which includes adherence to the medication regimen, is the key to maximizing the treatment effect in SLE patients.

Optimal adherence to medications may reduce the risk of disease flare. However, a recent 10-year report found that global adherence rates ranged 3–76% [5–8], and were 35–48.7% in China [7]. Diverse measures have been designed to improve adherence, including drug diaries, pill counters, automated reminders, patient counseling and improving social support [9]. However, all of these interventions involve substantial cost, time and effort, with a variable response dependent on health consciousness, treatment prescription and self-motivation. Such methods are not feasible in settings like China, with its poor health literacy, low health awareness and uneven distribution of medical resources.

As a part of medical policy reform in China, a large number of pharmacists have been liberated from traditional dispensing. Pharmacy-based interventions have been proven effective in improving treatment adherence in patients with chronic diseases such as diabetes, hypertension and coronary heart disease [10], but there is no report about the effectiveness in SLE patients in mainland China. Our study is aimed to assess the effect on clinical outcomes and adherence of a patient-centered, pharmacist-led multidisciplinary care model in Shanghai Renji Hospital, one of the largest rheumatology centers in China.

Aim of the study

To evaluate the effect of the patient-centered, pharmacist-led multidisciplinary care model on the disease activity, health quality and satisfaction with information about drugs in SLE patients.

Ethics approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (Renji Hospital Ethics Committee, [2016]195) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

Method

Study setting and sample size calculation

This study was conducted at Renji Hospital, Shanghai, China. This center is one of the largest rheumatology centers in China, and the patients are from all regions of the country. All participants completed questionnaires about their adherence to treatment, beliefs about medicines and satisfaction with information on the treatment drugs.

The sample size was calculated using our previous preliminary experiment data, to compare the mean systemic lupus erythematosus disease activity index-2000 (SLEDAI-2K) scores [11, 12] between the intervention and control group. The study was designed with 80% power (with a 2-sided alpha level of 0.05) to detect a difference of 1 in the mean SLEDAI-2K scores. With the anticipation of a 5% drop-out rate, a total of 40 patients was needed in each study group (Clinical Research Sample Size Calculator, CRESS version 1.3, Shanghai, China).

Participants

Patients using rheumatic drugs (glucocorticoids, immunomodulators and immunosuppressants, non-steroidal anti-inflammatory drugs [NSAID] and biological drugs) were considered for inclusion if they fulfilled the American College of Rheumatology (ACR) 2012 criteria for SLE and visited the outpatient clinic of the South Campus of Renji Hospital between October 1, 2017 and October 1, 2018.

Patients were excluded if they could not read, had a severe mental disorder, had serious physical constraints, had a life expectancy of fewer than 12 months or had changed doctors within the last 12 months. All others were included, regardless of demographic, disease or treatment characteristics. Data were collected on demographic characteristics (age, sex, marital status, education level, employment and type of medical insurance), disease characteristics (duration, comorbidities and health status based on the three-level EuroQol five-dimensions [EQ-5D-3L] [13, 14], the Systemic Lupus International Collaborating Clinics [SLICC] [15, 16] and SLEDAI-2 K scores) and treatment characteristics (types of pills prescribed daily, use of glucocorticoids, use of immunomodulators and immunosuppressants [e.g., tacrolimus, mycophenolate mofetil, hydroxychloroquine, cyclophosphamide], use of NSAIDs, use of a biological drugs [e.g., rituximab], dosing frequency and side effects).

Assignment of interventions

Patients in the intervention group received multidisciplinary care (from a physician, pharmacist and nurse) in addition to their routine clinical follow up. Initially, patients were interviewed by a pharmacist to get detailed medical, family and social histories, diet and exercise patterns. Each received a booklet to guide them in taking their medicines (Fig. 1). During the routine clinical follow up, the patient's medication history was reviewed by a pharmacist and counseling was provided on any inappropriate drug use. After the clinical session ended, medications were dispensed to the patient and education provided related to the medications. Scheduled in-person or telephone follow-up meetings were given to the patients at 3-week to 3-month intervals that coincided with the drug refills or clinical follow-up date. During each visit, structured individualized education was given on medications, complications and healthy lifestyle, according to the needs of each patient. The pharmacists had prior approval from the doctors to adjust the doses of prednisone when necessary. The steps of the intervention are shown in Fig. 2.

