

Intentional and Unintentional Treatment Nonadherence in Patients With Systemic Lupus Erythematosus

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Objective. Patients may be defined as nonadherent if they do not take their medications as prescribed by their physicians. Determinants of nonadherence may vary between and within patient groups. This study investigated the extent to which patients with systemic lupus erythematosus (SLE) show intentional and unintentional nonadherence, and the associations of nonadherence with psychological and medical parameters.

Methods. The study included 106 patients who were receiving at least one immunosuppressive agent to control their SLE. Level of self-reported adherence and a measure of both intentional and unintentional nonadherence were obtained. Questionnaires were completed to assess associations between adherence and problems with cognitive functioning, beliefs about medicines, illness perceptions, emotional health, and disease characteristics.

Results. The mean self-reported adherence rate for the total patient group was 86.7%. At least occasional intentional nonadherence was reported by 46.2% of patients and 58.5% of patients were at least occasionally unintentionally nonadherent. Problems with cognitive functioning, concerns about adverse effects of medication, and younger age were the strongest predictors of (non)adherence. Patients who were emotionally affected by their SLE were more likely to report low adherence, but this was not a significant predictor after accounting for other variables. Disease characteristics showed no relationship to measures of adherence.

Conclusion. Although SLE patients reported high levels of adherence on average, they commonly reported intentional and unintentional nonadherence. Adherence was associated with both cognitions and emotions. Nonadherence may be reduced by targeting emotional and cognitive functioning and by fine tuning doctor–patient communication to address patients' individual concerns about their medications.

INTRODUCTION

Treatment adherence in patients with systemic lupus erythematosus (SLE) has been shown to be low, with approximately 30% never failing to take their medications (1–3), between 20% and 40% stopping their medication on their own (2), and between 14.0% and 42.6% missing one or more clinic visits (1,4–6). Nonadherence may pose a severe problem, as it has been associated with higher mor-

bidity (5), hospitalization (6), and poor renal outcome (7). Few studies have investigated treatment adherence in SLE patients and generalization of the results is often limited because rheumatoid arthritis (RA) and SLE patients were treated as one patient group (2,8,9) or differences between specific ethnic groups were investigated (1,2,8–10). Moreover, psychosocial factors that may predict treatment adherence in SLE patients have not been sufficiently investigated (11). The present study aimed at assessing treatment adherence in a representative cohort of SLE patients and investigating associations with psychosocial and medical factors.

SLE is an autoimmune disease that can result in inflammation of multiple organ systems at the same time. The worldwide prevalence is estimated to be approximately 1 per 1,000 and the female to male ratio is 10:1 (12). The course of disease is characterized by alternating periods of either relatively stable disease or high disease activity. In the face of an exacerbation, patients may need to take high doses of immunosuppressive agents. But also when the disease is relatively stable, maintenance doses are often required to preserve low activity and patients are closely

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monitored for signs of flare-ups. Therefore, treatment adherence is important to control the course of disease.

A comprehensive assessment of treatment nonadherence should involve both intentional and unintentional nonadherence (13). In the case of intentional nonadherence, patients actively choose not to follow treatment recommendations. A social cognition model that aims to explain intentional nonadherent behavior was developed by Horne (1997) (14) and is based on the Health Belief Model (15) and the Illness Perceptions Model (16). According to Horne's model, adherence to medication is based on a combination of a range of beliefs concerning perceived severity, susceptibility, benefits, and barriers, and patients' illness perceptions, i.e., their understandings of the nature of the illness, its severity, cause, timeframe, likely prognosis, and treatability.

In contrast to intentional nonadherence, unintentional nonadherence is thought to be the result of a passive process that is less strongly associated with individuals' beliefs and perceptions (13). Factors associated with unintentional nonadherence can be categorized according to the following 3 groups: 1) patient factors (e.g., age), 2) treatment factors (e.g., side effects), and 3) patient-health care provider factors (e.g., doctor-patient interaction) (13).