Patients in the non-intervention (control) group were instructed to receive routine clinical follow up with nurses every 3 to 4 months. The received no education from a pharmacist. Patients' knowledge on medications, compliance, quality of life and disease activity in both groups were assessed at 0 and 12 months.

Fig. 1 Medication education booklet

Methylprednisolone Tablets

It is used to treat autoimmune diseases. Usage and dosage refer to prescription, **do not stop without doctor's advice!** It is best to take this medicine with food or milk to relieve side effects in digestive tract. The drug exists in active form and is suitable for patients with abnormal liver function.

This medicine may cause the following problems: susceptibility to infection, increased appetite, edema, weight gain, osteoporosis, cataract or glaucoma. If you use this drug for a long time, the following items need to be monitored, so you must revisit regularly: blood sugar, blood electrolyte, stool occult blood, blood pressure, osteoporosis, ophthalmic examination, etc.

Call your pharmacist right away if you notice any of these side effects: severe stomach pain or black stool. When go to dentist or any other doctor, please inform the doctor that you are using this drug.

Methotrexate Tablets

It is used to treat autoimmune diseases such as rheumatoid arthritis, dermatomyositis, systemic lupus erythematosus and so on. **Take it once a week!** It is best to take this medicine at fixed time weekly. Take Folic Acid Tablets at least one day after taking the drug to relieve the side effects.

This medicine may cause the following problems: nausea and poor appetite, hair loss, etc. Call your pharmacist right away if you notice any of these side effects: black stool, Multiple subcutaneous congestion, severe abdominal pain and diarrhea, etc.

If there is a bone marrow suppression adverse reaction, your blood cell count may be abnormal two weeks after your first medication, so you must revisit on time to check the blood routine. Because of the teratogenic effect of this medicine, man should be contraceptive for **at least 3 months** after withdrawal, and female patients should be contraceptive **at least within 2 menstrual cycles!**

Fig. 2 The flow chart of intervention

Study procedures

Patients were randomized by computer. Participants were assigned to groups in a parallel fashion in a 1:1 ratio. After allocation, the research supervisor (Prof. Li) explained the details of the intervention to the participants. Cases allocated to the usual care (control) group were informed of their date of follow up after every visit. The staff who randomized (Dr. Ding), those who assessed and those who delivered the intervention were all different.

Participants were invited to participate after assessment of eligibility and those who consented were interviewed to gather their demographic, medical and prescription information. The baseline characteristic for each patient was also recorded, followed by their randomization into either the usual care group or the intervention group. Patients' knowledge of medications, compliance, quality of life and disease activity were assessed during every visit.

Primary outcome measures

Disease activity

Organ damage was assessed using the SLICC and disease activity was evaluated using the SLEDAI-2K. These are valid, reliable and widely used criteria to measure disease activity in SLE patients. Based on the SLEDAI-2K score, the disease activity in patients were classified as inactive (0–4 points), mild (5–9 points), moderate (10–14 points) or severe (≥ 15 points).

Satisfaction with information on treatment

The main outcome of the study was patient satisfaction with information on treatment, using the Chinese version of the validated Satisfaction with Information about Medicines Scale (SIMS) [17]. SIMS evaluates the extent to which patients feel that they have been given adequate information on prescribed medicines [18]. The questionnaire consists of 18 items, each referring to a particular aspect of medicine use. Patients are asked to rate the information they have been provided using the following response scale: "too much," "about right," "too little," "none received," "none needed." Satisfaction with information (ratings "about right" or "none needed") was given a score of 1. Dissatisfaction (ratings "too much," "too little" or "none received") was scored as 0. The median scores of the three SIMS scales were used to define dissatisfaction (< 16 of 18 items, < 8 of 9 items and < 8 of 9 items for, respectively, overall satisfaction rating, subscale action and usage and subscale potential problems). Because the distribution of the three SIMS scales was left-skewed, the scales were dichotomized into dissatisfaction (0) versus satisfaction (1).

Measurement of health status

The general health status of patients was evaluated using the Chinese version of the general population-based EQ-5D-3L questionnaire. Each EQ-5D-3L health state was scored as 1 (no problems), 2 (some/moderate problems) or 3 (extreme problems) to indicate functional levels in five dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression). The "time-trade-off" EQ-5D-index was used to assess quality of life.

Secondary outcome measures

Self-reported adherence

Self-reported adherence was assessed using the Compliance Questionnaire for Rheumatology (CQR) [19]. Previous studies show it has proven good reliability and validity in SLE patients. The CQR consists of 19 items about taking medicine, for which patients are asked to score the degree to which they agree with each statement. Answers are based on 4-point Likert scales (4: agree very much; 3: agree; 2: do not agree; 1: do not agree at all). Non-adherence was defined by a CQR score below 80% [20].

Beliefs about medicines

The Beliefs about Medicines Questionnaire (BMQ) has 10 questions in two subscales that capture beliefs about the prescribed medication [21]. The subscales measure (1) patient beliefs about the necessity of a prescribed medication to control their illness and (2) their concerns about the potential adverse consequences of taking the medication. Each subscale is measured with 5 items rated on a 5-point Likert scale. A necessity–concerns differential was calculated by subtracting the individuals' concerns scores from the individuals' necessity scores, leading to a range from -20 to 20 [22]. Higher scores on this differential indicate higher perceived necessity and/or lower concerns about the drugs.

Statistical analysis

Descriptive statistics were used for the demographic and other patient characteristics. The categorical data were summarized as numbers and percentages; the continuous data in normal distribution were summarized using the mean and standard deviation, or using median and quartiles, as appropriate. Differences in the demographic and clinical characteristics between groups were examined using the Chi-square test for categorical variables and the Wilcoxon rank-sum test for continuous variables. The results were

significant if the P value was < 0.05. All analyses were performed with IBM SPSS Statistics for Windows, Version 21.0 (IBM Corp., Armonk, NY).

Results

Of the 208 patients approached for enrollment, 65 were excluded due to ineligibility (Fig. 3) and 143 were randomized into the groups. After the 12-month follow up, 40 participants in the control group and 42 in the intervention group remained for analysis.

Baseline characteristics

Of the 82 participants analyzed in the study, 74 (90.2%) were female. The mean age was 31.5 ± 11.1 years in the intervention group and 30.3 ± 11.8 years in the control group. Most of the participants were married (n = 53, 64.6%) and unemployed (n = 44, 54.7%). In terms of education, 16 (40%) patients in the control group had a primary education, and 15 (35.7%) patients in the intervention group had a secondary education. In the control group, 21 (52.5%) patients had been diagnosed with SLE for more than 5 years, versus 19 (45.2%) in the intervention group. Most of the patients in the control group (n = 19, 47.5%) had 2 comorbidities, whereas most in the intervention group (n = 25, 59.5%) had no comorbidity. Patients in each group took about 4 types of pills daily. Most were prescribed glucocorticoids (n = 75, 91.5%) and immunomodulators or immunosuppressants (n = 50, 61.0%). NSAIDs and biologic drugs were not widely used in these patients. Most patients (n = 74, 90.2%) experienced no adverse drug side effects. At baseline, none of the differences in characteristics between groups were statistically significant (Table 1).

Outcomes at 12 months

At baseline, none of the evaluating indicators were statistically different between the two groups ($P > 0.05$). The baseline median SLEDAI-2K scores were similar: 8 in the control group and 7.5 in the intervention group. After 12-month follow up, SLEDAI-2K scores significantly decreased in the intervention group (7.98–1.36 for control vs. 7.50–2.78 for intervention) ($P = 0.027$).

No statistical difference was detected in patients' initial satisfaction about their medication information between the two groups (7 participants were satisfied in the control group and 11 in the intervention group). After 12 months, satisfaction improved substantially in the intervention group (39 patients were satisfied). This difference between the two groups was statistically significant ($P < 0.000$).

In terms of quality of life, there was no statistically significant difference in the initial EQ-5D-index (0.85 in the control group and 0.81 in the intervention group). After follow-up, the patients' health status in the intervention group had a marked improvement. The EQ-5D-index of patients in the intervention group increased from 0.81 to 0.94 ($P = 0.006$). No differences in SLICC, CQR or BMQ scores were detected (Table 2).