Problems with cognitive functioning are frequently reported in SLE patients. The prevalence of cognitive dysfunctions is not only high (i.e., 27–52%) in patients with past or present neuropsychiatric manifestations of SLE, but also 20–42% of patients without neuropsychiatric lupus show cognitive impairments (17). Two previous studies have looked at the association between medication adherence and cognitive functioning in SLE patients (1,3). In both studies, the assessment of cognitive impairments was based on patients' performances on ability tests: reading ability and short-term memory in one study (1) and verbal learning and memory in the second study (3). Poor performance on short-term memory was associated with low adherence in African American patients, but not in white patients (1). However, the authors propose that this difference between ethnic groups is a result of socioeconomic disparity and it may not reflect a real barrier to adherence. Problems with verbal learning and memory did show a relationship to poor adherence, but were not important predictors after accounting for other variables (3). Contrary to measuring performance, the present study aimed to assess patients' self-reported problems in doing several cognitive functions and activities of daily life. From a clinical perspective, it is more informative to know which problems patients actually experience and how these real problems relate to nonadherent behavior.

The present study assessed intentional and unintentional treatment nonadherence in SLE patients. Moreover, we examined the associations between treatment nonadherence and sociodemographic and disease characteristics, cognitive functioning, and several psychosocial factors, including beliefs about medicines, illness perceptions, and emotional well-being.

PATIENTS AND METHODS

Participants. Patients were recruited from the rheumatology clinic at Greenlane Clinical Centre (i.e., the outpatient clinic of Auckland City Hospital) and from two lupus patients' associations. Patients were included when a diagnosis of SLE according to the revised American College Rheumatology criteria for SLE (18) was well documented in the electronic patient records, and when they received a current treatment with prednisone and/or another immunosuppressive agent. Two weeks after sending out invitation letters to potential participants, the patients were contacted by telephone. Of 141 patients who were approached, 106 patients participated (75% participation rate). Twenty-two patients did not indicate interest in joining the study, 4 patients did not attend their scheduled study appointment, and 9 patients stated they were either too busy or did not want to participate due to language barriers.

Participants provided informed consent prior to the assessment and completed 6 self-administered, paper-and-pencil questionnaires. After completion of the questionnaires, the principal investigator (GMND) assessed disease activity according to the SLE Disease Activity Index (SLEDAI) (19). Assessment took place in a private room at Greenlane Clinical Centre or at the patient's home. The study was approved by the Northern X Ethics Committee (Auckland region, New Zealand).

Materials. Treatment adherence was measured using part A of the Medication Adherence Self-Report Inventory (MASRI) (20), which has been shown to be a reliable (Cronbach's $\alpha = 0.70$ and intraclass correlation coefficient 0.93) and valid ($r_s = \geq 0.55$) measure of medication adherence in SLE patients. Part A of the MASRI is 87% sensitive and 86% specific for identifying patients who were nonadherent (21). Part A consists of five 4-point scale items and one visual analog scale (VAS) item. The VAS item asks patients to indicate how much medication they have taken in the past month on a scale from 0% to 100%. Only the VAS item is used to get a numerical estimate of the adherence level. The other 5 items are added to help patients develop this adherence estimate.

As a measure of adherence to clinic visits, hospital records were consulted to determine the number of visits that were missed in the past 12 months as a percentage of the total scheduled appointments in that period.

The distinction between intentional and unintentional nonadherence was made using the Medication Adherence Report Scale (22). This self-report scale consists of one statement to measure unintentional nonadherence (i.e., I forget to take my medications) and 4 statements to obtain a measure of intentional nonadherence: 1) I alter the dose of my medications, 2) I stop taking my medications for a while, 3) I decide to miss out on a dose, and 4) I take less than instructed. Answers are scored on a 4-point rating scale ranging from always to never. Two different variables were derived for both nonadherence measures: a continuous variable (mean score) and a dummy variable (0 represents a mean score of 1, never unintentionally or inten-

tionally nonadherent; 1 represents a mean score of >1 , at least occasionally unintentional or intentionally nonadherent).

The Cognitive Symptoms Inventory (CSI) was used to measure cognitive functioning (23). The CSI has been demonstrated to be a good screening measure of cognitive impairment in SLE patients in research settings (24). The CSI contains 21 questions to assess difficulties in daily activities that relate to 1) concentration, 2) recognition/planning, 3) intermediate memory, and 4) executive function.

The Beliefs about Medicines Questionnaire (BMQ) was used as a measure of commonly held beliefs about medicine (25). The BMQ consists of 18 items divided over 4 scales: 1) the specific necessity scale assesses the perceived necessity of the prescribed medication, 2) the specific concern scale addresses concerns about the potential adverse effects of prescribed medication, 3) the general harm scale measures the perceived level of harm and addiction caused by medications in general, and 4) the general overuse scale assesses beliefs about the use of medicines by doctors. An extended version of the BMQ also contains 4 single items about complementary or alternative medication use.

The Brief Illness Perception Questionnaire (IPQ-B) was used to measure illness perceptions (26). The IPQ-B contains 8 items to score on a scale from 0 to 10 and one open-ended question where the participants have to state the 3 most important causes for their disease. The reported causes were grouped into categories on the basis of common themes.

The subscale emotional health of the LupusQol was used as a measure of the emotional domain of health-related quality of life (27). The LupusQol is a validated SLE-specific health-related quality of life instrument. The subscale emotional health consists of 6 items with a 5-point scale response format.

The SLEDAI was used to measure disease activity at the time of the assessment (19). The SLEDAI is a reliable, valid, and widely used instrument to assess disease activity in SLE patients (28–30).

Design and procedure. Data were analyzed using SPSS software, version 17.0. Descriptive statistics and frequencies were obtained for the sociodemographic and disease characteristics. Associations between measures of adherence and other variables were explored with Pearson's or Spearman's correlation coefficients. In the presence of significant correlations, regression analyses were performed to further study the predictive associations between variables. Independent *t*-tests or chi-square tests were used to test differences in predictor variables between patients who were at least occasionally nonadherent and patients who were never nonadherent (i.e., dichotomized intentional and unintentional adherence variables). In the case of not normally distributed data, nonparametric *t*-tests (Mann-Whitney U tests) were performed. To test differences in adherence levels between more than 2 groups (e.g., ethnicity), an analysis of variance (ANOVA) or nonparametric ANOVA (Kruskal-Wallis test) with Bonferroni

Table 1. Demographic variables (n = 106)*

	Value
Women:men	100:6
Age, mean \pm SD years	43.34 \pm 14.96
Ethnicity	
New Zealand European	42 (39.6)
Pacific Islands	15 (14.2)
Maori	13 (12.3)
Indian	11 (10.4)
Asian	14 (13.2)
Other	11 (10.4)
Employment	
Full time	34 (32.1)
Part time	23 (21.7)
Sickness benefit	20 (18.9)
Housewife	9 (8.5)
Retired	9 (8.5)
Student	8 (7.5)
Unemployed	7 (6.6)
Marital status	
Unmarried	33 (31.2)
Married or living together	55 (51.9)
Divorced	11 (10.4)
Widow/widower	7 (6.6)
Education	
Primary education	5 (4.7)
Secondary education	63 (59.4)
Bachelor degree	31 (29.2)
Master degree	5 (4.7)
Doctoral degree	2 (1.9)
Children (1 or more)	65 (61.3)
Religion	
None	60 (56.6)
Christianity	37 (34.9)
Other	9 (8.5)

* Values are the number (percentage) unless otherwise indicated.

correction was used. An alpha level of 0.05 was used for all statistical tests.

RESULTS

Patients. The participant group consisted of 100 women and 6 men, and had a mean \pm SD age of 43.4 \pm 15.0. New Zealand Europeans formed the largest ethnic group (39.6%). The distribution of ethnicities in the current sample is a good representation of the general Auckland population (31). Table 1 gives an overview of the sociodemographic characteristics.

Two-thirds of the patients (62.3%) were receiving 2 or more immunosuppressive agents. The majority of patients (54.7%) had experienced one or more organ involvements. Nearly three-quarters of the patients (71.7%) had one or more comorbidities. An overview of the disease characteristics is provided in Table 2.