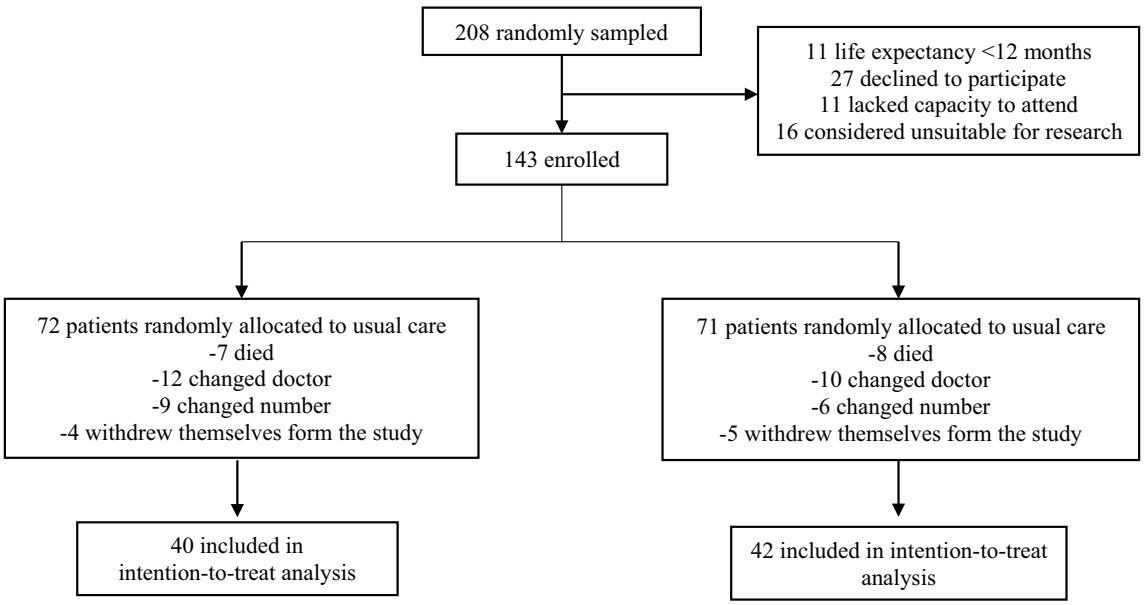

Fig. 3 Trial profile

Table 1 Baseline demographic and clinical characteristics of outpatients with lupus (n = 82)

Characteristics	Descriptive		*P* value
	Usual care group (n = 40)	Intervention group (n = 42)	
Age (years), mean (SD)	30.3 (11.8)	31.5 (11.1)	0.6314
Sex, female, n (%)	36 (90)	38 (90.5)	0.9430
Marital status, n (%)			0.3917
Married	24 (60)	29 (69.1)	
Other marital status	16 (40)	13 (31.0)	
Education level, n (%)			0.6876
Primary (0–6 years)	16 (40)	13 (31.0)	
Secondary (7–12 years)	12 (30)	15 (35.7)	
Higher (≥ 13 years)	12 (30)	14 (33.3)	
Employment, n (%)			0.8373
Employed	19 (47.5)	19 (45.2)	
Unemployed	21 (52.5)	23 (54.8)	
Disease duration, n (%)			0.1318
< 1 year	0 (0)	4 (9.5)	
1–5 year	19 (47.5)	19 (45.2)	
≥ 5 year	21 (52.5)	19 (45.2)	
Comorbidities, n (%)			0.0922
0	13 (32.5)	25 (59.5)	
1	19 (47.5)	12 (28.6)	
2	5 (12.5)	4 (9.5)	
≥ 3	3 (7.5)	1 (2.4)	
Types of pills prescribed daily, median (p25, p75)	4 (2.8, 6)	4 (2.3, 6)	0.0888
Use of GC, n (%)	38 (95)	37(88.1)	0.2634
Number of immunomodulators and immunosuppressants, n (%)			0.7140
0	14 (35)	18 (42.9)	
1	16 (40)	16 (38.1)	
≥ 2	10 (25)	8 (19.1)	
Use of NSAID, n (%)	4 (10)	5 (11.9)	0.9421
Use of biologic drugs, n (%)	2 (5)	7 (16.7)	0.0912
Daily dosing frequency, n (%)			0.0713
< Once daily	10 (25)	15 (35.7)	
Once daily	7 (17.5)	13 (31.0)	
Twice daily	14 (35)	5 (11.9)	
≥ Thrice daily	9 (22.5)	9 (21.4)	
Side effects, n (%)			0.2116
0	34 (85)	40 (95.2)	
1–2	4 (10)	2 (4.8)	
≥ 3	2 (5)	0 (0)	

GC glucocorticoid, *NSAID* non-steroidal anti-inflammatory drug, *SD* standard deviation, *SLEDAI* systemic lupus erythematosus disease activity index, *SLICC* the Systemic Lupus International Collaborating Clinics

Discussion

To the best of our knowledge, this is the first randomized prospective study to evaluate the effect of a patient-centered, pharmacist-led multidisciplinary care model on clinical outcomes in SLE patients in mainland China. In our study, an innovative pharmacist-led intervention was provided to SLE patients, including prescription review and adjustment, patient-centered medicine education and guidance, and periodic follow-up assessment. Satisfaction with drug information, quality of life and disease activity were set as the primary outcomes.