Adherence measures. The mean self-reported adherence rate for the total patient group was 86.7%. Therefore, on average, patients reported they had taken mean \pm SD 86.7% \pm 18.0% of their medication in the past month. The

Table 2. Disease characteristics (n = 106)*

	Value
Disease duration, mean ± SD years	10.2 ± 9.1
SLEDAI score (range 0–105), mean ± SD	10.2 ± 6.2
Organ involvement	
None	48 (45.3)
Lupus nephritis	31 (29.2)
NPSLE	17 (16.0)
Pleuritis	13 (12.3)
Pericarditis	10 (9.4)
Hepatitis	7 (6.6)
Eyes	8 (7.5)
Comorbidity	
None	30 (28.3)
Other autoimmune disease	18 (17.0)
Hypertension	18 (17.0)
Fibromyalgia	12 (11.3)
Antiphospholipid antibody syndrome	12 (11.3)
Secondary Sjögren’s syndrome	11 (10.4)
Dyslipidemia	10 (9.4)
Medication	
Hydroxychloroquine	89 (84.0)
Prednisone	56 (52.8)
Azathioprine	42 (39.6)
Other immunosuppressants	15 (14.2)
Psychopharmaceuticals	26 (24.5)
Analgesics	30 (28.3)

* Values are the number (percentage) unless otherwise indicated. SLEDAI = Systemic Lupus Erythematosus Disease Activity Index; NPSLE = neuropsychiatric systemic lupus erythematosus.

dichotomous distinction between intentional and unintentional nonadherence showed that 46.2% of patients were at least occasionally intentionally nonadherent, 58.5% of patients were at least occasionally unintentionally nonadherent, and 25.5% of patients stated they were never either intentionally or unintentionally nonadherent. Unintentional nonadherence was significantly more common than intentional nonadherence (mean ± SD 1.63 ± 0.059 versus 1.30 ± 0.044; $t[105] = 7.47, P < 0.001$). The most common form of intentional nonadherence was altering the dose of the medications (35.8%).

Twenty-three patients (22.8%) did not attend one or more clinic visits in the past year. On average, 5.2% of scheduled visits were not attended. The more visits patients did not attend, the lower the self-reported adherence levels ($r = -0.28, P = 0.004$). In addition, patients who reported frequent unintentional nonadherence tended to miss more clinic visits ($r_s = 0.24, P = 0.018$).

Associations between adherence measures and sociodemographic characteristics. Adherence measures were associated with some sociodemographic characteristics. Older patients were more likely to report high adherence levels ($r = 0.23, P = 0.017$) and unintentional nonadherers were younger than patients who were never unintentionally nonadherent (mean ± SD 40.13 ± 14.10 versus 47.86 ± 15.12; $Z = -2.68, P = 0.007$). Ethnicity showed a relationship with self-reported adherence level, nonattendance at clinic visits, and unintentional nonadherence (Figure 1). Patients from the Pacific Islands missed out on

more clinic visits than patients from all other ethnicities ($\chi^2 = 10.02, 4 \text{ df}, P = 0.040, 2\text{-sided}$) and reported lower adherence levels than patients from Asian countries ($\chi^2 = 10.15, 4 \text{ df}, P = 0.038, 2\text{-sided}$). Patients of Indian ethnicity showed more unintentional nonadherence than New Zealand Europeans and patients from Asian countries, and Pacific peoples reported more unintentional nonadherence than New Zealand Europeans ($\chi^2 = 16.72, 4 \text{ df}, P = 0.002, 2\text{-sided}$).

Disease characteristics (e.g., SLEDAI scores, disease duration, number of comorbidities, number of organ involve-