Table 2 Outcomes at 12 months

	Usual care group (n = 40)		Intervention group (n = 42)		Between group *P* value	
	Baseline	End	Baseline	End	Baseline	End
Primary outcomes						
SLEDAI, median (p25, p75)	8 (2, 12)	2 (0.8, 3.3)	7.5 (4, 11)	0 (0, 2)	0.665	0.027*
SIMS, satisfied (n, %)	7, 17.5	0, 0	11, 26.2	39, 92.86	0.342	0.000***
Eq5D, median (p25, p75)	0.85 (0.64, 0.88)	0.85 (0.76, 0.94)	0.81 (0.67, 0.94)	0.94 (0.85, 0.94)	0.640	0.006**
Secondary outcomes						
SLICC, median (p25, p75)	1 (0, 1.3)	0.5 (0, 2.3)	0 (0, 1)	0 (0, 2)	0.593	0.146
CQR, median (p25, p75)	55 (51.8, 64)	59 (53, 63.3)	56.5 (52.3,63.8)	55 (51, 65)	0.943	0.318
BMQ, median (p25, p75)	2.5 (0, 6.3)	3 (1.8, 5)	2 (0, 6.8)	3 (0, 7)	0.993	0.981

*$P < 0.05$; **$P < 0.01$; ***$P < 0.001$

BMQ beliefs about medicines questionnaire, *CQR* compliance questionnaire rheumatology, *EQ-5D* EuroQol five-dimensions, *SLEDAI* systemic lupus erythematosus disease activity index, *SLICC* the Systemic Lupus International Collaborating Clinics, *SIMS* satisfaction with information about medicines scale

We found that the intervention was associated with greater satisfaction with drug information ($P = 0.000$). Previous studies have shown that educational interventions and counselling tips can improve patient understanding of drugs in those with diabetes [23], hypertension [24] and cancer [18]. The control group had much lower satisfaction with medication education than the intervention group (0 satisfied vs 7 satisfied, respectively). The reason for this result might be that some patients in the control group got a refill of their medications at their local hospital, and so did not re-visit the main hospital during the follow-up period. So, during this period they may not have received adequate health education, which led to a decline in their satisfaction with patient education [25]. However, in the intervention group, we arranged regular meetings or phone calls to ensure patients received timely health consultations.

Unlike previous studies, we found that our intervention could improve disease remission ($P = 0.027$). This result may be due to the fact that patient-centered multidisciplinary disease management helped improve patient compliance with treatment. As a chronic disease, SLE requires treatment compliance in order for clinical outcomes to improve. Past studies aimed at improving patient compliance failed to achieve the desired results because of switching among drugs [26], patients' lack of knowledge about disease and drugs [27] and contextual factors [28]. Because of the small sample size in this study, we could focus on each patient's specific problems and make up for the defects of previous studies. From our findings, patient-centered medication education and management can resolve the specific treatment-related problems of each patient, thereby improving treatment compliance and ultimately improving clinical outcomes.

Quality of life was also improved in the intervention arm after 12-month follow up. Previous studies have shown that the quality of life in patients with chronic diseases can be improved through disease management [29, 30]. In view of our previous research outcomes [7], patients had many concerns about the side effects of drugs; these concerns affected their health status in terms of depression and anxiety. Previous studies also found that depression is an important factor affecting the quality of life in SLE patients [31–33]. For this study, a professional pharmacist reinterpreted the information on adverse drug reactions for patients. The SIMS results showed significant improvement in both patients understanding of drug side effects and patient satisfaction with patient education. Patient education may reduce the negative emotions caused by fear of adverse reactions, and ultimately improve patient quality of life. In future studies, we should improve the assessment of patients' mental status to verify this hypothesis.

There were some limitations in our work. First, the study enrolled a small number of patients, partly due to the rarity of SLE. Second, our patients may not be completely representative of Chinese patients in general. However, our hospital is one of the largest rheumatology centers in the country, with patients from all parts of China, so our research results are representative of the SLE patient population. Further research on this topic should seek to enroll more patients from different areas. Nevertheless, our results prove the effectiveness of patient-centered, pharmacist-led multidisciplinary care in SLE patients.