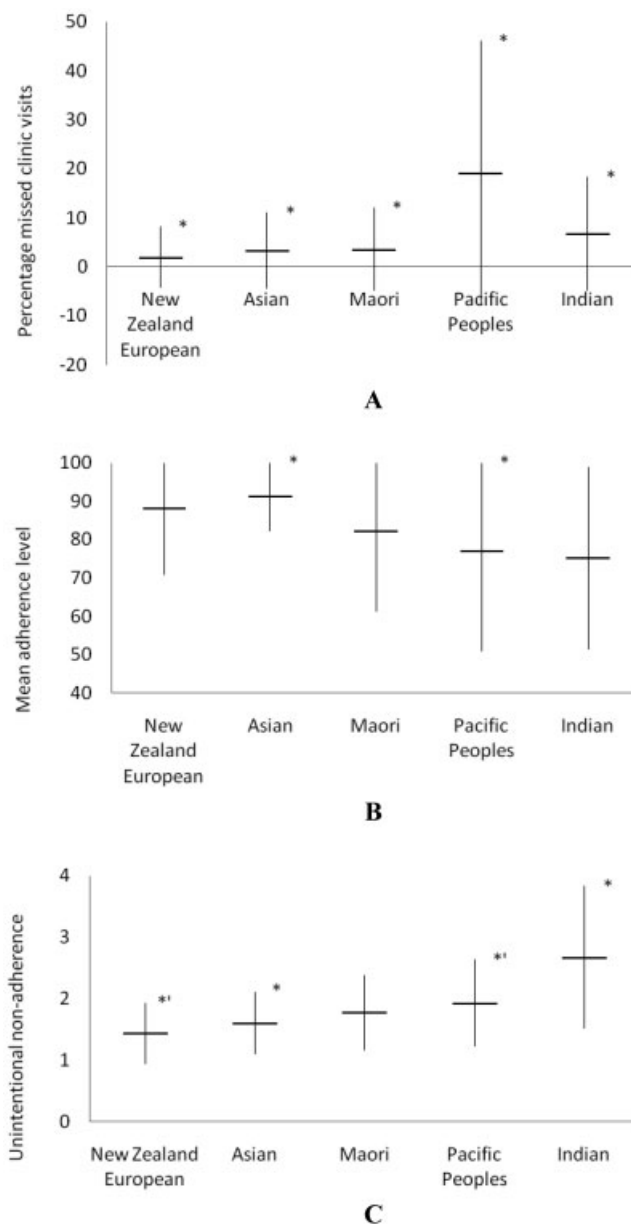


Figure 1. Percentage of missed clinic visits, mean adherence level, and unintentional nonadherence per ethnic group. **A**, Pacific peoples missed more clinic visits than patients from all other ethnicities. **B**, Pacific peoples reported lower adherence levels than Asians. **C**, Indians showed more unintentional nonadherence than New Zealand Europeans, and Asians and Pacific peoples reported more unintentional nonadherence than New Zealand Europeans. * = significant group differences.

Table 3. Mean \pm SD scores for the Cognitive Symptoms Inventory (CSI) for the total patient group and for unintentional versus non-unintentional nonadherers

	Total patient group (n = 106)	Unintentional nonadherent (n = 62)	Never unintentional nonadherent (n = 44)	P
Concentration	14.3 \pm 4.2	15.2 \pm 4.3	13.0 \pm 3.6	0.005*
Recognition/planning	4.9 \pm 1.3	5.2 \pm 1.5	4.5 \pm 0.90	<0.001†
Intermediate memory	3.4 \pm 1.3	3.5 \pm 1.2	3.2 \pm 1.3	0.181
Executive function	2.6 \pm 1.0	2.5 \pm 0.80	2.7 \pm 1.3	0.785
Total CSI score	30.9 \pm 8.0	32.2 \pm 8.3	28.9 \pm 7.2	0.017‡

* $P < 0.01$.
† $P < 0.001$.
‡ $P < 0.05$.

ments, and number of medications) showed no relationship with measures of (non)adherence.

Associations between adherence measures and cognitive functioning. Patients who reported low adherence rates were more likely to experience problems with cognitive functioning in general ($r_s = -0.24$, $P = 0.013$) and specifically with concentration ($r_s = -0.24$, $P = 0.014$) and recognition/planning ($r_s = -0.30$, $P = 0.002$). Problems in these 3 domains were more common in unintentional nonadherers than in patients who did not show unintentional nonadherence (Table 3). There was no effect for intentional nonadherence. Age was not associated with problems with cognitive functioning.

Relationships between adherence measures and psychological variables. *BMQ.* A total of 80.2% of patients supported the necessity of taking SLE medications to maintain good health. However, the majority of patients (63.2%) also expressed concerns about the possible negative effects of SLE medications.