Conclusion

The pharmacist-led multidisciplinary care program significantly improved the disease remission, satisfaction with medicine information and health quality of SLE patients at Renji Hospital, Shanghai, China. This multidisciplinary care

model should be validated by a wider range of studies and extended to other chronic diseases.

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Conflicts of interest Le Zhang, Shikai Geng, Liping Qian, Shuang Ye, Xiaodong Wang, Guohong Lu, Yang Ding and Ting Li declare that they have no conflict of interest.

Informed consent Informed consent was obtained from all individual participants included in the study.

Data availability statements The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

References

1. Di Battista M, Marcucci E, Elefante E, Tripoli A, Governato G, Zucchi D, et al. One year in review 2018: systemic lupus erythematosus. Clin Exp Rheumatol. 2018;36(5):763–77.
2. Carter EE, Barr SG, Clarke AE. The global burden of SLE: prevalence, health disparities and socioeconomic impact. Nat Rev Rheumatol. 2016;12(10):605–20.
3. Wang Z, Li M, Wang Y, Xu D, Wang Q, Zhang S, et al. Long-term mortality and morbidity of patients with systemic lupus erythematosus: a single-center cohort study in China. Lupus. 2018;27(5):864–9.
4. de Larrinoa IR-FF. What is new in systemic lupus erythematosus. Reumatol Clin. 2015;11(1):27–32.
5. Osterberg L, Blaschke T. Adherence to medication. N Engl J Med. 2005;353(5):487–97.
6. Oliveira-Santos M. Erratum to: effectiveness of pharmaceutical care for drug treatment adherence in patients with systemic lupus erythematosus in Rio de Janeiro, Brazil: study protocol for a randomized controlled trial. Trials. 2017;18(1):96.
7. Zhang L, Lu GH, Ye S, Wu B, Shen Y, Li T. Treatment adherence and disease burden of individuals with rheumatic diseases admitted as outpatients to a large rheumatology center in Shanghai, China. Patient Prefer Adherence. 2017;11:1591–601.
8. Costedoat-Chalumeau N, Tamirou F, Piette JC. Treatment adherence in systemic lupus erythematosus and rheumatoid arthritis: time to focus on this important issue. Rheumatology (Oxford). 2018;57(9):1507–9.
9. Williams EM, Lorig K, Glover S, Kamen D, Back S, Merchant A, et al. Intervention to improve quality of life for African-American lupus patients (IQAN): study protocol for a randomized controlled trial of a unique a la carte intervention approach to self-management of lupus in African Americans. BMC Health Serv Res. 2016;16(a):339.
10. Choudhry NK, Isaac T, Lauffenburger JC, Gopalakrishnan C, Lee M, Vachon A, et al. Effect of a remotely delivered tailored multicomponent approach to enhance medication taking for patients with hyperlipidemia, hypertension, and diabetes: the STIC2IT cluster randomized clinical trial. JAMA Int Med. 2018;178(9):1182–9.
11. 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 SLE. Arthritis Rheum. 1992;35(6):630–40.
12. Butler JA, Peveler RC, Roderick P, Horne R, Mason JC. Measuring compliance with drug regimens after renal transplantation: comparison of self-report and clinician rating with electronic monitoring. Transplantation. 2004;77(5):786–9.
13. Liu GG, Wu H, Li M, Gao C, Luo N. Chinese time trade-off values for EQ-5D health states. Value Health. 2014;17(5):597–604.
14. Jorgensen TS, Turesson C, Kapetanovic M, Englund M, Turkiewicz A, Christensen R, et al. EQ-5D utility, response and drug survival in rheumatoid arthritis patients on biologic monotherapy: a prospective observational study of patients registered in the south Swedish SSATG registry. PLoS One. 2017;12(2):e0169946.
15. Gladman DD, Goldsmith CH, Urowitz MB, Bacon P, Fortin P, Ginzler E, et al. The Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index for Systemic Lupus Erythematosus International Comparison. J Rheumatol. 2000;27(2):373–6.
16. Flynn A, Gilhooley E, O'Shea F, Wynne B. The use of SLICC and ACR criteria to correctly label patients with cutaneous lupus and systemic lupus erythematosus. Clin Rheumatol. 2018;37(3):817–8.
17. Horne R, Hankins M, Jenkins R. The Satisfaction with Information about Medicines Scale (SIMS): a new measurement tool for audit and research. Qual Health Care. 2001;10(3):135–40.
18. Boons C, Timmers L, van Schoor NM, Swart EL, Hendrikse NH, Janssen J, et al. Patient satisfaction with information on oral anticancer agent use. Cancer Med. 2018;7(1):219–28.
19. Zhu GH, Wang YZ, Tong ZW. Reliability and validity of Chinese compliance questionnaire for rheumatology. Chin Gen Pract. 2013;16:2803–5.
20. van den Bemt BJ, van den Hoogen FH, Benraad B, Hekster YA, van Riel PL, van Lankveld W. Adherence rates and associations with nonadherence in patients with rheumatoid arthritis using disease modifying antirheumatic drugs. J Rheumatol. 2009;36(10):2164–70.
21. Kumar K, Gordon C, Toescu V, Buckley CD, Horne R, Nightingale PG, et al. Beliefs about medicines in patients with rheumatoid arthritis and systemic lupus erythematosus: a comparison between patients of South Asian and White British origin. Rheumatology (Oxford). 2008;47(5):690–7.
22. Menckeberg TT, Bouvy ML, Bracke M, Kaptein AA, Leufkens HG, Raaijmakers JA, et al. Beliefs about medicines predict refill adherence to inhaled corticosteroids. J Psychosom Res. 2008;64(1):47–54.
23. Gabarron E, Dorronzoro E, Bradway M, Rivera-Romero O, Wynn R, Arsand E. Preferences and interests of diabetes social media users regarding a health-promotion intervention. Patient Prefer Adherence. 2018;12:2499–506.
24. Morgado M, Rolo S, Castelo-Branco M. Pharmacist intervention program to enhance hypertension control: a randomised controlled trial. Int J Clin Pharm. 2011;33(1):132–40.
25. Miller NH, Hill M, Kottke T, Ockene IS. The multilevel compliance challenge: recommendations for a call to action: a statement for healthcare professionals. Circulation. 1997;95(4):1085–90.
26. Kesselheim AS, Misono AS, Shrank WH, Greene JA, Doherty M, Avorn J, et al. Variations in pill appearance of antiepileptic drugs and the risk of nonadherence. JAMA Intern Med. 2013;173(3):202–8.
27. Chambers SA, Raine R, Rahman A, Isenberg D. Why do patients with systemic lupus erythematosus take or fail to take their