The extent to which patients expressed concerns about their SLE medications was associated with all measures of adherence. The more concerned patients were about taking SLE medications, the lower their mean self-reported adherence rate ($r_s = -0.23$, $P = 0.019$). Table 4 shows the scores on all 4 subscales for patients who reported intentional or unintentional nonadherence versus those who did not. Intentional and unintentional nonadherers were more concerned about the possible side effects of their

medications than patients who reported no intentional or unintentional nonadherence.

With regard to medicines in general, 24.5% of patients regarded them as harmful and 40.6% of patients thought doctors overuse medicines. Intentional nonadherers held stronger beliefs about overuse than patients who were not intentionally nonadherent (Table 4).

Alternative or complementary medicines were used by 50.9% of patients to relieve symptoms, but only a minority of patients agreed that these medicines could control their lupus between acute episodes (36.8%). The belief that alternative medicines were more natural and less damaging was supported by 24.5% of patients, and one-third of patients agreed that Western medicines should be substituted by alternative medicines. Beliefs about alternative or complementary medicines were not associated with adherence measures.

IPQ-B. Patients' illness perception scores in general clustered around the midrange of the items. An exception is the item timeline, which had the highest mean score (mean \pm SD 8.43 \pm 2.53). This indicates that patients held chronic perceptions of their SLE. Patients who experienced strong emotional effects from their SLE showed lower self-reported adherence levels ($r_s = -0.25$, $P = 0.012$). The first most important reported causes were grouped into 5 broad categories: psychosocial causes (33.3%), genetics (32.0%), environmental causes (10.7%), previous bacterial or viral infections (13.3%), and pregnancy (10.7%). There were no associations with adherence measures.

Table 4. Mean \pm SD scores on the Beliefs about Medicines Questionnaire for intentional versus unintentional nonadherers and unintentional versus non-unintentional nonadherers

	Intentional nonadherent (n = 49)	Never intentional nonadherent (n = 57)	P	Unintentional nonadherent (n = 62)	Never unintentional nonadherent (n = 44)	P
Necessity	20.1 \pm 4.1	19.5 \pm 3.9	0.389	20.1 \pm 3.9	19.3 \pm 4.0	0.192
Concern	18.0 \pm 3.5	15.2 \pm 3.9	0.001*	17.5 \pm 3.4	14.2 \pm 4.2	0.003†
Harm	10.7 \pm 3.2	10.6 \pm 2.9	0.896	10.8 \pm 2.9	10.4 \pm 3.1	0.439
Overuse	12.6 \pm 2.8	11.4 \pm 2.7	0.023‡	12.3 \pm 2.9	11.5 \pm 2.0	0.145

* $P < 0.001$.
† $P < 0.01$.
‡ $P < 0.05$.

Table 5. Summary of regression analyses to predict treatment nonadherence*

Predictor variables	VAS level		Unintentional nonadherence		Intentional nonadherence	
	β	<i>P</i>	β	<i>P</i>	β	<i>P</i>
Cognitive functioning						
Recognition/planning	-1.342	0.001†	0.632	0.015‡	N/A	N/A
Concentration	-0.003	0.976	0.069	0.332	N/A	N/A
Beliefs about medicines						
Concern	-0.046	0.631	0.173	0.006§	0.204	0.001§
Overuse	-0.005	0.959	0.035	0.696	0.063	0.463
Sociodemographic						
Age	-1.089	0.001†	-0.039	0.014‡	N/A	N/A
Ethnicity	-0.043	0.627	N/A	N/A	N/A	N/A
Religion	N/A	N/A	N/A	N/A	0.130	0.694
Psychosocial						
Emotional health	N/A	N/A	N/A	N/A	-0.012	0.240
IPQ-B emotions	-0.050	0.592	N/A	N/A	N/A	N/A

* VAS = visual analog scale; N/A = not applicable; IPQ-B = Brief Illness Perception Questionnaire.
 † *P* < 0.001.
 ‡ *P* < 0.05.
 § *P* < 0.01.

LupusQol. Emotional health for the total patient group was moderate (mean ± SD 72.2 ± 2.2, range 0–100). Patients who were at least occasionally intentionally nonadherent showed worse emotional health than patients who were never intentionally nonadherent (mean ± SD 66.6 ± 25.3 versus 77 ± 18.1; *Z* = -2.09, *P* = 0.036). There was no effect for unintentional nonadherence.

Regression analyses. Stepwise linear regression analysis was used to test whether problems with cognitive functioning, concerns about medication (i.e., concern), and emotions were stronger predictors of self-reported adherence level than demographic variables (age and ethnicity). A significant model emerged in which recognition/planning and age explained 35.9% of the variance in self-reported adherence levels (*F*[3,101] = 20.45, *P* < 0.001). Recognition/planning was the strongest predictor, accounting for 18.8% of the explained variance. Age added a further 8.3% to the proportion of explained variance. Table 5 shows the regression coefficients.

Logistic regression analyses were performed to assess the strongest predictors of intentional and unintentional nonadherence as dummy variables. The forward:likelihood ratio method was used to test whether intentional nonadherence could be predicted by concern, beliefs about medication overuse, and emotional health. A significant model emerged with concern as the only significant predictor of intentional nonadherence (omnibus χ^2 = 13.56, 1 df, *P* < 0.001). The model accounted for between 12.0% and 16.0% of the variance in intentional nonadherence (Table 5). Using a similar analysis to predict unintentional nonadherence showed that a model with the predictors recognition/planning, age, and concern was significant (omnibus χ^2 = 24.56, 3 df, *P* < 0.001). The model accounted for between 20.7% and 27.8% of the variance in unintentional nonadherence (Table 5).

In conclusion, regression analyses showed that prob-

lems with recognition/planning, concerns about medication use, and age were the strongest predictors of nonadherence.

DISCUSSION

This study assessed the prevalence and predictors of intentional and unintentional treatment nonadherence in SLE patients. The high mean self-reported adherence level indicates good adherence, but patients also commonly report intentional or unintentional nonadherence. Unintentional nonadherence was more common than intentional nonadherence and was associated with nonattendance of clinic visits. Problems with cognitive functioning, concerns about potential adverse effects of medication, and age were the best predictors of nonadherence.

Treatment nonadherence has been identified as a substantial problem in patients with chronic inflammatory rheumatic diseases (32). However, few studies have focused on treatment nonadherence in SLE patients specifically and no prior studies have included self-report adherence questionnaires that have been validated for use in SLE patients. Previous studies that have assessed adherence in SLE patients report levels between 69.1% and 83% (2,6,10,33,34). Even though every study used a different measure to assess adherence, the mean adherence level of 86.7% found in the present study seems to be at the high end of the range. This may be partly explained by a difference in the regulation of the health care system. Three of the previous studies have been conducted in the US or Mexico, where costs of medication may be a barrier to adherence (2,6,33). This is less likely to be a problem for patients in New Zealand due to the publicly funded health care system. Health care costs have indeed been identified as potential threats to adherence for SLE patients in the US and developing countries (8,35). Higher health care costs

may also explain the difference in the percentage of missed clinic visits: 5.2% in the present study versus rates between 14% and 42.6% in previous studies (1,4–6).

Only one known study, in which patients with RA and SLE were assessed together, has made the distinction between intentional and unintentional nonadherence (2). Two-thirds of patients reported forgetting their medication at least occasionally, and between 20% and 40% of patients said they intentionally did not take their medication at least occasionally (2). These results are comparable to the findings in the present study that both intentional and unintentional nonadherence were frequently reported and unintentional nonadherence seems to be more common.

Problems with cognitive functioning, more specifically with recognition/planning, were the strongest predictors of self-reported adherence level and unintentional nonadherence. Activities that pertain to recognition/planning are managing money and paying bills, remembering to take medication, and recognizing people. As mentioned before, two previous studies have looked at the association of cognitive functioning with adherence measures in SLE patients (1,3) and both could not support a predictive effect of cognitive impairments. A study that looked at the relationship between adherence and cognitive impairments in 3 different patient groups does propose that cognitive dysfunctions may identify patients at risk of poor adherence regardless of diagnosis or regimen (36).