prescribed medications? A qualitative study in a UK cohort. Rheumatology (Oxford). 2009;48(3):266–71.
28. Feldman CH, Costenbader KH, Solomon DH, Subramanian SV, Kawachi I. Area-level predictors of medication nonadherence among U.S. medicaid beneficiaries with lupus: a multilevel study. Arthritis Care Res (Hoboken). 2018. https://doi.org/10.1002/acr.23721.
29. Smith SM, Wallace E, O'Dowd T, Fortin M. Interventions for improving outcomes in patients with multimorbidity in primary care and community settings. Cochrane Database Syst Rev. 2016;3:Cd006560.
30. Salisbury C, Man MS, Bower P, Guthrie B, Chaplin K, Gaunt DM, et al. Management of multimorbidity using a patient-centred care model: a pragmatic cluster-randomised trial of the 3D approach. Lancet. 2018;392(10141):41–50.
31. Peralta-Ramirez MI, Perez-Marmol JM, Castaneda-Cabestany M, Santos-Ruiz AM, Montero-Lopez E, Callejas-Rubio JL, et al. Association between perceived level of stress, clinical characteristics and psychopathological symptoms in women with systemic lupus erythematosus. Clin Exp Rheumatol. 2018;36(3):434–41.
32. Macedo EA, Appenzeller S, Costallat LTL. Depression in systemic lupus erythematosus: gender differences in the performance of the Beck Depression Inventory (BDI), Center for Epidemiologic Studies Depression Scale (CES-D), and Hospital Anxiety and Depression Scale (HADS). Lupus. 2018;27(2):179–89.
33. Lee JW, Kang JH, Lee KE, Park DJ, Kang SW, Kwok SK, et al. Effects of risk factors for and components of metabolic syndrome on the quality of life of patients with systemic lupus erythematosus: a structural equation modeling approach. Qual Life Res. 2018;27(1):105–13.