Concern about potential adverse effects of medication was the second most important predictor of unintentional nonadherence and the only predictor of intentional nonadherence. Although most studies on treatment adherence in SLE patients have also looked at associations with sociodemographic and psychological factors, only few have used validated questionnaires to measure these variables (1,2,33). Despite this limitation, fear of side effects of medication was an important barrier to adherence in 5 of 6 studies (1,2,8,10,35).

Age was a third significant predictor of self-reported adherence level and unintentional nonadherence. One other study has examined the relationship between age and adherence in SLE and found a nonsignificant tendency for adherent patients to be older than nonadherent patients (33). A similar effect of age on adherence has been reported in a study investigating predictors of adherence in 4 chronic illnesses (37).

Adherence measures did tend to differ between ethnic groups, with patients from the Pacific Islands reporting lower adherence and missing more clinic visits than patients from the other ethnicities. However, ethnicity was not a significant predictor on the basis of regression analyses. Previous studies have reported mixed results on the relationship between ethnicity and adherence levels, and comparison with the present study is limited because prior research involved different ethnic groups. Three studies report a lower self-reported adherence in African Americans compared with whites (2,5,33), but one study used a physician's assessment of adherence (5) and another study only found an effect for hydroxychloroquine, and not for prednisone or other immunosuppressants (33). Studies that involved the same ethnic groups as the present study, but looked at medication adherence in patients with dia-

betes mellitus, support a poorer medication self-care (38) and lower adherence rates (39) in Pacific peoples compared with Europeans.

Although 3 previous studies have found a relationship between adherence and education (2,33,34) and 2 studies found a relationship between adherence and marital status (2,33), the present study could not confirm these results. Similarly, none of the disease characteristics (disease activity, disease duration, number of comorbidities, number of involved organs, and number of medications) were related to measures of adherence. However, the disease activity index that was used in the present study, the SLEDAI, may have failed to detect a relationship with adherence because of a lack of the inclusion of subjective symptoms. For instance, the assessment of fatigue is not part of the SLEDAI but has been identified as a highly prevalent and disturbing symptom (40). Other indices, such as the European Consensus Lupus Activity Management (41), do include these subjective measures and may be better correlated with adherence measures.

The high prevalence of unintentional nonadherence and its association with missing clinic visits suggests that a primary focus on reducing unintentional nonadherence would greatly improve treatment adherence. This approach is supported by findings from a previous study in which the main self-reported barriers to adherence among SLE patients were examples of unintentional nonadherence (e.g., "just having forgotten" or "being busy at work") (33). In addition, suggestions by these patients on how to improve adherence all referred to actions that are related to preventing unintentional nonadherence (e.g., pill boxes or task lists). Apart from these direct methods to reduce unintentional nonadherence, adherence can be further improved indirectly by resolving problems with cognitive functioning and concerns about adverse effects of medication. A recent study found a significant improvement in cognitive functioning of SLE patients after an 8-week psychoeducational intervention (42). With regard to concerns about possible side effects, addressing a patient's specific concerns may not only reduce fear of adverse effects and thereby improve adherence, but it may also improve the doctor-patient relationship. Problems with communication and trust have been identified as important barriers to adherence in SLE patients (1,8,10,33).

A limitation of this study is that it was cross-sectional and correlational, which limits interpretations about causality. In addition, several potential barriers to adherence were not investigated. For instance, assessment of the patient-doctor relationship (1,10,33), perceived costs and evaluation of the health care system (8,10), and frequent dosing of medication (8,33) have been identified as a threat to adherence but were not assessed in the present study. Also, the majority of patients were of New Zealand European origin, which limits comparisons between different ethnic groups. A substantial proportion of SLE patients of Asian origin could not be included in the study because of language barriers. Finally, there is a potential selection bias because the participating group and nonparticipating group could not be compared.

In conclusion, intentional and unintentional nonadherence are common in SLE patients. Adherence measures

were associated with age, cognitive functioning, and illness-related emotions. Nonadherence may be reduced by targeting cognitive functioning and by fine tuning doctor-patient communication to address patients' individual concerns about their medications.

AUTHOR CONTRIBUTIONS

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

Study conception and design. Daleboutd, Broadbent, McQueen, Kaptein.

Acquisition of data. Daleboutd, McQueen.

Analysis and interpretation of data. Daleboutd.

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